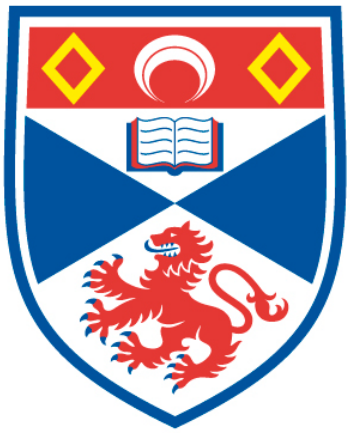
Fertility issues and fear of cancer recurrence in young women with gynaecological or breast cancer

Aleksandra Sobota

A thesis submitted for the degree of PhD
at the
University of St Andrews



2016

Declaration

1. Candidate's declarations:

I, Aleksandra Sobota hereby certify that this thesis, which is approximately 80 000 words in length, has been written by me, and that it is the record of work carried out by me, or principally by myself in collaboration with others as acknowledged, and that it has not been submitted in any previous application for a higher degree.

I was admitted as a research student in [November, 2012] and as a candidate for the degree of PhD in [November, 2012]; the higher study for which this is a record was carried out in the University of St Andrews between [2012] and [2016].

Date …… signature of candidate ……

2. Supervisor's declaration:

I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of PhD in the University of St Andrews and that the candidate is qualified to submit this thesis in application for that degree.

Date …… signature of supervisor ……

3. Permission for publication: (*to be signed by both candidate and supervisor*)

In submitting this thesis to the University of St Andrews I understand that I am giving permission for it to be made available for use in accordance with the regulations of the University Library for the time being in force, subject to any copyright vested in the work not being affected thereby. I also understand that the title and the abstract will be published, and that a copy of the work may be made and supplied to any bona fide library or research worker, that my thesis will be electronically accessible for personal or research use unless exempt by award of an embargo as requested below, and that the library has the right to migrate my thesis into new electronic forms as required to ensure continued access to the thesis. I have obtained any third-party copyright permissions that may be required in order to allow such access and migration, or have requested the appropriate embargo below.

The following is an agreed request by candidate and supervisor regarding the publication of this thesis:

PRINTED COPY

No embargo on print copy

ELECTRONIC COPY

Embargo on all or part of electronic copy for a period of 2 years on the following ground(s):

- Publication would preclude future publication

Date …… signature of candidate …… signature of supervisor ……

Acknowledgements

First, I would like to thank the Richardson Family for their generosity in funding the scholarship thanks to which I was able to undertake this PhD. This was a truly life-changing experience which, without their kindness, would have never been possible.

My thanks go to my supervisor – Dr Gozde Ozakinci who has given me the opportunity of coming to St Andrews, offered invaluable guidance and support throughout the project I found absolutely fascinating, and most importantly kept her cool through the most difficult of times and made me believe that despite all the adversities I would one day see this PhD to an end. I am grateful to my thesis committee, Professor Gerry Humphris and Professor Candace Currie for taking interest in my research and providing all the constructive feedback and advice. I am indebted to my internal and external examiners, Dr Damien Williams and Professor Marie Fallon for giving up so much of their time.

I would also like to thank all my collaborators from the NHS Lothian: Professor Charlie Gourley, Dr Mark Zahra, Dr Alison Stillie, and Dr Camille Busby-Earle; NHS Tayside: Erica McGaughay, Pamela Duthie, Dr Marta Reis, Dr Caroline Michie, and Dr Douglas Adamson; NHS Fife: Dr Scott Fegan and Jennifer Anderson; Anna Mazowiecka Clinical Hospital: Professor Roman Smolarczyk, Professor Krzysztof Czajkowski, and Dr Kazimierz Pietrzak; Swietokrzyskie Cancer Centre: Dr Marcin Misiek and Dr Kamil Zalewski; and the Military Medical Institute: Professor Włodzimierz Baranowski and Dr Dariusz Tarwacki for all the help with the project and assistance with recruitment. My thanks also go to all the cancer charities and support organisations who kindly distributed the information about the study and particularly Jo's Trust, Womb Cancer UK, Ovacome, Breast Cancer Care, CoppaFeel!, Young Breast Cancer Network, Maggie's Centres (especially Dr Lesley Howells), and Shine Cancer Support.

Most importantly, I would like to thank all the participants who gave me their time and participated in the study. This project could never have happened without them.

Last but not least I would like to thank my friends and family. Agata, for always being there for me (even if that was thousands of kilometres away and on the other end of the phone), supporting me through the good and the bad, and never once doubting that I

would succeed (at getting this PhD project finished and sorting out the rest of my life). Maria, for always knowing how to make me laugh. Alina, for all the dinners she cooked for me when I was exhausted after whole days of writing, and trips to the Highlands – this is what kept me sane in those last couple of months. And Rob, for bringing out the best in me and never letting me give up. I am one lucky girl to have them all in my life.

I would also like to thank my parents, Mrs and Mr Sobota who are responsible for instilling in me the passion for science and who have always encouraged me to pursue my dreams (even the wildest ones). Who I am and where I am now I owe to them, and they are the ones I would like to dedicate this thesis to.

Contents

Table of Contents

List of Figures

List of Tables

Abbreviations

A-DAS – Abbreviated Dyadic Adjustment Scale

ARTs – assisted reproductive technologies

ATLAS – Adjuvant Tamoxifen: Longer versus Shorter trial

aTTom - adjuvant Tamoxifen—To offer more? trial

Brief-IPQ – Brief Illness Perceptions Questionnaire

CARES – Cancer Rehabilitation Evaluation System

CES-D – Center for Epidemiologic Studies Depression Scale

CSI(4) – 4-item version of the Couples Satisfaction Index

CSI_T – Couples Satisfaction Index total scale

CSM – Common Sense Model

FCR – Fear of recurrence scale

FP – fertility preservation

FSFI – Female Sexual Functioning Index

GCP – Gynecologic Problems Checklist

GnRH – gonadotropin releasing hormone

GP – general practitioner

HADS – Hospital Anxiety and Depression Scale

HER2 – Human Epidermal Growth Factor Receptor

IES – Impact of Event Scale

IES-R – Impact of Event Scale Revised

IESR_A – Impact of Event Scale Revised avoidance subscale

IESR_H – Impact of Event Scale Revised hyperarousal subscale

IESR_I – Impact of Event Scale Revised intrusion subscale

IESR_T – Impact of Event Scale Revised total scale

IPQ – Illness Perceptions Questionnaire

IPQ-R – Illness Perceptions Questionnaire-Revised

IVF – in vitro fertilisation

MCS – Mental Component Summary

NHS – National Health Service

NICE – The National Institute for Health and Care Excellence

PANAS – Positive and Negative Affect Scale

PCS – Physical Component Summary

QLACS – Quality of Life Adult Cancer Survivors

QLACS_A – Quality of Life Adult Cancer Survivors appearance subscale

QLACS_B – Quality of Life Adult Cancer Survivors benefits subscale

QLACS_CP – Quality of Life Adult Cancer Survivors cognitive problems subscale

QLACS_DF – Quality of Life Adult Cancer Survivors distress family subscale

QLACS_F – Quality of Life Adult Cancer Survivors fatigue subscale

QLACS_GT – Quality of Life Adult Cancer Survivors generic subscale

QLACS_NF – Quality of Life Adult Cancer Survivors negative feelings subscale

QLACS_P – Quality of Life Adult Cancer Survivors pain subscale

QLACS_PF – Quality of Life Adult Cancer Survivors positive feelings subscale

QLACS_SA – Quality of Life Adult Cancer Survivors social avoidance subscale

QLACS_SP – Quality of Life Adult Cancer Survivors sexual problems subscale

QoL – quality of life

QoL-CS – Quality of Life – Cancer Survivors

RCAC – Reproductive Concerns After Cancer

RCS – Reproductive Concerns Scale

SAQ – Sexual Activity Questionnaire

SHARE – Scottish Health Research Register

VOC – Value of Children

VOC_P – value of children psychological subscale

VOC_S – value of children social subscale

VOC_U – value of children utilitarian subscale

Abstract

Fertility and cancer recurrence fears have been identified as important issues among young cancer patients (1-3), which frequently remain unaddressed (4, 5). This thesis aims to investigate the role that these issues play in the lives of young women diagnosed with breast or gynaecological cancer.

This project consisted of three components – a systematic review of literature, a qualitative, and a quantitative study. The literature review included both the quantitative and qualitative evidence and sought to a) identify factors associated with fertility issues; b) characterise the relationship between fertility issues and psychological well-being; and c) explore decision-making about treatments that can affect fertility potential among women diagnosed with cancer during their reproductive years. It used narrative and thematic synthesis as methods of analysis, and provided the rationale for the qualitative and quantitative components of this PhD project. In the qualitative study, twenty-four young women who had finished active cancer treatment were interviewed over the phone about the importance of their fertility at the time of treatment decision-making. In the quantitative study, 164 women completed a survey investigating the determinants of the psychological experience of fertility issues, cancer recurrence fears, and QoL. The Common Sense and the Shared Decision Making Models have been used to frame and analyse the data collected throughout the qualitative and quantitative studies..

The literature review suggests that there is a paucity of evidence with respect to the factors associated with psychological experience of fertility issues among young women with cancer. It indicates, however, that fertility issues can have a profound impact on young women's post-cancer lives in terms of their QoL and ability to regain normality after cancer treatment. Finally, it provides evidence in favour of the shared decision-making being women's preferred strategy in terms of making choices about treatments that can affect their fertility potential. These findings, and the gaps identified within the literature are addressed by either the qualitative or the quantitative component of this PhD project.

The qualitative findings suggest that prior to treatments women engaged in a process of balancing survival and fertility which serves to clarify their priorities with respect to the treatment outcome. When making treatment decisions, women wished: a) to involve

their physicians and their significant others, b) to be informed about treatments, and c) for their priorities to be taken into account as much as possible in the process. This is in line with the basic premises of the Shared Decision Making Model.

Determinants of the psychological experience of fertility issues, recurrence fears, and QoL have been identified throughout the quantitative study. While some of these determinants differed depending on the psychological outcome, illness perceptions significantly predicted all of them. This supports the assumptions of the CSM which suggests that one's own conceptualisation of disease plays a key role in adapting to an illness.

The findings of this thesis provide insight into the importance of fertility issues and recurrence fears among young women with breast or gynaecological cancer. The use of theories enables the design of potential future interventions to improve the patients' well-being in survivorship.

Chapter 1 Introduction

This chapter first discusses the epidemiology of cancer among young women (section 1.1) and given the increasing incidence of the disease in this population it subsequently presents particular cancer-related needs expressed by this group of patients (section 1.2). One of the needs frequently mentioned in the literature and pertaining to young women in particular is fertility. The impact of cancer of female fertility is therefore described in detail (section 1.3). The reasons why fertility might be of importance to young women who face a cancer diagnosis (section 1.4) as well as why its loss can add to the psychological burden already attached to a life threatening disease (section 1.5) are discussed next. As fear of cancer recurrence has been identified as another prominent issue affecting cancer patients, and young sufferers in particular, it is also described (section 1.6). Finally, drawing on the existing evidence, the rationale for this PhD project is provided (section 1.7) and detailed aims and objectives are presented (section 1.8). The outline of the thesis concludes this chapter (section 1.9).

1.1. Cancer in young women

Due to its biology, cancer is most often diagnosed at an older age. However, it can occur at any time in life (6). Cancer among teenagers and young adults aged 15 to 24 is relatively rare and accounts for less than 1% of all new cancer cases diagnosed in the UK per year (7). Female patients in this age group are most often diagnosed with carcinomas, including female-specific carcinomas of the cervix, ovary, and breast (8).

In the years 2000-2009, the incidence of carcinomas observed among women between the age of 19 and 24 rised from 3 per million among 19-year olds to 56.4 per million among 24-year olds for cervical cancer; from 1.5 per million for 19-year olds to 22.4 per million among 24-year olds for breast cancer, and from 12.9 per million among 19-year olds to 24.1 per million among 24-year olds for ovarian cancer (9). Between 2009 and 2011, the incidence rates of all these cancers continued to increase among women aged 25 to 49. Breast, cervical, and ovarian cancers accounted for 45%, 9%, and 5% of all new cancer cases diagnosed in this age group, respectively (10). Statistics are similar for the Polish female population where cervical and ovarian carcinomas constituted approximately 6% and 7%, respectively of all cancer cases diagnosed among women aged 15 to 49 between 2010 and 2012 (11). Although only approximately 14% of all

cancers in women are diagnosed between the age of 15 and 49 (10, 11), these patients should not be overlooked as they constitute a specific group with particular cancer-related needs.

1.2. Cancer-related needs in young women

More effective screening programmes and progress in cancer treatment effectiveness mean that an increasing number of people survives cancer diagnosis (12). Hence, improving patients' QoL becomes an important challenge for healthcare professionals and needs to be a priority when planning cancer treatment.

Young adults are a unique population among cancer patients in terms of their cancer-related needs. Their diagnosis occurs during the time of intense developmental changes including forming relationships and building families as well as making education and career-related decisions (1) and can pose a challenge to achieving developmental milestones and life goals. Consequently they have particular health-related, information, and supportive needs.

Evidence shows that young cancer survivors report the need for age-appropriate cancer information and state-of-the-art treatments that fit within their lifestyle (2, 3), information on health behaviours (e. g., diet, exercise, and nutrition) (1, 2), complementary and alternative therapies (1, 2), peer support (e. g., retreats for young people with cancer) (2), as well as information and counselling regarding sexuality and fertility (1-3).

Several systematic reviews have stressed the importance of fertility-related information to young cancer patients in general (4) and young women in particular (13, 14). Unfortunately, despite the presence of guidelines issued by the American Society of Clinical Oncology (15, 16) and the National Institute for Health and Care Excellence (NICE) in the United Kingdom (17) both of which clearly recommend that healthcare professionals discuss the risk of infertility posed by cancer treatments at the earliest opportunity and refer patients for FP where possible, these needs often remain unmet (1, 4).

1.3. The impact of cancer on female fertility

Cancer can affect fertility both directly, when localised in the reproductive organs and indirectly through treatments. This can occur through the following mechanisms:

1. Surgical removal of all or some of the reproductive organs for gynaecological cancers or tumours localised in the lower pelvis can lead to difficulties with, or inability to conceive or carry a pregnancy.
2. Total body irradiation and pelvic irradiation may result in ovarian failure and damage to the uterine musculature and vascular system (18).
3. Cranial irradiation can alter the functioning of hypothalamic-pituitary-gonadal axis resulting in reduced serum levels of sex-steroids and hence the absence of menstruation (amenorrhea) (18).
4. The negative effect of systemic chemotherapy on reproductive function is widely acknowledged and depends on the age of the patient at drug administration, drug dosage, duration of therapy, and type of medications used (18, 19). Chemotherapy is known to diminish the ovarian reserve which may result in an early-onset menopause even in women who continue menstruating after having received systemic treatment (20).
5. Hormonal therapy employed in hormone-positive breast cancer has been shown to increase the risk of amenorrhea in cancer survivors (21). Moreover, tamoxifen, the most commonly prescribed drug is considered to be a teratogen, meaning that pregnancy should be contraindicated during the time of therapy (22, 23). According to the guidelines, tamoxifen should be continued for five years after diagnosis (24). However, the findings from the ATLAS (25) and aTTom (26) trials which investigated the benefits of extended endocrine therapy suggest that taking tamoxifen for 10 years reduces recurrence rates and mortality among hormone-receptor positive breast cancer patients. This new and lengthy recommended use of tamoxifen means that for some patients with an already reduced ovarian reserve due to adjuvant chemotherapy, a window for childbearing would be very short or even non existent.

1.4. The importance of fertility for young women diagnosed with cancer

Not only do cancer rates among young people continue to rise (27, 28) but they increase faster than those among children and older adults (29). At the same time, due to 'postponement transition' (30) resulting from sociocultural changes including the introduction of reliable contraceptive methods as well as women joining the workforce and pursuing educational and career goals, women have started to delay childbearing (31). According to recent statistics, average maternal age at first birth among women in the UK was 28.1 in 2012 compared to 26.8 in 2002, and the average age of all mothers was 29.8 in 2012 compared to 29.7 in 2011 (32). Polish census also confirms a steady increase in the mean maternal age from 27.2 in 2000 to 28.4 in 2010 (33).

With childbearing becoming increasingly a matter of personal preference, women can also choose to pursue the route of voluntary childlessness (31, 34). However, some postpone having children until later in life and with natural fertility declining steadily from the age of 25 (35-37), they might find themselves unable to conceive and hence become involuntarily childless. A cancer diagnosis can be an additional factor contributing to involuntary childlessness.

1.5. Psychological impact of infertility

The evidence suggests that, although voluntary childlessness might be perceived as a deviation from social norms (38, 39), it does not have detrimental effects for women's psychological well-being (40, 41). Compared to women who are involuntarily childless, voluntary childless women have higher levels of overall well-being, feel more autonomous, and are less likely to express child-related regret (41).

Although pathways to remaining childless are not straightforward in either of these groups (42), it is important to acknowledge the distinction the literature makes between the two. While voluntary childlessness is more likely to be described as a matter of choice and hence a preferred term to describe it is 'childfree' (43), involuntary childlessness is often constructed in medical terms and associated with infertility (39). Lechner, L. et al. (44) who investigated psychological distress among involuntarily childless women found that they experienced more anxiety, depression, and complicated grief than the general population.

Yet, research into psychological consequences of infertility does not give a straightforward answer to how not being able to have children affects psychological outcomes. Cockburn, J. and M. Pawson (45) list some of the emotions frequently accompanying infertility in women such as mourning and grief over a non-existent baby, guilt, and shame. They also associate fertility issues with changes in personal identity, loss of sexual pleasure, and the feelings of loss of control over one's choices. This last emotion has also been highlighted by Cousineau, T.M. and A.D. Domar (46) who suggest that in a world in which a woman is under the impression that she can control her body (either through dieting, exercise, or contraception), inability to be in charge of one's own reproduction can lead to feelings of failure and disorganisation of one's sense of order. A review by Greil, A.L. et al. (47) suggests that although infertile women are not more likely to experience higher levels of psychopathology, their levels of distress are greater when compared to those of the healthy population or other women in family practice clinics. Yet, the authors also acknowledge that some studies fail to show this difference (47). According to the systematic review investigating QoL of infertile patients by Chachamovich, J.R. et al. (48), infertile women reported worse mental health, as well as social and emotional role functioning when compared to the healthy population.

1.6. Fear of cancer recurrence

Although fertility-related needs are reported to be one of the most important ones to young female cancer patients, they are not the only cancer-related needs or concerns prevalent in this population. According to a systematic review of unmet supportive needs among the general cancer patient population, 'fear of cancer spreading or recurring' constituted the most frequently identified psychosocial issue in the treatment and post-treatment phases (5).

Fear of cancer recurrence is defined as 'fear, worry, or concern about cancer returning or progressing' (Gozde Ozakinci, personal communication, 27.01.2016). Even though it is a rational response to a potential health threat, it can have serious effects on people who experience it. Preliminary evidence suggests that fear of cancer recurrence affects women's treatment-related decisions and higher levels of fear of recurrence might be associated with choosing more aggressive cancer treatment regimens (49). In the case of

young women leaning towards more aggressive treatments, this could mean choosing regimens potentially detrimental to their fertility.

This finding is particularly important since Simard, S. et al. (50)'s systematic review investigating the correlates of fear of cancer recurrence among various cancer patients populations presented strong evidence for the negative association between age and fear of recurrence as well as moderate evidence for the relationship between female gender and recurrence fears. Recent studies have found that among women who were aged less than 50 at the time of cancer diagnosis, fear of recurrence was still associated with age, with the youngest groups being the most affected (51-53). Thewes, B. et al. (53) who investigated recurrence fears in a group of 218 women diagnosed with breast cancer at the age 18 to 45 reported that 70% of participants showed clinically significant levels of fear of recurrence. The evidence would, therefore, suggest that young women are at risk of experiencing fear of cancer recurrence (49).

Because of the specific needs of this population of cancer patients, it has been hypothesised that fear of cancer recurrence in young women could be related to fertility and parenthood issues. Two studies (52, 53) failed to find a significant association between fear of cancer recurrence and either childbearing status or attitudes towards childbearing (considering future pregnancy vs. not). Contrary to these findings, Mehnert, A. et al. (54), Lebel, S. et al. (51), and Arès, I. et al. (55) all reported a significant relationship between being a mother and the level of recurrence fears. Additionally, Arès, I. et al. (55) noted that among mothers, fear of recurrence was positively associated with the age of the children with women caring for adolescents experiencing higher levels of fear of recurrence than mothers of young children. This evidence suggests that fear of cancer recurrence and fertility issues might somehow be related in young women diagnosed with cancer, however, the evidence remains as yet scarce and inconclusive.

1.7. Conclusions and rationale for the project

Although the prevalence of cancer in young people remains relatively low (6), research suggests that when diagnosed, young people constitute a particular patient population facing distinctive, age-specific issues (1-3, 29). These include, among others, fertility-related needs such as the need for information about the impact of cancer treatments on

fertility as well as counselling regarding fertility issues after the end of treatment (4, 13, 14). Even though the majority of young cancer patients express these needs, they often remain unmet (4) which might lead to negative psychological consequences (56). Another psychological consequence that the majority of cancer patients experience which is, however, most pronounced in younger cancer patients (50) is fear of cancer recurrence persisting long into survivorship (53).

This PhD research project aims to explore psychological consequences of cancer related to fertility and fear of recurrence in detail. To do this I first conducted a systematic review of literature about fertility and parenthood issues among young women with cancer. Based on its findings, I designed and conducted two studies – one qualitative and one quantitative which explored different aspects of fertility issues in young women diagnosed with breast or gynaecological cancer during their reproductive years.

I chose to concentrate specifically on reproductive-age female population with the diagnosis of breast, cervical, or ovarian cancer firstly, because these malignancies tend to occur most frequently in this group of patients (10) and secondly, because they often require treatments that can temporarily or permanently impair women's fertility. By the means of the quantitative study I also chose to investigate the cultural aspect of fertility issues related to cancer by comparing two populations – British and Polish. This is because the concept of fertility is embedded in the broader socio-cultural context (47), yet, the cross-cultural research of cancer-related fertility issues is lacking. Finally, I chose to conceptualise both parts of the study using the theoretical framework of the CSM. I also applied the Shared Decision Making model to the quantitative data. This is because underpinning empirical research with theoretical models allows to uncover important concepts or processes, and their explanations in the data which, if no theory is used, might remain unnoticed. The next section outlines in detail the specific aims and objectives of this PhD project.

1.8. Aims and objectives

1.8.1. Aims

The aim of this thesis was to investigate the role that fertility and reproductive issues play in the lives of young women who were diagnosed with breast or gynaecological cancer. Both qualitative and quantitative methodologies were used to achieve this aim.

The qualitative study concentrates specifically on whether fertility issues affect women's treatment-related decision-making and if yes, to what extent, and in what way. This study focuses exclusively on women living in the United Kingdom.

The quantitative study explores the psychological experience of fertility issues following treatment. On the one hand, it focuses on the determinants of psychological experience related to reproductive issues and on the other, on its association with women's psychological well-being. Additionally, since perceptions of fertility are largely influenced by one's socio-cultural background (47), this study was designed to account for the possible cross-cultural differences in the psychological outcomes by including participants drawn from two populations – British and Polish. Finally, this study incorporates the concept of fear of cancer recurrence and explores the interplay between fear of recurrence and fertility issues, and their impact on women's QoL.

1.8.1.1. Objectives

The following specific objectives addressing the elements of the thesis were established to achieve the above aims:

1. To establish the importance of fertility issues and fear of disease recurrence among young female cancer patients (as outlined above in sections 1.1 – 1.7).
2. To understand how individuals perceive their illness and cope with it from the perspective of the CSM, and how this model can be applied to young women dealing with cancer and fertility issues (Chapter 2).
3. To conduct a systematic review of literature examining fertility issues in young female cancer patients (Chapter 3).
4. To investigate how women in the UK diagnosed with either gynaecological or breast cancer make treatment-related decisions which can affect their

reproductive potential and whether fertility issues play a role in those decisions (Chapter 4).

5. To identify the determinants of psychological experience of fertility issues and fear of cancer recurrence among young women diagnosed with gynaecological or breast cancer drawn from the British and Polish populations (Chapter 5).
6. To examine whether fertility issues and fear of cancer recurrence are associated with QoL and relationship functioning among young women diagnosed with gynaecological or breast cancer drawn from the British and Polish populations (Chapter 5).

1.9. Thesis outline

Following this introductory chapter, this thesis consists of five chapters. Chapter 2 discusses the theoretical models applied to the project. It describes in detail the overreaching theoretical framework that brings together the qualitative and the quantitative parts of the project, namely the CSM. It also introduces the decision-making models applicable to the clinical setting and focuses in particular on the Shared Decision Making model which was applied to the qualitative data. Finally, it discusses the concept of decision regret as well as the impact of the broader socio-cultural context on the conceptualisation of both cancer diagnosis and fertility issues. Chapter 3 discusses the systematic review of literature conducted as part of the PhD project. It brings together the findings from the quantitative and qualitative literature investigating various factors affecting the levels of fertility-related distress among young women diagnosed with cancer as well as the impact of fertility issues on (1) women's psychological well-being, and (2) their decisions about cancer treatments. Finally, the chapter draws on the literature findings and the gaps identified within to provide a rationale for both the qualitative and the quantitative study. Chapters 4 and 5 describe the qualitative and the quantitative components of this project, respectively. They present the rationale for each study, the research questions and the methods used to answer them, and the obtained results. The findings are discussed within the context of the theoretical frameworks applied as well as drawing on the evidence from the systematic review of literature. Finally, the limitations of each study and their impact on the conclusions that can be drawn from the data are presented. Chapter 6 provides a summary of the most important points outlined in Chapters 1 – 5. It also offers a

synthesis of the qualitative and quantitative findings of this project referring to the CSM. It discusses the limitations of the project and delineates areas of research that need further investigations. Finally, it suggests the implications of the findings of this project for both medical and health psychology practice.

Chapter 2 Theoretical considerations

This chapter outlines the theoretical considerations that help understand and place this PhD project within the context of broader health psychology research. The rationale for choosing the CSM – a model stemming from the self-regulatory tradition is discussed first (section 2.1). The components of the model – particularly the illness representations (section 2.2.1) and coping mechanisms (section 2.2.2) are then discussed in detail. The decision-making models applicable to clinical setting are presented (section 2.2.2.2) as treatment-related decision-making is conceptualised as one of the strategies to cope with illness. Particular attention is given to the Shared Decision Making model as the gold standard of clinical care (57). Related to treatment decision-making is decision regret. This concept is also briefly discussed (section 2.2.2.3). Since the CSM acknowledges the importance of a broader socio-cultural context in perceiving and dealing with one's illness, its influence on one's representation of cancer and fertility issues is outlined (section 2.2.3). The chapter concludes with the explanation of how both the CSM and the Shared Decision Making model were applied to both the qualitative and quantitative components of this PhD project (section 2.3).

2.1. Introduction

Health psychology is a discipline that focuses on investigating how psychological factors (i.e., one's beliefs, values, feelings, thoughts, and attitudes) affect health and illness, and what impact they have on health-related behaviours (58). There are multiple theories that have been developed within the field (e.g., Transtheoretical Model, Health Belief Model, Protection Motivation Theory, Theory of Planned Behaviour, or CSM) (59). While there are obvious differences between those various theoretical frameworks, their common assumption is that for a given health behaviour to occur, this particular behaviour needs to become a personally important goal (60). Setting personally important goals is in turn part of a broader concept of self-regulation (60).

Within the self-regulation framework, a goal serves as a standard which an individual tries to achieve by diminishing the discrepancy between the perceived and the desired state of affairs. Behavioural processes lead to the achievement of the desired goals. The outcome of behaviour is constantly assessed and if it is not deemed satisfactory, an

individual modifies the behaviour in order to achieve the goal (60). Also, human behaviour does not operate in a vacuum, but is nested in a broader context of environmental and personal factors and is influenced by them (61).

As mentioned previously, the first phase of self-regulation, namely the goal setting is common to the majority of the models used in the field of health psychology. The model that also reflects the phases of goal attainment and appraisal is the CSM (62) and it has been chosen as a framework to guide this PhD project for two main reasons.

First, as opposed to other models in health psychology, the CSM not only concentrates on predicting the occurrence of particular health behaviours (coping strategies as a result of the cognitive representation of illness), but also incorporates the emotional impact an illness can have on an individual (as a result of both cognitive and emotional illness representations). As this PhD project includes a qualitative study which explores coping with illness (i.e., treatment-related decision making in the context of fertility), and a quantitative study which investigates the emotional impact of disease on an individual (i.e., psychological outcomes resulting from cancer-related fertility issues and fear of disease recurrence), the CSM appears to be the best suited to bring the results of the two studies together in a coherent manner and allow for a synthesis of the findings to provide additional insights that could not otherwise be achieved.

Second, as suggested by systematic reviews of both fertility and parenthood issues among young female cancer survivors (63), and fear of recurrence in a general cancer population (50), neither fertility-related distress nor recurrence fears seem to be affected by the objective characteristics of the disease. The two reviews suggest, however, that it is the patient's subjective conceptualisation of illness that is associated with psychosocial outcomes. As the CSM provides a framework to explore one's lay theories of one's illness (i.e., illness perceptions), it was deemed the most applicable in the context of this PhD project. The CSM is therefore described in detail in the next section.

2.2. Leventhal's Common Sense Model (CSM)

Leventhal formulated CSM on three fundamental propositions:

1. People are problem solving agents who define their worlds, select coping strategies to deal with threats, and modify their problem representations and reactions based on the obtained feedback;
2. Problem-solving does not occur in vacuum but within a specific socio-cultural context; and
3. People make their decisions to enhance health or treat disease based on what is identified as the most urgent threat and these decisions are limited by the available resources and evaluated against one's expectations with regards to the outcome (named as 'satisfaction rule') (64).

What differentiates CSM from other models based on the underpinnings of self-regulation theory is that it supplies the details of 'what' is being regulated and 'how', when people try to maintain health or control illness (65). In other words, it offers a framework and psychological constructs which provide a specific 'content' of the model for the health threat in question (65). The framework that CSM is based on constitutes the extension of the parallel processing model (66) which suggests that a health threat elicits two simultaneous responses in individuals – an emotional response (such as fear or distress) and subsequent coping strategies to manage these emotions as well as a cognitive response (a representation of threat) and procedures to cope with the threat itself (see Figure 2.1). CSM also conceptualises how people think about health threats, namely the 'what' they respond to. According to CSM, individuals create their own illness representations which are defined as an individual's understanding of a health threat (62, 64). In other words, what is important when creating an illness representation is the patient's rather than the medical observer's perspective (67).

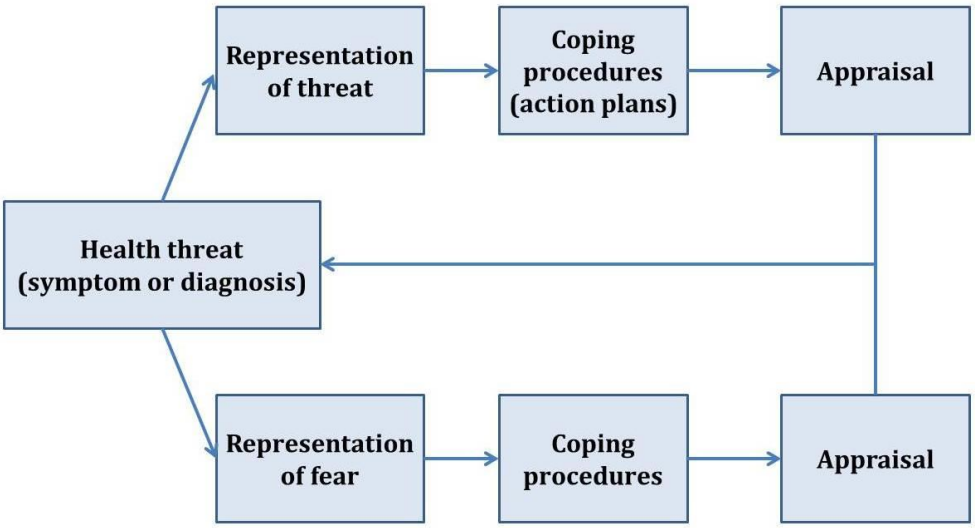


Figure 2.1. Leventhal's parallel processing model

Illness representations are primarily characterised by their content (64) which refers to the nature of a health threat and are conceptualised according to the five following categories:

1. *Identity* that includes the label of an illness [its name (e.g., diabetes)] and the associated symptoms.
2. *Timeline* that represents different time frameworks relating to an illness such as the time needed to diagnose it, its duration, or time needed for recovery.
3. *Causes* that can be classified as intrinsic or extrinsic to an individual or as environmental, biological, emotional or psychological (68). Causal attributions differ depending on the disease stage they are made at (e.g., attribution about a symptom; attribution about a disease) (69).
4. *Consequences* that refer to the seriousness of an illness and its influence on different life domains.
5. *Cure/control* that represents the degree to which an individual has control over an illness and assesses it as curable (70).

Illness representations are activated by specific stimuli that can either be concrete, such as somatic symptoms of a disease, or abstract, such as a diagnosis given by a healthcare professional, or even information from the media (64, 68, 71). The processing of

information from concrete and abstract sources results in the formation of a cognitive representation. This process is based on the rule of symmetry which implies that to form an illness representation, one needs to integrate the information from both the concrete and abstract levels (64). Regardless of which information is acquired first – the awareness of symptoms or the disease label – they need to go hand in hand. Symptoms need a label to define them and a label needs symptoms to explain it. Only when the disease representation acquires this bi-level organisation is it fully formed (64) and one can develop appropriate strategies to cope with an illness. Consequently, a failure to fully form the disease representation can affect patients' choice of coping mechanisms as well as psychological outcomes. For example, Bradley, E.J. et al. (72) who studied illness perceptions among early stage gynaecological cancer patients found that because gynaecological cancers were often asymptomatic in the beginning, patients did not go through a self-diagnosis stage which resulted in anxiety about not being able to detect cancer recurrence. The primary mechanism of coping with these feelings of fear about cancer recurrence was seeking reassurance from physicians which, in turn, led to an increase in healthcare utilisation (72).

The cognitive process of forming an illness representation is accompanied by a parallel emotional pathway. Coping procedures including cognitive (e.g., action plans to deal with the health threat), emotional, and behavioural mechanisms (e.g., execution of action plans) follow the appraisal of a stimulus. Coping leads to the achievement of two types of outcome –cognitive and emotional, which are then appraised. The results of the appraisal process feed back to the illness representations and emotional responses (65). This cyclical model also permits for the cognitive illness representations to directly affect and be affected by emotional responses (see Figure 2.2).

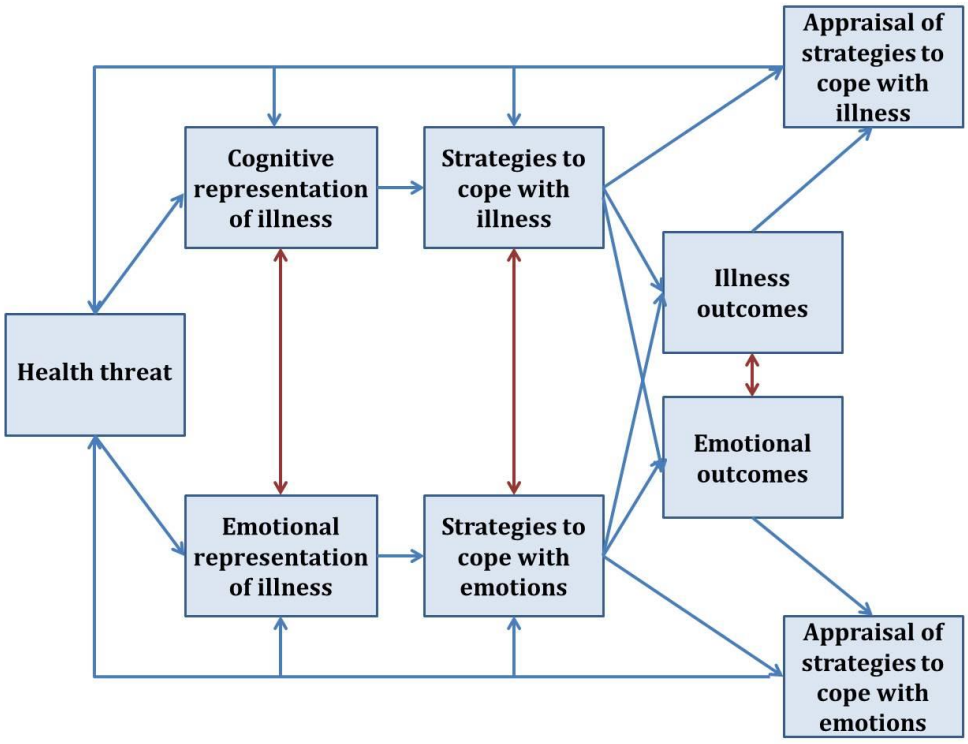


Figure 2.2. Cognitive and emotional pathways of the CSM

The way an individual processes inner or outer health-related stimuli greatly depends on multiple factors. These include not only the characteristics of a particular stimulus but also the attributes of an individual. Leventhal, H. et al. (64) describes the perceived vulnerability to an illness as an example of a factor related to the self (self-identity) which could potentially influence one's response to a health-related stimulus. Felt age, self-assessment of health (67), and family history of illness are all considered to determine one's perception of how vulnerable one is towards a particular illness (64). Research also emphasises the role of personality traits such as neuroticism and extraversion in affecting one's responses to health-related stimuli (68, 73).

Another important determinant of how one interprets health-related stimuli includes heuristics. Heuristics are problem-solving strategies defined in cognitive psychology as 'rules of thumb that are cognitively undemanding and often produce approximately accurate answers' (74, p. 634). Some heuristics have proved useful from the perspective of CSM. The 'age-illness heuristic' helps one decide whether the perceived symptoms and signs are indicative of an illness or rather of the ageing process (67). More

specifically, age can be perceived as a source of risk for or a protection against cancer diagnosis (64). For example, young people can feel that the threat of cancer is irrelevant to them because of their age (67). Another such heuristic is the 'prevalence heuristic' which people use to downgrade the severity of their symptoms when they are aware that these symptoms are frequently encountered in the population (67). These heuristics along with the factors related to the self (e. g., self-identities, and personality traits) can affect the perception of one's vulnerability to a specific health threat.

Finally, CSM is also embedded in a broader context of social and cultural norms which play an important role in forming illness representations, emotionally responding to health threat, and selecting coping strategies (75) (see Figure 2.3). Baumann, L.C. (75) provides a definition of culture suggested by Giger, J.N. and R.E. Davidhizar (76) which explains culture as 'a metacommunication system based on non-physical traits, such as values, beliefs, attitudes, customs, language, and behaviours that are shared by a group of people and passed down to generations through formal communication and imitation' (p. 242). Even though according to CSM, an individual is a problem solver who interprets a health threat, this individual is at the same time immersed in a particular culture and constantly influenced by it. Whether one lives within an egocentric culture embracing a biomedical model or a sociocentric one adopting a more holistic model, culture is a non-negligible factor affecting self-regulation processes (75). Studies have shown that effective self-regulation of physical and mental health depends on the presence of others (65). One's social network including family, friends (65), and nowadays also extending to the Internet (77, 78) constitutes a source of important social input when illness representations are formed.

Probably the most straightforward demonstration of self-regulation being a social process comes from the fact that when faced with symptoms, individuals, especially in egocentric cultures, turn to medical professionals for advice regarding diagnosis and treatment. Through this process they acquire a label for what was beforehand only a cluster of symptoms and this enables them to form an illness representation (65). According to Leventhal, H. et al. (64), culture not only provides a linguistic label for defining an illness but also personal contacts through which one learns how to interpret physical stimuli and ways to manage them. Once diagnosed with an illness, individuals

tend to compare themselves to other patients in a similar situation in search for cues for how one should feel or to normalise one's disease experience (65). Socio-cultural context acts as a reference point for both cognitive and emotional illness experiences. For example, illness representations have a prototypical structure created within a specific socio-cultural context. This means that a representation of a particular disease reflects the most common presentation of the condition in that culture. However, if one's experience of illness differs from the prototypical representation, one considers oneself to be an exception to this common experience rather than discards the cultural belief (75).

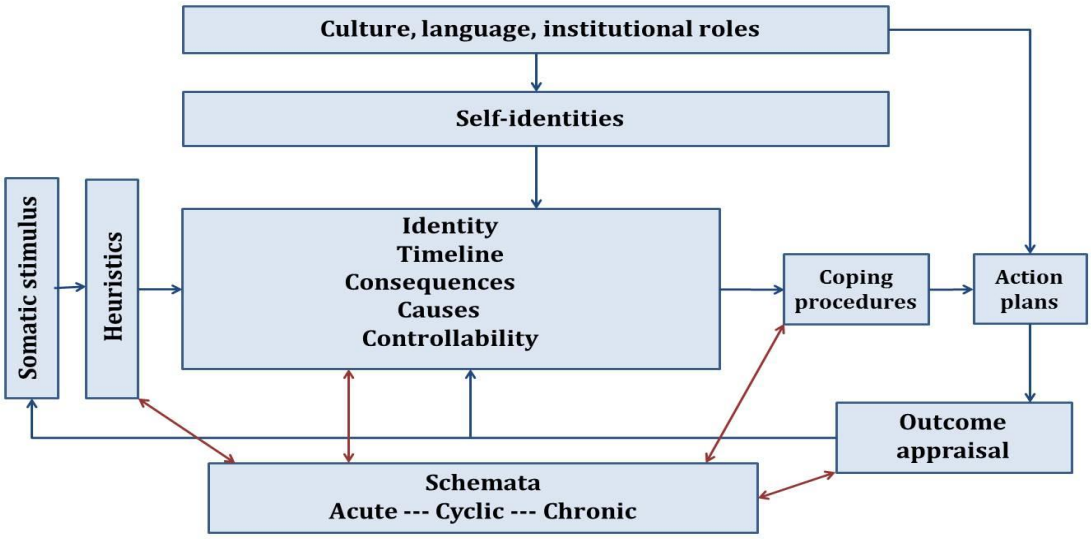


Figure 2.3. The common-sense model of self-regulation. Adapted with permission from Leventhal et al. (2004)

2.2.1. Illness representations

As mentioned above, illness representations refer to an individual's understanding of a health threat. A meta-analysis of studies guided by the CSM conducted by Hagger, M.S. and S. Orbell (68) found a pattern in illness representations consistent across a broad range of different chronic conditions such as cardiovascular disease, diabetes, asthma,

or cancer. As suggested by Leventhal, H. et al. (67), these conditions, although different in nature, share certain similarities in that they all:

1. are systemic and alter multiple body organs, which has an effect on physical and therefore social functioning of an individual;
2. develop over a long time and persist throughout one's life;
3. can be treated and controlled rather than cured;
4. may have insidious character and gradually affect an increasing number of valued life activities; and
5. may have phasic trajectory with quiet periods and episodic flares intertwined.

Hagger, M.S. and S. Orbell (68) operationalised the categories of illness representation according to the most commonly used measures – the Illness Perceptions Questionnaire (IPQ) (79) and the Illness Perceptions Questionnaire-Revised (IPQ-R) (80). While IPQ measures the dimensions of illness representations mentioned in section 2.2.1, the IPQ-R introduces the following additional categories of illness perceptions:

1. Cyclical timeline which refers to the periodicity of symptoms.
2. Illness coherence which describes the way an individual makes sense of one's own illness and sees the representation as useful.
3. Emotional representation which reflects the emotional response to an illness.

Furthermore, the category of control is divided into treatment and personal control of an illness. In both IPQ and IPQ-R, higher scores on identity, timeline, and consequences subscales signify respectively a larger number of reported symptoms, a more chronic pattern, and more serious consequences of a disease. Higher scores on cure/control subscale indicate stronger beliefs in curability and controllability of a disease.

Hagger, M.S. and S. Orbell (68) reported positive correlations between illness identity and consequences, identity and timeline, and finally timeline and consequences. They also found negative correlations between cure/control and consequences, identity and cure/control as well as timeline and cure/control (68). This review supports the notion that characteristics of illness representations are separate and valid constructs and that their specific patterns can describe groups of similar conditions (e. g., chronic *or* acute) but also enable to discriminate between the dissimilar ones (e. g., chronic *and* acute).

2.2.1.1. Illness representations, emotional distress and QoL

In their systematic review Hagger, M.S. and S. Orbell (68) also identified links between illness cognitions and various psychological outcomes. Across the studies they reviewed, psychological distress was positively related to the consequences, the identity, and the timeline of a disease and negatively associated with the cure/control representations.

As mentioned above, Hagger, M.S. and S. Orbell (68) found patterns of illness representations consistent across various chronic conditions. This would suggest that even when conditions differ in nature (e.g., cardiovascular disease and cancer), illness representations attached to them, if similar, should also engender similar psychological responses. However, since this thesis concentrates specifically on cancer and cancer-related infertility, a rapid review[1] of literature was conducted to investigate the relationship between illness representations and psychological outcomes including emotional distress and QoL among:

1. patients with different types of cancer; and
2. women suffering from infertility not related to cancer.

The decision to examine the associations between the conceptualisation of fertility problems and psychological well-being among otherwise healthy infertile women was dictated by the fact that no studies involving women with cancer-related infertility exist to date. The results of this review are described in sections 2.2.1.1.1 and 2.2.1.1.2.

2.2.1.1.1. Cancer

2.2.1.1.1.1. Distress

The findings of eight studies providing the analysis of cross-sectional data suggest that distress (operationalised as either general distress related to illness, anxiety, or depression) was most strongly and positively related to illness identity, timeline, consequences, and emotional causes of the disease (81-88). Those observations are supported by the findings of longitudinal studies which indicate an association between illness identity and timeline measured before cancer treatment and the distress at post-

[1] Two databases (PubMed and Web of Science) were searched using the following keywords: 'illness perceptions' OR 'illness representations' AND 'quality of life' OR 'distress' AND 'cancer' OR 'infertility'. The search was delimited to years 2003-2013.

treatment follow-up (83, 89). Some of the cross-sectional studies additionally found a negative relationship between depression and personal control as well as illness coherence (81, 82, 86). Two studies using cluster analysis (90, 91) provide evidence that a general pattern of more negative illness cognitions and their deterioration over time were related to higher levels of both anxiety and depression.

Only two studies, one longitudinal and one cross-sectional concentrated on a specific type of distress among cancer patients, namely fear of cancer recurrence. In the cross-sectional study (92), fear of recurrence was predicted by illness identity, timeline, treatment control, and emotional representation of the disease. The longitudinal study (93) confirms the association of recurrence fears with illness representations (the consequences and the emotional representation), however, long-term (six to eight months after finishing treatment) recurrence fears were not predicted by any of the pre-treatment illness perceptions.

2.2.1.1.1.2. QoL

The results of four cross-sectional studies indicate that the overall QoL might be predicted by illness identity, consequences, and emotional representation of the disease (85, 88, 94, 95). This pattern is also supported by the findings of one longitudinal study (96), where the global QoL at 2-years follow-up was related to illness identity and consequences measured at the time of diagnosis. However, different domains of QoL could be associated with different types of illness representations. Physical functioning seems to be strongly and negatively associated with illness identity (97, 98), whereas both mental and emotional functioning appear to be negatively related to emotional representation of the disease and positively to the treatment control (95, 97, 99, 100). Cross-sectional (98, 100) as well as a longitudinal study (96) also reveal that attributing illness to behavioural causes was a predictor of lower levels of functioning in multiple QoL domains. It is, however, important to note that one longitudinal study did not find any relationship between QoL at 6 to 8-months post-treatment follow-up and the pre-treatment illness perceptions (89).

2.2.1.1.2. Infertility

Illness perceptions in infertility patients and their relation to distress and QoL seem to be a highly understudied area with only three articles pertaining to the subject as revealed by the scoping literature review.

Both studies by Benyamini et al. (71, 101) show that among women, lower perceived controllability of the disease and more severe consequences were associated with higher distress related to infertility. In a study by Lord, S. and N. Robertson (102), anxiety was predicted by the cyclical timeline of an illness and depression was related to lower illness coherence and stronger illness identity in a mixed-gender sample of infertile patients.

The existing literature placing cancer and infertility in the framework of the CSM reveals several potentially important illness cognitions that might affect patients' levels of distress and QoL. Distress seems to be particularly influenced by illness identity, timeline, and consequences (81-84, 87-89, 91-93) whereas QoL appears to be affected by illness identity, consequences, and attributing the cause of the disease to one's own behaviour (such as smoking, drinking alcohol, or diet) (85, 88, 95-100). Also, controllability of an illness appear to be a factor affecting distress in infertile patients (71, 101) and to a lesser extent in patients suffering from cancer (81, 82, 84, 91, 92).

2.2.2. Information-seeking and treatment decision-making as coping procedures

Illness representations are a driving force that determine the selection of a procedure or a set of procedures to cope with a particular health threat (65). Coping involves both cognitive and behavioural actions that serve to eliminate an illness or its consequences (64). Illness representations and coping procedures are intrinsically intertwined since the former influence the selection of the latter and the latter in turn affects the former via an appraisal process. Moreover, specific illness representations lead to a choice of specific coping procedures which is known as an 'IF-THEN' rule where IF represents an illness perception and THEN represents a specific act (64). For instance, if one has a headache, then one takes a painkiller to numb the pain.

However, faced with any health threat, one can choose from a vast number of options to deal with the situation. In Western cultures [also referred to as 'egocentric' or

'individualistic' and defined as those 'in which the ties between individuals are loose: everyone is expected to look after him/herself and his/her immediate family' (103, p. 11)] which include the European and Northern American ones and where the biomedical model prevails (75), individuals tend to turn to the healthcare system, especially when they suspect their condition might be serious. They apply an 'IF-THEN' rule in a way whereby if they experience symptoms, then they seek medical advice.

Seeking medical advice and help for a set of symptoms has two aims: (1) defining the problem, that is, diagnosing an illness, and (2) solving the problem, that is, treating the diagnosed condition. Although physicians are responsible for accurately diagnosing and treating a condition the patient presents with, it is the patient who will live with the consequences of an illness. Coping with these consequences, especially in the case of a serious illness such as cancer, might be a challenging process. Information-seeking and treatment-related decision-making have been identified as coping strategies often used by cancer patients (104-107).

2.2.2.1. Information-seeking as a coping strategy

Knowledge and information have been recognised as powerful tools to deal with cancer diagnosis that grant patients cognitive control over the difficult situation they found themselves in (106). Literature suggests that the majority of cancer patients prefer to be given all the information pertaining to their diagnosis and treatment regardless of whether the news is good or bad (106). In a study by Jenkins, V. et al. (108) that surveyed a sample of 2331 cancer patients attending out-patient clinics across the UK, 87% of participants wanted all information relevant to their illness and 98% specifically wanted to know whether they had cancer.

Information can play multiple roles in restoring cancer patients' well-being. Henman, M. et al. (104) interviewed women with early breast cancer diagnosis and identified four main reasons why they wanted to be provided with information regarding their diagnosis. First of all, knowledge about cancer allowed women to regain some of the control that cancer took away from them. It made their diagnosis less mysterious and restored their ability to plan for the future. It also made it possible to somewhat predict what would happen in terms of their cancer journey which in turn made the experience

less scary and more manageable. Additionally, information reduced women's anxiety by allowing them to dispel cancer-related misconceptions and therefore put some of their worries aside. Finally, it motivated women to adopt new behaviours that could potentially reduce their risk of cancer recurrence (104).

These qualitative results corroborate the existing quantitative evidence on the role of cancer-related information. Mills, M.E. and K. Sullivan (109)'s literature review on the topic concluded that information helped patients gain control over their lives, reduced their anxiety, improved compliance with treatment, created more realistic expectations regarding their illness, promoted self-care and participation in treatment as well as generated feelings of safety and security. These findings were also supported by a more recent systematic review of cancer patients' information needs (105). Rutten, L.J.F. et al. (105) reported that information benefitted patients in that they were able to partake in treatment-related decision-making and were subsequently more satisfied with treatment choices.

Knowledge is an obvious prerequisite to decision-making as without necessary information one cannot make an informed choice. Yet, wanting information is not always equal to wanting to actively participate in the decision-making process (106). Research has shown that cancer patients often prefer to assume a passive role when it comes to decisions regarding their treatment. In a seminal study, Degner, L.F. and J.A. Sloan (110) investigated treatment-decision preferences in a sample of 436 cancer patients in Canada and found that 59% of participants chose their physician as a principal decision-maker and only 12% indicated they wanted to assume an active role in the decision-making. Similarly, Beaver, K. et al. (111) studied 150 women newly diagnosed with breast cancer in the UK and reported that 52% of participants preferred their physician to decide about their treatment while 20% wanted to play an active role in the decision-making. A more recent report that compiled data from six studies involving 3491 cancer patients in the US and Canada showed that approximately equal numbers of patients wanted to assume active or passive role in treatment decisions making (26% and 25%, respectively) with the majority (49%) preferring a collaborative role (112).

Although wanting information might not mean wanting to participate in decision-making, it gives patients a choice of whether to participate or not (106). This leads to the question of whether there is a group of cancer patients that would be more likely to want to participate in the decision-making process. Research has been conducted into this area to enable physicians to predict which patients would be interested in partaking in decision-making regarding their treatment and it has shown that generally younger and well-educated women wanted to assume a more active role in treatment decisions (113).

As previously mentioned in section 1.2, young women diagnosed with cancer have specific information needs (1). Zebrack, B. (1) suggested that this is because cancer diagnosis at a young age poses major and unanticipated developmental challenges that young people do not usually have to face. Threat to fertility is one of them. Two systematic reviews focusing on breast cancer survivors (14, 56) and one targeting women with variable chronic non-communicable diseases (13) investigated their information needs concerning fertility and found that women wanted information about fertility, however, only 34-72% of women across different studies reported having had a conversation about it with their physician. Yet, fertility and menopause-related information are important to young female cancer patients with fertility-related information being particularly relevant at the time of diagnosis and treatment decision-making, suggesting that women might wish to take this factor into account while making treatment decisions (114). Still, apart from socio-demographic variables, other factors such as physician's inclination to involve the patient and the relationship and communication with the clinical team also play a role in patients' preferences to be involved in treatment decision-making (113).

2.2.2.2. Treatment-related decision-making as a coping strategy

The involvement in the process of treatment decision-making can be an empowering experience for the patient (107) and another strategy to cope with cancer. Therefore it is important to outline how medical decisions take place within the clinical setting and what that might mean for the patient. Current literature conceptualises health-related decision-making depending on the amount of control attributed to and the involvement of the patient in the process and categorises it into passive ('paternalistic' or 'physician

as agent'), shared or active ('informed') decision-making models (115-118). These models are explained by adopting the perspective delineated by Charles, C. et al. (116) who divided treatment decision-making process into three stages: (1) information exchange, (2) deliberation about treatment options, and (3) deciding on the treatment to implement. Additionally, since respect for autonomy is one of the basic principles widely recognised as crucial while making treatment decisions (119-121), the representation of patient's autonomy within each model is discussed.

Passive decision-making models assume minimal, or even no patient involvement in the decision-making process (115, 117). In both the paternalistic and physician as agent models, the physician is an expert who possesses medical knowledge to treat an illness (115). The difference lies in the direction of information exchange. In the paternalistic model, the information flow is unidirectional, from physician to patient (116). The physician informs the patient of the nature of his or her condition and the preferable course of action (115, 116). The doctor acts in the patient's best interest, however, this best interest is understood as medical only. In the paternalistic model, the patient does not communicate his or her values to the physician and therefore those values are not taken into account in the deliberation or the final, decision-making stage of the process (115-117).

In contrast, in the 'physician as agent' model, physician first elicits patient's preferences regarding treatment and then makes a decision trying to select the option the patient would have chosen had she or he had the expertise of the healthcare professional (115, 118). In both of these models, the physician is the sole decision maker who informs the patient of the treatments he or she is about to receive for the purpose of obtaining informed consent (107, 116). The patient is, therefore, seen as a passive recipient of treatments and his or her autonomy is expressed in his or her assent to what the physician determined as the best course of action (117).

Paternalistic decision-making model prevailed in medicine for a long time. This is because physicians were seen as the ones with the most valid and up-to-date knowledge regarding medical treatments which they were expected to apply while choosing the one appropriate for their patient (116). They were guided by their professional code of conduct and therefore seen as acting in the patient's best interest (116). Finally, their

expertise put them in the best position to assess trade-offs between different types of treatments (116). This model is still applicable to certain treatment decisions, particularly when one single best treatment option exists or when time to make a decision is very limited (e.g., in emergency medicine). However, with the rapid evolution of treatment modalities for many conditions, including cancer, and the trade-offs becoming more difficult to judge, the assumption that physicians are in the best position to select treatments has been challenged (116). Patients' input in deciding about treatments has become more important and this shift in perspective has brought about shared and active decision-making models.

The 'informed decision-making' model stems from the consumerist approach to medicine that started developing in 1970s as a reaction to the paternalistic model (122). This model, similar to 'physician as agent' model, can be classified as an agency model, where an agent makes decisions for another person (e.g., patient) who would be subject to these decisions (a principal) (118). The difference between these two models lies in who the agent in each case is.

As discussed previously, in the physician as agent model, the patient (or the principal as defined within agency models) delegates the decision-making responsibility to the physician. In contrast, in the informed decision-making model, the patient retains the authority to make decisions (118). However, he or she cannot make an informed choice without necessary information. While in the physician as agent model, the patient transfers information about his or her values to the physician, in the informed decision-making model, the transfer of information is again unidirectional, but in this case it is the physician who transfers his knowledge about a disease and treatment options to the patient (115, 118). The physician acts as an expert and is a primary provider of information, however, his or her preferences are not accounted for in the decision-making process (115). It is the patient who undertakes the deliberative process alone and subsequently makes an autonomous decision regarding his or her course of treatment (116). Autonomy is therefore understood as patient's complete control over medical decision-making (117). That said, Emanuel, E.J. and L.L. Emanuel (117) dispute whether this model truly preserves patient autonomy by stating: 'Freedom and control over medical decisions alone do not constitute patient autonomy' (p. 11). They

suggest that a deliberation process involving a physician is essential to achieving an autonomous decision.

Hence, in opposition to the models where only one person goes through the decision-making process, the shared decision-making model is often seen as 'middle ground' between the passive and active decision-making models (123). According to Charles, C. et al. (115), for the shared decision-making process to occur, four conditions have to be fulfilled:

1. There needs to be at least two participants in the decision-making process – the physician and the patient [however, this is the minimum and often family, friends, and other physicians participate in the process which renders it more complex (116)],
2. Both parties have to be willing to participate in the decision-making process,
3. Information must be shared between physician and patient, and
4. A treatment decision that both parties agree to has to be reached at the end of the process.

What is crucial in the shared decision-making model is the bidirectional exchange of information whereby the physician shares his or her medical knowledge as well as the opinions about different treatment modalities with the patient and the patient in turn provides the information about his or her values and preferences regarding treatments as well as shares the pre-existing knowledge he or she has about his or her condition (116). Once the information exchange process has taken place, both the patient and the physician enter the deliberation stage where information is discussed in an interactional manner (116). In this process of negotiation, a decision regarding treatment is reached and implemented (116).

Building on these basic characteristics of shared decision-making, Makoul, G. and M.L. Clayman (123) provided a more detailed description of what shared decision-making entailed. They reviewed the relevant literature and concluded that there were certain essential and ideal components of the shared decision-making process. They listed the following as essential elements that need to occur during shared decision-making: defining the problem under discussion, presenting options, discussing risks and benefits

as well as patient values and preferences, acknowledging doctor's recommendations, clarifying the understanding, making or deferring the decision, and arranging follow-up (123).

These models proposed by Charles (115, 116) and Makoul, G. and M.L. Clayman (123) widely overlap and more importantly both emphasise the mutual exchange of knowledge and preferences between the patient and the physician as a crucial characteristic of shared decision-making. It is through this process that both the patient and the physician acquire an in-depth understanding of the illness situation. According to Emanuel, E.J. and L.L. Emanuel (117), this is what constitutes the key to preserving patient autonomy because 'the patient is empowered not simply to follow unexamined preferences or values but to consider, through dialogue, alternative, health-related values, their worthiness and their implications for treatment' (p. 7).

Charles, C. et al. (116) suggest that there are no right or wrong decision-making models and the choice of the decision-making strategy needs to be based on the characteristics of the clinical situation. Whitney, S.N. et al. (107) recommend that when choices are made under high risk and low certainty (such as choices regarding cancer treatments), shared decision-making would be an ideal model to adopt. In their study exploring treatment-related decisions among breast cancer patients, Henman, M. et al. (104) found that women wanted to feel included in the decision-making process since that gave them back some of the control over their lives and made them feel like a person and not like a medical case. On a broader scale, shared decision-making has proved to be beneficial to patients in terms of their satisfaction with the decision-making process (124), the post-decision satisfaction as well as physical and psychological well-being (125).

However, for the shared decision-making process to occur, both the physician and the patient need to feel that there are actual choices to be made (116) and this might not always be the case for cancer patients. In two studies investigating treatment decisions among breast cancer patients (104, 126), women reported how they felt they had no choice regarding treatments since doing nothing was not a viable option and deciding between variations of chemotherapy regimens was not considered an important decision. If that is the case and shared decision-making model is not always applicable to oncology setting, does that mean that cancer patients are worse-off than individuals

with other chronic illnesses for whom perceived treatment choices exist? A systematic review of optimal matches of patient preferences for information and decision-making by Kiesler, D.J. and S.M. Auerbach (127) suggests that it is the extent to which patient's expectations regarding the amount of information provided and desired decision participation match the physician's communication and practice styles that is actually associated with patient outcomes in terms of satisfaction, QoL, and depression. By extension, the mismatched patient-physician relationship could have detrimental effects on patient outcomes and lead to dissatisfaction with medical decisions including decision regret.

2.2.2.3. The concept of decision regret

Decision regret is commonly defined as a negative emotion related to the cognitive evaluation of future or past choices (128, 129). Joseph-Williams, N. et al. (130) conducted a systematic review of regret instruments and provided a theoretical model based on the research by Zeelenberg, M. and R. Pieters (131) (Theory of Regret Regulation 1.0) and work by Connolly, T. and J. Reb (129). According to this model, a decision can be conceptualised as either action or inaction, and regret can be either anticipated or experienced after the decision has been made and executed. Experienced regret is further divided into the immediate and delayed regret, depending on the time elapsed since the decision. Finally, the model proposes three types of targets of regret as outlined by Connolly, T. and J. Reb (129): the 'process or role regret' that pertains to the decision process preceding the choice; the 'option regret' pertaining to the alternative chosen; and the 'outcome regret' pertaining to the final result of the decision. Joseph-Williams, N. et al. (130) also acknowledge that while regret is generally considered to be a negative emotion it can also lead to positive outcomes as it can motivate and shape future decisions. This means, for example, that once an individual has experienced decision regret, he or she will learn from the experience and seek to avoid regret the next time he or she is making a decision.

In terms of research referring to treatment decision-making, it has been shown that decision regret concerning treatment is common among cancer patients (129). Hack, T.F. et al. (132) investigated decision-making among breast cancer patients and reported that a significant number of women experienced role regret. Most of these women

would have preferred to have been more involved in their treatment decision-making process (132). Similarly, Clark, J.A. et al. (133) explored decision-making among prostate cancer patients and found that men who expressed more regret regarding the treatment regimen they underwent were less likely to be satisfied with both their role in the decision-making and the outcome of their treatment.

The issue of regret might be particularly salient in the case of young female cancer patients who, by making decisions concerning the type of treatment to undergo, might irrevocably change their future possibility of having a family they may have wanted. The scarce evidence that exists in this area suggests that women may experience regret regarding their treatment choices in the context of maintaining fertility (14) and that counselling or receiving a decision aid specifically targeting fertility treatments can decrease young female cancer patients' decision regret (63).

2.2.3. Cancer and fertility in a broader socio-cultural context

As mentioned in section 2.2, the self-regulatory processes activated in response to an illness are embedded in a broader context and influenced by it (see Figure 2.3). One's socio-cultural background might affect all stages of illness experience – from the formation of cognitive and emotional representations, through the selection and implementation of coping strategies to the appraisal of the effects of actions taken.

2.2.3.1. Cancer representations and culture

So far, scarce evidence exists from the comparative studies on how socio-cultural context influences different stages of the self-regulation process in cancer patients. In two studies, Kaptein et al. (134, 135) analysed illness representations of breast and lung cancer among Dutch and Japanese patients and reported certain differences between the two populations. Among lung cancer patients, the Japanese reported more perceived control over treatment as well as more personal control over illness than the Dutch, indicating their higher sense of belief that medical treatment was going to be helpful in eradicating cancer (134). Differences between Japanese and Dutch breast cancer patients were less pronounced with generally similar illness perceptions and QoL responses between the two groups of patients (135). However, aside from a country level factor, neither of the studies included specific culture-related items to explain those differences and similarities.

2.2.3.2. Culture and family-related norms

Some cultural norms might be more important than others in influencing individual's health-related behaviours. Family-related norms and customs pertaining to domestic life are among the most salient ones as indicated by their stability even in the context of immigration and acculturation processes. Therefore, family building, having children, but also the issue of not having them may have different meanings across societies (136).

It is assumed that fertility depends on individual decision-making where the benefits and costs of having children are weighed against each other. These are influenced by socialisation experience, within the family but also the broader socio-cultural context (137). They differ across countries but also change from generation to generation within the same culture, paralleling socio-cultural transformations.

Originating from those considerations, the concept of the 'value of children' (VOC) first emerged in the work of Hoffman, L.W. and M.L. Hoffman (138). It referred specifically to the role children may have for and the needs they fulfil in their parents' lives. Hoffman, L.W. (139) primarily classified VOC into nine categories which were subsequently narrowed to three major values following the cross-cultural studies of the concept: the utilitarian/economic VOC, the social VOC, and the psychological VOC (140). The empirical studies showed that there existed inter- as well as intra-cultural (urban vs. rural regions) differences in values attached to children, with modern societies attaching more importance to psychological VOC and traditional societies being more inclined towards the economic-utilitarian VOC (141-143).

However, even within the countries with a common European heritage there seems to be differences in the meanings attributed to having children, as well as the levels of acceptance of not having children. In a study by Merz, E.-M. and A.C. Liefbroer (144), the acceptance of not having children appeared to be positively related to the levels of individualism (high in Scandinavian countries and Great Britain compared with Southern and Eastern Europe) and negatively associated with religiousness and traditional orientation. According to Huijts, T. et al. (145) who analysed data from 24 European countries, residents who did not have children in the countries where not having children was socially disapproved had worse psychological well-being than

those living in the countries with less severe opinions on not having children. It has been argued that simply living in a pronatalist society and being aware of rigid social norms concerning family structure, not necessarily accompanied by explicit signs of social disapproval, can lead to self-stigmatisation and distress in infertile people, and particularly women (146, 147).

2.2.3.2.1. Childbearing in Polish and British societies

Childbearing is an important issue valued for different reasons around the world. In 20th century Western Europe a phenomenon known as a 'Second Demographic Transition' (148) took place resulting in decreased fertility rates. It stemmed from a shift of values towards individualism, self-fulfilment, importance of professional career, and also secularisation of societies and liberalisation of norms (see section 1.4).

In Europe, the United Kingdom is perceived to be one of the most individualistic societies (149, 150) with a long tradition of market economy and well-established women's rights which can all influence fertility. Poland, as part of the former Soviet Bloc only underwent an economic and political transition in the early 90s. It resulted in the decrease of fertility rates and also in the increase of the age at which women have their first child. However, the pattern of such changes in Poland does not seem to follow the one in other post-Soviet countries. Thus, the aforementioned transition might not be the only factor influencing childbearing practices and attitudes in Poland.

According to Mynarska, M. (151) 'Polish culture is marked by a strong orientation towards family and children and Catholicism, and its most distinct feature is religious homogeneity' (p. 375). The last census data (152) showed that 87.6% of Poles declared their affiliation to the Roman Catholic Church while in 2011, only 15.9% of Scottish population declared the same, with 53.8% identifying themselves as Christians in general and 36.7% declaring no religious affiliation (153). Similar numbers were recorded in England and Wales where 59.3% of the population identified as Christian and 25.1% declared no religious affiliation (154).

The Catholic Church in Poland has a strong influence on how marriage and family life are perceived, stressing the importance of having children and at the same time condemning contraception, abortion, and the use of ARTs (155). Religion has always

shaped values around fertility either directly or indirectly (156), hence unsurprisingly, there exists a strong social pressure in Poland to have children (151). Moreover, this social control does not cease to influence those young women who emigrate from the country and decide to live in a different society. For example, a recent report about attitudes towards fertility and motherhood among non-Irish national minority ethnic women living in Ireland suggests that while Polish women live in what they perceive a liberal Irish culture, they keep feeling pressured to have children by the more traditional family-related values internalised from the Polish culture (157).

2.3. The application of the CSM and Shared Decision Making model to cancer and fertility issues

Thus far this chapter has discussed theoretical models pertaining to (1) the way individuals conceptualise illness; and (2) the way medical decisions are made within the clinical setting. Two of the presented models – the CSM and the Shared Decision Making model were adopted for the purpose of this study in the following manner:

(1) The CSM was used as an overreaching theoretical framework to guide and analyse both the quantitative and the qualitative data. It served to explore the nature of women's breast or gynaecological cancer experience as well as the fertility issues within.
(2) The Shared Decision Making model was used within the CSM to structure and analyse the data pertaining specifically to the decision-making processes obtained through the qualitative part of the project.

The research questions for the quantitative study were partially designed based on the CSM. Fear of cancer recurrence as well as distress related to fertility issues were conceptualised as emotional responses to illness. I tested the association between these emotional responses to illness and illness perceptions. I also investigated how these emotional responses to illness were related to QoL. This part of the project was conducted in two populations (Polish and British) to study whether any cross-cultural differences in terms of cancer or fertility issues experiences existed. This is particularly important given the cultural and religious differences between the two populations and the fact that the Polish ethnic group has grown to become one of the largest minorities in the UK (158). I addressed the shortcomings of the previous studies by using a

separate scale referring specifically to the value different cultures attach to having children (139).

The qualitative study, more exploratory in nature, used the Common Sense as well as the Shared Decision Making models to explain cancer treatment-related decision-making in the context of maintaining fertility among young women. Although the codes and initial themes in the qualitative analysis were derived inductively, the two models were applied as a framework to organise the findings. Since I was interested particularly in how women made their treatment decisions in the context of maintaining fertility the data pertaining specifically to the decision-making process were analysed in light of the Shared Decision Making model. However, other relevant information regarding the first suspicion of disease, circumstances of diagnosis, treatment, and survivorship issues were also gathered throughout the interviews. These topics and how they related to treatment decision-making were explained using the CSM. The details of how the two models were applied are presented in detail in section 4.3.2.

Chapter 3 Fertility issues in young female cancer patients – a systematic review of quantitative and qualitative evidence

This chapter discusses the systematic review of both quantitative and qualitative literature that was conducted as part of this PhD project. It first describes a published review of fertility and parenthood issues among young women diagnosed with cancer (63) providing the basis for the review which is the focus of this chapter (section 3.1). Second, the objectives of the review are presented (section 3.1.1). The methodology of the review is then described, detailing the search strategy (section 3.2.1), inclusion and exclusion criteria (sections 3.2.2 and 3.2.3), study selection (section 3.2.4), data management (section 3.2.5), data extraction (section 3.2.6), analysis (section 3.2.7), and quality assessment (section 3.2.8). The results of the review (section 3.3) are presented in a manner that reflects the review objectives and where both qualitative and quantitative studies were included, these are summarised separately for the reasons described in the appropriate sections (3.3.2 and 3.3.3). The findings of the review are discussed within the broader context of psychooncology literature and drawing on the theoretical frameworks discussed in Chapter 2 (section 3.4.1). Finally, the limitations of the review are presented (section 3.4.2) with potential bias introduced into the metasynthesis discussed in the reflexivity statement (section 3.4.3), and the rationale for conducting additional research in the field of oncofertility is provided (section 3.4.4).

3.1. Introduction

Recent years have witnessed the emergence and adoption of evidence-based practice (EBP) across many healthcare disciplines including medicine (159, 160) and psychology (161). EBP involves using both clinical expertise and the best existing clinical evidence to make high quality decisions regarding patient care (160). The latter can be obtained by reviewing the literature and synthesising it to inform practice but also guide future research as it identifies gaps in the existing body of research.

Several reviews addressing different aspects of oncofertility have been published to date (4, 13, 14, 56, 162, 163). They investigate female cancer patients knowledge (13), information needs (4, 14), and preferences regarding discussions about fertility (13). They contribute to our understanding of the meaning of fertility to women with cancer (163) and how it changes over time (162). While they undeniably provide practitioners

and researchers with valuable information, the majority only concentrate on patients diagnosed with breast cancer (14, 56, 162, 163). Although malignancy of the breast constitutes the most frequent cancer diagnosis among reproductive age women, other cancers diagnosed in this group can equally impair women's fertility. It would therefore be beneficial to synthesise the evidence available for those other cancer diagnoses. Also, while some of these reviews do mention the impact of fertility issues related to cancer treatment on psychosocial outcomes (56, 162), they do not focus specifically on the topic. Finally, the only review that investigates women's reproductive decisions (163), while including exclusively breast cancer patients also concentrates primarily on decisions related to pregnancy after cancer, without examining other important decisions which could affect women's reproductive potential (e.g., FP or decisions about fertility-sparing or compromising cancer treatments).

To address these gaps and define research questions for this PhD project, we have conducted a systematic review of quantitative literature investigating fertility and parenthood issues among women diagnosed with various types of cancer during their reproductive years (63). This review focused, on the one hand, on the relationship between women's fertility issues and their psychological well-being in survivorship and, on the other, on the impact of fertility issues on women's reproductive decisions understood as both decisions about pregnancy and decisions about treatments which could impact on fertility (including FP). The findings of this review suggest that the way fertility issues were defined for the purpose of the included studies was important. In other words, the review shows that subjective experience of reproductive issues was associated with young women's well-being while the objective fertility status was not. Furthermore, the findings indicate that cancer can have mixed effects on women's reproductive decisions (understood both as FP and pregnancy decisions post-cancer), and that fertility decisions specifically could be facilitated by providing women with adequate information and decision aids (for full review see Appendix 1). Based on the review findings, the initial aims for this PhD research project were established. This review also provided basis for the new review which is the focus of this chapter. The aim of this new review was to better reflect the final questions addressed by this PhD project (see section 1.8.1) and provide the synthesis of the most relevant and up-to-date literature in the field.

The new review used the search strategy employed in the published review (referred to as Search 1) to address objectives 1 & 2 (see section 3.1.1). An additional search (referred to as Search 2) was conducted to address objective 3 (see section 3.1.1). This review also combined the synthesis of both quantitative and qualitative research concentrating on various aspects of fertility issues in young women diagnosed with cancer during their reproductive years.

While systematic reviewing of quantitative evidence has been used to inform evidence-based practice and research for a long time, the importance of incorporating qualitative literature into the process has only been recognised fairly recently (164). Qualitative synthesis can provide insight into human behaviours, emotions, and experiences beyond what a systematic review of quantitative literature could ever achieve (165). Its advantages lie in the ability to elucidate the results of quantitative systematic reviews and develop models that could explain the results of multiple similar qualitative studies (166). For these reasons this review incorporates both quantitative and qualitative literature to address the following objectives.

3.1.1. Objectives of the review

1. To identify factors associated with fertility issues in women diagnosed with cancer during their reproductive years;
2. To characterise the relationship between fertility issues and psychological well-being of reproductive-age women diagnosed with cancer;
3. To explore how women diagnosed with cancer during their reproductive years make treatment-related decisions that can affect their reproductive potential and outcomes in the future.

For the purpose of this review, fertility issues were conceptualised as subjective experience of reproductive potential. This is following the findings of the pulished review (63) which suggested that psychological well-being seemed to be associated with the psychological experience of fertility potential rather than the objective fertility status conceptualised as receiving particular type of treatment (e.g., fertility sparing vs. radical treatment) or experiencing prolonged amenorrhea following cancer therapy. Therefore, when referring to fertility issues in Objectives 1 & 2 of this review, the focus is on self-assessed problems with conceiving (e.g., not being able to complete one's

family or have a desired number of children; self-assessed infertility), distress related to impaired fertility, or reproductive concerns as commonly measured by Reproductive Concerns Scale (RCS) (167).

It is also perhaps important to specify FP options which are available to women in the context of cancer treatment since these are widely referred to when addressing Objective 3. De Vos, M. et al. (168) divide FP strategies into two groups – the established, and the experimental methods. The former include oocyte and embryo cryopreservation as well as ovarian transposition (for women scheduled for pelvic irradiation) (168). NICE guidelines suggest offering embryo or oocyte cryopreservation to female cancer patients who are well enough to undergo the necessary FP procedures, whose condition would not deteriorate due to these procedures, and for whom there is enough time to undergo FP (17). Although its effectiveness has not been supported by clinical data (169) and hence is not supported by the guidelines, ovarian suppression using gonadotropin-releasing hormone analogues can be used in women planned for chemotherapy. This method is supposed to limit ovarian damage by chemotherapeutic agents through inducing prepubescent stage in the ovaries (170). Experimental methods outlined by De Vos, M. et al. (168) include ovarian tissue cryopreservation and its transplantation, or in-vitro growth and maturation of oocytes for future fertilisation. While these strategies can be used across a range of cancer diagnoses, there exist cancer-specific options such as radial trachelectomy in case of early stage cervical cancer (171), hormonal treatments for early stage endometrial cancer (172), or unilateral salpingo-oophorectomy for ovarian malignancies (173, 174).

3.2. Materials and methods

3.2.1. Search strategy

Two literature searches performed by one researcher (AS) were conducted to complete this literature review. Search 1 was performed using the keywords presented in Table 3.1 and covered the literature published before November 2014.

Table 3.1. Keywords for Search 1

Column 1	Column 2	Column 3	Column 4
'woman'	'cancer OR tumor OR neoplasm OR malignancy'	'fertility OR sterility OR reproduction OR childbearing OR pregnancy'	'psychology OR distress OR depression OR anxiety OR fear OR PTSD OR quality of life OR self-esteem OR sexual OR recurrence OR reproductive decision OR decision making OR intervention OR counseling OR communication'

Search 2 was an additional search run to cover the literature focusing on tamoxifen-related decision-making (objective 3). Keywords presented in Table 3.2 were used and the search covered articles published up to January 2015.

Table 3.2. Keywords for Search 2

Column 1	Column 2	Column 3	Column 4
'wom*n' OR 'female'	breast cancer	'tamoxifen' OR 'endocrine' OR 'hormonal'	'treatment adherence' OR 'treatment compliance' OR 'treatment discontinuation'

Both searches were performed using the following medical and social sciences search engines: NCBI (PubMed), OVID (Medline and Embase), Web of Science (Science Citation Index Expanded, Social Sciences Citation Index, Art & Humanities Citation Index, Conference Proceedings Citation Index – Science and Conference Proceedings Citation Index – Social Sciences & Humanities), Cochrane Central Register (Cochrane systematic reviews, Cochrane controlled trials and Cochrane methodological register) and PROQUEST (PsycArticles and Applied Social Sciences Index & Abstracts) or EBSCO (PsycArticles, PsycInfo and Psychology and behavioural sciences collection).

3.2.2. Inclusion criteria

3.2.2.1. Population

Studies were included in the review as long as they met the following criteria:

- The study sample consisted, in total or in part, of women who were diagnosed with cancer (excluding childhood cancers and cancer co-occurring with pregnancy) during their reproductive years. Being of reproductive age was characterised as (1) being between 14 and 50 years of age at the time of diagnosis or (2) being pre-menopausal at the time of diagnosis. The age range for reproductive age was defined based on the average age of menarche and menopause worldwide (175).
- Where the study sample consisted of women of all ages, results for the target age group were presented separately.
- Where the study sample consisted of both men and women, results for women from the target age group were presented separately.
- Where the study sample consisted of women with various cancer diagnoses including childhood cancers and cancer co-occurring with pregnancy, results for the target diagnoses group were presented separately.

3.2.2.2. Outcomes

For objective 1: determinants of the psychological experience of fertility issues

For objective 2: QoL; relationship functioning or dating experience; sexual functioning; depression; anxiety; fear of recurrence.

For objective 3: decisions about initial potentially fertility reducing treatments (e.g., surgery; chemotherapy; full body irradiation; bone marrow transplant); decisions about endocrine therapy (tamoxifen for breast cancer); decisions about FP (e.g., egg or embryo cryopreservation; ovarian tissue cryopreservation; the use of gonadotropin-releasing hormone agonists).

3.2.2.3. Study design

Controlled trials, experimental, quasi-experimental and observational studies (cohort and case control studies) as well as qualitative studies were included in the review.

3.2.3. Exclusion criteria

Studies were excluded from the review for the following reasons:

- Where combined results were presented for women of all ages.

- Where combined results were presented for both genders.
- Where results for women diagnosed with childhood cancers and/or cancer co-occurring with pregnancy were presented together with results for women with other cancer diagnoses.
- The publication was not an original study (e.g., book chapter, review, editorial, commentary, letter, guidelines).
- The article was published before 1990[2].
- For objectives 1 and 2: Where fertility issues were conceptualised only in objective terms such as type of treatment received (e.g., fertility sparing vs. radical gynaecological surgery, chemotherapy, radiotherapy to the pelvic area, full body irradiation or bone marrow transplant); occurrence of amenorrhea post-treatment; symptoms or hormonal indicators of menopause.

3.2.4. Study selection

The study selection process was conducted by one reviewer (AS). The selection processes were performed separately for searches 1 and 2, however, the same protocol was followed for both screening processes. At first, duplicates were removed and then the titles were screened for potential relevance. Where the title seemed relevant to one of the review objectives, the abstract was evaluated. Based on abstract relevance, full-text copies of the articles were obtained and these were assessed against the inclusion criteria for the review. Details of the screening processes for searches 1 and 2 are presented below.

3.2.4.1. Search 1

A total number of 10343 publications were identified through the databases searches. After automatic and manual removal of duplicates this number decreased to 8343. Titles of those articles were visually screened and 827 publications were retained and their abstracts were assessed. One hundred and twenty abstracts were selected as potentially relevant and the full-text copies of these articles were obtained and evaluated against the predefined eligibility criteria. Fifty-three articles met all the inclusion criteria. A further seven articles which narrowly missed one of the predefined criteria (age range or

[2] Year 1990 was chosen as a cut-off because of considerable advances in medical technology and the emergence of new procedures allowing for fertility sparing and preservation for female cancer patients (171).

diagnosis criterion), were also included (see Flowchart in Appendix 2) as excluding them could have potentially biased the results of the review. Two studies by Gorman et al. (177, 178) included women diagnosed below the age of 14 (defined by the authors as childhood cancers) and these participants constituted 23% and 10% of the study samples, respectively. The age range at diagnosis criterion was not met by four other studies: Perz, J. et al. (179) presented data from an open-ended question referring to the way in which cancer affected participants' fertility. They reported the average age of their participants to be 54.1, however, their results are supported by quotes from participants who were mostly within the acceptable age range (the oldest quoted participant being 53). Ferrell, B. et al. (180) who analysed the content of correspondence between ovarian cancer patients and *Conversations!: The International Newsletter for Those Fighting Ovarian Cancer* did not provide the age range of their participants, however, fertility concerns were mentioned spontaneously by participants. Therefore the assumption was made that these patients were of reproductive age. Based on a similar assumption, two other studies (181, 182) were retained for synthesis. Participants in the study by Molassiotis, A. et al. (181) were aged 21 to 64 at diagnosis, yet fertility issues emerged as one of the themes in the study. While Reis, N. et al. (182) did not provide an exact age range of their participants, the qualitative data about fertility issues analysed in this review came from a sample of 30 women 53.3% of which were younger than 50. Finally, Bastings, L. et al. (183) who explored FP decisions among women who required gonadotoxic treatment included in their analysis one woman with a benign condition (1.5% of the total sample size).

3.2.4.2. Search 2

This search has yielded 2422 articles. Automatic and manual de-duplication process reduced this number to 1945. Titles of those publications were screened and 176 were selected as potentially relevant. Abstracts for those articles were evaluated and 56 were deemed relevant to the review objectives. The full-text copies of these articles were assessed against the inclusion criteria and while five of them met all the criteria, one missed the age criterion, however, the decision was made to include all of them in the review (see Flowchart in Appendix 3). The study that missed the age criterion was by Bell, R.J. et al. (184) which included participants 58 years old on average, yet it

specifically refers to pregnancy as one of the factors to discontinue tamoxifen suggesting that these participants were of reproductive age.

In total, 67 papers describing 60 separate studies were included in the review (studies by Letourneau, J.M. et al. (185) and Letourneau, J.M. et al. (186); Hershberger, P.E. et al. (187) and Hershberger, P.E. et al. (188); Corney, R. et al. (189) and Corney, R.H. and A.J. Swinglehurst (190); Halliday, L.E. et al. (191) and Halliday, L.E. et al. (192); Kirkman, M. et al. (193) and Kirkman, M. et al. (194); Cluze, C. et al. (195) and Huiart, L. et al. (196); Carter, J. et al. (197) and Carter, J. et al. (198) referred to the same respective datasets). Of the included 67 articles, 32 used quantitative methodology, 30 were qualitative and five being predominantly quantitative, combined both methodologies.

3.2.5. Data management

QSR International's NVivo 10 software (199) was used as data management software and relevant articles were uploaded to objective-specific files. Articles within a file were categorised into qualitative or quantitative (based on the type of data presented in the article relevant to the given objective) and then relevant data were highlighted and coded into *Relevant data* node. For qualitative studies the result sections of the articles were treated as data.

3.2.6. Data extraction

One reviewer (AS) extracted the following data from each included article: authors, date, location of study, study sample (including cancer type, age at diagnosis, sample size), study design, definitions of fertility, outcomes (constructs and measures), and results for outcomes of interest. These along with the quality scores (see section 3.2.8) are summarised in a tabular format (see tables in Appendices 5, 6, and 7) to facilitate access to the relevant study information.

3.2.7. Analysis

The process of data analysis was completed by one reviewer (AS). Quantitative studies were analysed using narrative synthesis technique. Narrative synthesis is an approach used in systematic reviews and is based on words and text to summarise and explain the results of the included studies (200). Although it might be seen as 'second best' to meta-analysis, the 'Guidance on the Conduct of Narrative Synthesis in Systematic Reviews'

(200) suggests it is used as a first step in every systematic review to enable authors to decide whether any other methods of evidence synthesis might be suitable for their data. The meta-analytic approach was not deemed appropriate for this review due to the heterogeneity of study designs and outcome measures.

Thematic synthesis proposed by Thomas, J. and A. Harden (201) was used to analyse qualitative data. This method was employed for two reasons. First, it has already been applied to qualitative literature in the domain of healthcare research (202-205). Second, thematic synthesis is similar to the method I chose to adopt when handling the original qualitative data collected for the purpose of this PhD project, namely the thematic analysis. Using thematic synthesis in combination with the thematic analysis across this project assures the comparability of the findings of the literature review and those of the original qualitative study.

Following the method of thematic synthesis as outlined by Thomas, J. and A. Harden (201), in the first stage textual data from the result sections of the included articles were coded inductively and sets of codes were obtained (28 codes for objective 2 and 67 codes for objective 3). The next step involved organising codes into descriptive themes (seven for objective 2 and nine for objective 3). Finally, analytical themes were generated based on the descriptive themes and pertaining specifically to objective 2 (three analytical themes) and objective 3 (four analytical themes).

3.2.8. Quality assessment

The quality of the included papers was formally assessed by one reviewer (AS) using 'QualSyst' (206). 'QualSyst' consists of two separate checklists for the evaluation of quantitative and qualitative studies. An example of the completed instrument for one quantitative and one qualitative paper is provided in Appendix 4. While multiple quality assessment tools exist (e.g., CONSORT for randomised trials, STROBE for observational studies, and COREQ for qualitative studies) the 'QualSyst' was chosen for two reasons. First, the checklist devised to evaluate quantitative studies is easily adaptable to various study designs and therefore allows for direct comparisons of the quality of quantitative studies differing in terms of design. Second, while a separate checklist is provided for the assessment of the quality of qualitative studies, the end product of both instruments is a number ranging from 0 to 100% and representing the

quality of a particular study. The uniformity of the final output of both checklists is useful when synthesisisng quantitative and qualitative literature as it makes comparisons between different types of studies possible. It is, however, important to acknowledge the criticism of quality assessment tools using summary scores in that the final obtained number might provide a biased representation of study quality if interpreted outwith the context of the checklist items (207). This is why, although scores were calculated for all the papers included in this review and these are provided in the summary tables (see Appendices 5, 6, and 7), the quality criteria most frequently missed by the included studies were also investigated and are summarised in section 3.4.2.

3.3. Results

The articles included in this review were in the first instance classified according to the objective they were relevant to and further according to the factors associated with the outcome of interest (objective 1) or the outcome they described (objectives 2 and 3). Where appropriate, quantitative and qualitative studies were analysed and summarised separately.

3.3.1. Objective 1: To identify factors associated with fertility issues in women diagnosed with cancer during their reproductive years.

Four studies meeting all the inclusion criteria (208-211) and one study narrowly missing the age criterion (178) investigated factors associated with the psychological experience of fertility issues in young women diagnosed with cancer. All these studies used quantitative methodology. Two of them (208, 209) operationalised fertility issues using the RCS (167) whereas others used alternatives such as a single Likert scale based question about fertility concerns (211), the Impact of Event Scale (IES) adapted to post-cancer infertility (208), the Reproductive Concerns After Cancer (RCAC) scale (178), or did not specify how fertility concerns were measured (210).

The process of identifying factors associated with the psychological experience of fertility issues was driven by the literature. In other words, factors related to fertility issues were highlighted while reading the articles and compared across the studies. Identical or similar factors investigated by the included studies were then grouped into the following categories: socio-demographic characteristics, childbearing/parenthood status, desire to have children, and medical factors. Their associations with fertility

issues are described respectively (for details of included studies and factors significantly associated with fertility concerns, see Table in Appendix 5). Studies investigating psychological factors were excluded under this objective and are presented under Objective 2, which specifically explores the relationship between fertility concerns and psychological well-being.

3.3.1.1. Socio-demographic characteristics

All of the included studies investigated the associations between socio-demographic factors and fertility issues to some extent. Partridge, A.H. et al. (210) who explored fertility concerns in a group of breast cancer survivors <40 years old at diagnosis found that being younger, having higher education level, being unmarried, and being employed full-time were positively related to fertility concerns in univariate analyses. These, however, were not significant in multivariate analysis. Other factors they tested for but found non-significant were race and financial comfort (210).

In a study by Ruddy, K.J. et al. (211) concentrating again on young breast cancer patients being <35 years old at diagnosis, non-white race, and being unmarried were significantly associated with more fertility concerns in univariate analyses and the former two factors retained their significance in multivariate analysis. Similar to the study by Partridge, A.H. et al. (210) described above, Ruddy, K.J. et al. (211) found no association between financial status and fertility concerns. They also concluded that education level and employment status were not related to fertility concerns (211).

In a study conducted among a group of young women with mixed cancer diagnoses (178), there were no significant differences in RCAC total scores between groups based on age (18-29 vs. 30-35), race (white vs. non-white), Hispanic ethnicity (yes vs. no), or employment status (full time vs. part time vs. student vs. other). However, unpartnered women had significantly higher RCAC scores than partnered women (3.38 vs. 3.17, $p < 0.05$) and women with high school education had higher scores than women with college or graduate education (3.42 vs. 3.18, $p < 0.05$). An earlier study by Gorman, J.R. et al. (209), which focused on young women with breast cancer, found that being younger than 35 was not significantly related to the RCS scores. Finally, according to Canada, A.L. and L.R. Schover (208) who investigated fertility issues in young women

with mixed cancer diagnoses, younger age, lower income, and better education level accounted for some of the variance in the scores of both IES and RCS scales.

3.3.1.2. Childbearing/parenthood status

Two studies (209, 211) investigated whether having children prior to cancer diagnosis was associated with fertility concerns, whereas the study by Canada, A.L. and L.R. Schover (208) explored how different types of parenting (biological and social[3]) or not having children were related to fertility concerns. Gorman, J.R. et al. (209) found that not having children at the time of diagnosis as well as not having them at all (prior to or after cancer) were both significantly associated with higher RCS scores. In a study by Ruddy, K.J. et al. (211), childbearing status was significantly related to fertility concerns in both univariate and multivariate analyses with women who had children being less likely to experience fertility concerns. Canada, A.L. and L.R. Schover (208) compared RCS and IES scores between groups of women who were raising biological children only, combined biological and social children, social children only, or did not have children. They suggested that there were significant differences between these groups in terms of IES and RCS scores with women who only had biological children scoring consistently lower on both scales, followed by women with biological and social children, those who had social children only, and finally women who did not have children. The latter scored highest on both scales indicating that they experienced the most reproductive concerns and distress related to infertility (208).

3.3.1.3. Desire to have children

Four studies (178, 208, 209, 211) examined the role that the desire to have children played in relation to fertility concerns. Gorman, J.R. et al. (209) reported that a more pronounced desire to have children both before and after breast cancer diagnosis was associated with higher RCS scores. Similarly, in another group of breast cancer survivors, a wish to have (more) children was significantly associated with fertility concerns in both univariate and multivariate analyses with women desiring to have more children being also more concerned about their fertility (210). Another study by Gorman, J.R. et al. (178) suggests that total RCAC scores were significantly higher for women who wanted a baby compared to those who did not (3.34 vs. 2.99, $p < 0.01$) and

[3] Social parenthood was defined by Canada, A.L. and L. R. Schover (208) as 'raising a stepchild, adopted child, informally adopted child, or child conceived with donor oocytes' (p. 139).

also for women who considered a biological child to be very important compared to those who were not as concerned about the biological link to the child (3.37 vs. 3.13, $p < 0.05$). Finally, Canada, A.L. and L.R. Schover (208) compared RCS and IES subscales (Intrusion and Avoidance) and total scores related to post-cancer infertility between two groups of women: those who had biological children if desired and those who had an unfulfilled desire for a biological child at cancer diagnosis. Women with an unfulfilled desire for a child scored consistently higher on all the scales which indicated higher reproductive concerns as well as distress related to cancer's impact on being able to conceive and carry a pregnancy to term. They also showed that even after taking socio-demographic and treatment-related factors into account, an unfulfilled desire for a child still accounted for significant variation in the IES and RCS scores (208).

3.3.1.4. Medical factors

All included studies investigated the association among various medical factors and fertility concerns. These medical factors were grouped as follows: general, gynaecological and obstetric history, cancer characteristics, and cancer treatment characteristics and are discussed separately.

3.3.1.4.1. General

Alcohol or tobacco use, family history of breast or ovarian cancer, and additional comorbid conditions all proved to be non-significant in both univariate and multivariate analyses in a study by Ruddy, K.J. et al. (211). Similarly, Partridge, A.H. et al. (210) did not find any significant relationship between having additional comorbidities, or family history of breast or ovarian cancer and fertility concerns in univariate analysis. Having a first degree relative with any type of cancer was associated with more fertility concerns in univariate analysis, however, was not significant in multivariate analysis (210).

3.3.1.4.2. Gynaecological and obstetric history

Partridge, A.H. et al. (210) examined a large set of variables related to reproductive history and found that several variables were significantly associated with more fertility concerns in univariate analyses. These included a regular menstruation pattern at diagnosis, smaller number of pregnancies before cancer diagnosis, fewer prior live births, previous experience of difficulty conceiving, and no history of: having tried to become pregnant before diagnosis, miscarriages, tubal ligation, or infertility treatment.

At the same time, prior abortions, pregnancies resulting in stillbirth, history of unilateral oophorectomy, and prior infertility evaluation were not related to fertility issues (210). Of all these factors, the number of pregnancies before diagnosis (OR, 0.78; $p = 0.01$) and history of prior difficulty conceiving (OR, 1.86; $p = 0.08$ for yes and OR, 3.15; $p = 0.0001$ for not applicable if women had never tried to conceive) remained significant in multivariate analysis indicating that women who had more pregnancies prior to cancer diagnosis and who had no difficulty becoming pregnant were less concerned about their fertility (210). According to Ruddy, K.J. et al. (211), being pregnant at diagnosis, no history of pregnancy, history of miscarriage and history of fertility treatments were all associated with more fertility concerns in univariate analyses whereas being pregnant at the time of the study, history of abortion, and history of difficulty conceiving were not. Nonetheless, none of these factors were related to fertility concerns in multivariate analyses. In the study by Gorman, J.R. et al. (178), there were no differences in total RCAC scale score between women who experienced a previous live birth and those who did not; women who had normal menstruation subsequently to cancer and those who did not, and women who had history of infertility and those who did not. Only having experienced a miscarriage was associated with scoring higher on RCAC scale (3.67 vs. 3.22 for women who have not experienced miscarriage; $p < 0.01$). In another study by Gorman, J.R. et al. (209), irregular periods during or after cancer treatment were not related to the score on the RCS. Yet, according to Canada, A.L. and L.R. Schover (208) experiencing menopausal symptoms accounted for some of the variance in the scores of both RCS and IES.

3.3.1.4.3. Cancer characteristics

Cancer stage was not significantly associated with fertility concerns in two studies (210, 211) and neither were time since diagnosis (210) or grade and hormone receptor or HER2 status (211). Cancer recurrence and second primary cancer explained some of the variance in RCS and IES scores as suggested by Canada, A.L. and L.R. Schover (208).

3.3.1.4.4. Cancer treatment characteristics

While having received breast conserving surgery was associated with more fertility concerns in univariate analysis in one study (210), another study (211) suggested that having undergone a mastectomy was related to more fertility issues. Both of these

factors were not significant in respective multivariate analyses. Receiving endocrine therapy post-cancer was not associated with fertility concerns in univariate analysis yet having been treated with chemotherapy was significant in both univariate and multivariate analyses (OR, 1.61; 95% CI 1.04,2.5; $p = 0.03$) indicating that women who received chemotherapy were more concerned about their fertility (211). Chemotherapy, along with surgery and radiotherapy explained some of the variance in Canada, A.L. and L.R. Schover (208)'s models predicting RCS and IES scores. Finally, as suggested by Gorman, J.R. et al. (209), treatment that resulted in ovarian damage and the decision to undergo treatment based on FP were associated with higher RCS scores.

3.3.2. Objective 2: To characterise the relationship between fertility issues and psychological well-being of reproductive-age women diagnosed with cancer

Twenty-three original studies meeting all the criteria and five studies narrowly missing one of the criteria explored the relationship between fertility issues and psychological well-being of reproductive age women diagnosed with cancer (for details of included studies see Table in Appendix 6). The studies that missed one of the criteria and specifically the criterion missed were discussed in section 3.2.4.1. Quantitative data from eight studies and qualitative data from 20 studies are synthesised for the purpose of this review.

Quantitative and qualitative studies are summarised separately. This is because forcing qualitative findings into categories used for quantitative findings would mean losing some of the finer details provided by the thematic synthesis. Therefore, the results of quantitative studies are categorised based on the outcome they described (QoL, relationship functioning/dating experience, anxiety, depression, and fear of recurrence, or sexual functioning) whereas the summary of qualitative studies is presented based on themes which were identified in the process of synthesis.

3.3.2.1. Quantitative findings

3.3.2.1.1. QoL

Three studies explored the relationship between fertility issues and QoL. Two of these studies used the Medical Outcomes Scale SF-36 (212, 213) and one study used the Medical Outcomes Scale SF-12 (208) to measure QoL. Medical Outcomes Scale SF-12

is a short version of Medical Outcomes Scale SF-36 and both can be summarised into two component summary scores representing mental (MCS) and physical (PCS) health. One study additionally used a cancer-specific QoL questionnaire – QoL-CS (214).

Wenzel, L. et al. (213) investigated QoL among cervical cancer patients and found that better MCS scores were significantly related to fewer reproductive concerns as measured by RCS. They also showed that less reproductive concerns were significantly associated with better survivor-specific QoL as measured by QoL-CS (213). In a study by Mancini, J. et al. (212) which concentrated on young patients with various cancer diagnoses, those who considered themselves infertile scored significantly lower on both MCS and PCS subscales as compared to those who did not report infertility. Canada, A.L. and L.R. Schover (208) also focused on young women with various cancer diagnoses and found that women who could not fulfil their desire to have children had lower MCS scores than women who were able to have desired children. Contrary to the study by Mancini, J. et al. (212) however, they have not shown differences in PCS scores between the two groups of patients.

3.3.2.1.2. Relationship functioning/dating experience

Two studies explored relationship functioning (208, 212) and one also investigated dating experience among young female cancer survivors (208). Neither Canada, A.L. and L.R. Schover (208)'s study which used the A-DAS (215) nor Mancini, J. et al. (212)'s study which assessed relationship functioning using a single question found the association between the quality of close relationship and self-evaluated fertility significant. Dating experiences as measured by the dating subscale of the CARES (216) were also not significantly different between participants who had desired biological children and those who were not able to fulfil this wish (208).

3.3.2.1.3. Sexual functioning

Four studies investigated the relationship between fertility issues and sexual functioning. Two of them used the FSFI (208, 217), one study used two measures – the GCP as well as the SAQ (213) and lastly, in one study, sexual functioning was assessed using a single question (212). The study by Canada, A.L. and L.R. Schover (208) suggested that women who were not able to have desired children post-cancer scored significantly lower on FSFI than women who were able to have children if they wished

so. That same study also showed that women who self-identified as infertile were less sexually satisfied than those who did not. Similarly, Mancini, J. et al. (212) reported that women who viewed themselves as infertile were more likely to state that their disease impacted negatively on their sexual life than those who perceived themselves as fertile. Wenzel, L. et al. (213) who used two different instruments to evaluate sexual functioning suggested that more reproductive concerns were associated with greater gynaecological pain as measured by GCP and poorer sexual functioning as measured by SAQ. Finally, in the study by Eeltink, C.M. et al. (217), the relationship between self-assessed fertility and sexual functioning (FSFI) only approached significance ($p = 0.07$).

3.3.2.1.4. Anxiety, depression, and fear of recurrence

Four studies (209-211, 218) examined the association between fertility concerns and anxiety, depression, or fear of cancer recurrence. Two of them measured anxiety and depression using HADS (210, 211), and neither found an association between depression or anxiety and reproductive concerns. Brånvall, E. et al. (218) investigated fertility issues in long term survivors of acute myeloid leukaemia and found that the psychological well-being of women who unsuccessfully tried for children after diagnosis was not overall impaired. However, they scored higher on anxiety and depression (as measured by one Likert-type question with a scale from 1 = never to 7 = all the time) compared to other women in the study (2.75 vs 2). Gorman, J.R. et al. (209) used the Centre for Epidemiologic Studies-Depression scale and reported that more reproductive concerns were associated with more depressive symptoms in a group of young breast cancer survivors, however, the strength of this relationship was not reported. Finally, the study by Partridge, A.H. et al. (210) was the only one to explore the relationship between reproductive concerns and fear of cancer recurrence (measurement not specified). Less fear of recurrence was significantly associated with more fertility concerns among breast cancer survivors in univariate analysis, however, it was non-significant in multivariate analysis (210).

3.3.2.2. Qualitative findings

Thematic synthesis (201) of the 20 qualitative studies provided three broad themes summarising the relationship between fertility issues and psychological well-being among young women diagnosed with cancer. These themes include:

1. Consequences of cancer-related fertility issues
2. Being different/Comparisons with other women
3. Identity as a social construct (see Figure 3.1).

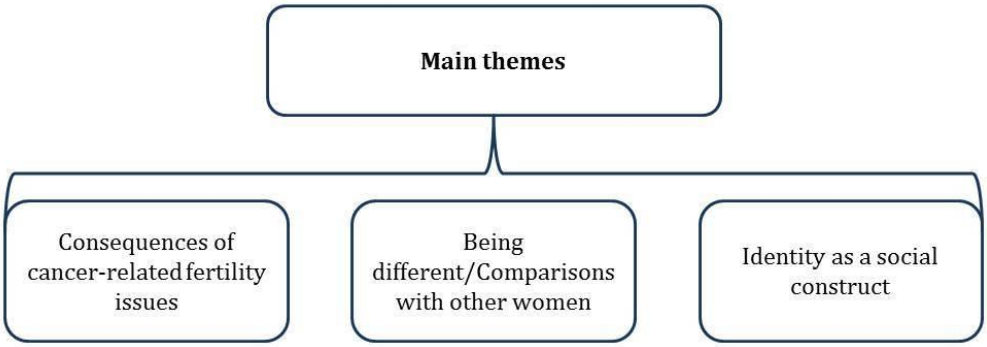


Figure 3.1. Visual representation of the main themes identified within the qualitative literature addressing objective 2 of the review

While the first theme is a more descriptive one and outlines the emotional and relationship-related consequences of fertility issues resulting from cancer treatment, the latter two try to explore and explain the reasons behind those consequences. Some of the studies included in the review concentrated mostly on describing psychological repercussions of infertility related to cancer and therefore, it seemed important to gather the evidence from those various sources and summarise it first. However, the purpose behind thematic synthesis is to add to the body of literature by going beyond the content of the original studies (201). I attempted to do this by developing the themes that not only list the emotional consequences of cancer-related infertility but also try to explain why these emotions occur using a broader social context in which they develop.

3.3.2.2.1. Consequences of cancer-related fertility issues

The following four subthemes were identified within this broader theme: *Cancer and infertility – adding insult to injury; Grieving the loss of fertility; Challenge to relationships;* and '*It is not all bad'* (see Figure 3.2).

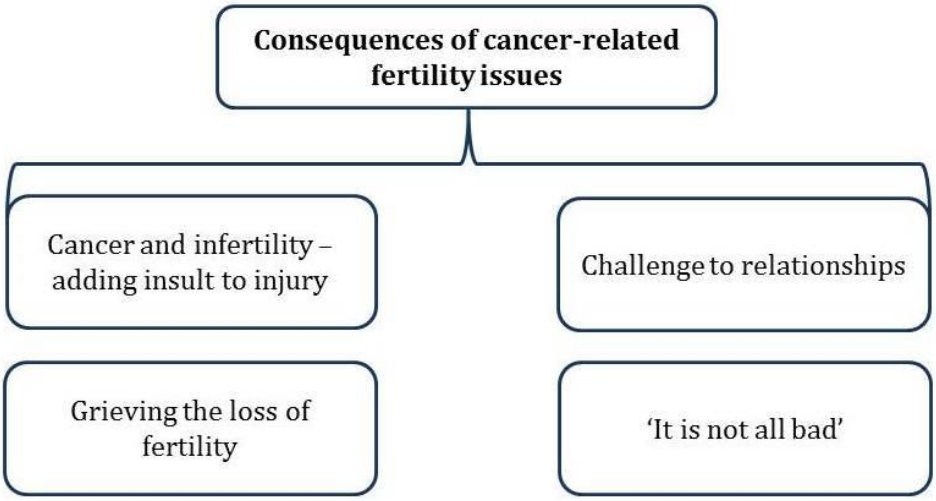


Figure 3.2. Visual representation of the subthemes identified within the theme *Consequences of cancer related fertility issues*

3.3.2.2.1.1. Cancer and infertility – adding insult to injury

Women admitted that cancer was a frightening diagnosis yet perceived it as something that could be dealt with thanks to a wide range of available treatments (188). It transpired from women's accounts that cancer was a 'bump in the road' (188, p. 63), and although a difficult experience, one that could eventually become just a memory, if not for the loss of fertility (219). Women often put their experience of being diagnosed with cancer in the context of fertility loss resulting from various treatments they received (179, 180, 188, 219-224). Losing one's fertility to cancer was hard to accept because contrary to a cancer diagnosis, not being able to have children was likely to affect women for the rest of their lives (188, 219). As one of the participants in a study by Gorman, J.R. et al. (219) succinctly said: *'That was way bigger a blow than "you have breast cancer" because the breast cancer you treat and it's over with. And, but the fertility issue stays with you for life… it changes the whole course of your life.'* (p. 38).

Women described the situation where choice about having children was taken away from them by cancer as particularly upsetting. One of the participants in the study by Perz, J. et al. (179) reflected on it saying: *'I ended up having a hysterectomy and all that just as a safeguard but that was quite confronting. I wasn't in a relationship at the time but I could have still had children and to have that taken away from me. […] to have*

that choice taken away from me was a little bit confronting on top of everything else' (p. 516). Even women who were not planning to have children after their diagnosis (220) or were considered infertile before the cancer (221) were severely shaken and shocked by the fact that cancer took away their chance of ever having a child. For women who tried but could not conceive before cancer diagnosis it was the definitiveness with which cancer took away any hope for pregnancy that made dealing with infertility harder than coping with cancer diagnosis (221). Women resented that in the process of saving their life they became infertile (220) and questioned whether receiving life-saving but cytotoxic treatments was worth the effort (222). Some of them even doubted whether their life was still meaningful if they could not realise their dream of having children (180).

3.3.2.2.1.2. Grieving the loss of fertility

Fertility issues resulting from cancer treatment evoked a variety of emotional responses in young women. One that was mentioned by several studies was grief (194, 220, 223, 225, 226). Women engaged in a grieving process while trying to adjust to the loss of their fertility, yet this was not always straightforward. Some studies suggested that women who lost their reproductive potential to cancer and its treatments were more likely to suffer from 'disenfranchised grief' (194, 223, 226). Disenfranchised grief is a term coined by Doka (227) and it occurs when a loss, or a person who is grieving is not openly recognised by society. This could be the case of fertility loss due to cancer as women reported the lack of acknowledgement of the importance of fertility by healthcare professionals. Physicians were generally perceived by women as not being concerned by the value their patients attached to fertility (179) but rather focused on administering life-saving treatments. This attitude might have contributed to the way women processed their emotions towards the loss of fertility. Women also described how they were heartbroken and devastated about not being able to have children (180, 228) and about the way cancer brought about the definitive end to their idea of potential motherhood (194, 221). Some were scared of the prospect of not being able to reproduce (228, 229). The removal or destruction of reproductive organs in the course of cancer treatment, even if it was curative, symbolised a loss of all the future children that women might have planned for (191, 220, 222, 230). It also represented a loss of a

normal age-appropriate experience of becoming pregnant and giving birth to a child (191, 222).

One of the most prominent emotions represented in women's accounts was anger related not only to the inability to have children (179, 221) but also to the fact that cancer took away the sense of control over one's reproduction (230), that life-saving cancer treatments came at a cost of fertility (192, 221) and that fertility was taken for granted by other women while they had to struggle (191).

3.3.2.2.1.3. Challenge to relationships

Fertility was perceived as necessary for many women to be able to form and maintain a healthy romantic relationship with a partner (229). Single women perceived being infertile as a limitation and a burden to a future partner and therefore, were unsure whether they would ever be able to form a romantic relationship (181, 182, 229). Loss of fertility, along with other consequences of cancer such as perceived imperfect body and potentially limited lifespan were also seen as barriers to ever finding a partner who would accept that (180, 190, 194). Single women also spoke about their anxiety of broaching the topic of cancer and its impact on fertility with new partners (177) and where they were uncertain of fertility status, whether they would ever be able to decide to try for children (190). Some were concerned that going through fertility treatments or deciding upon alternative parenting such as adoption could be a deal breaker especially if the partner did not experience cancer treatments with them (177). Single women also anticipated that not being able to have children could be a reason for a potential future partner to cheat or get angry and possibly leave (229). Some women who experienced relationships post-cancer reported that cancer-related loss of fertility might have contributed to their relationship break-up (177, 229).

In the narratives of married and partnered women, relationship and sexual issues were intertwined. Some recounted how their sexual relationships have not changed (181) whereas others, for whom sexual life was impeded by their cancer treatment, described feeling guilty that they were letting their partners down or that their partners were missing out on an important part of a relationship (179). Fertility issues further complicated sexual relationships and even though for some, not being able to have children took the pressure off planning for that and allowed them to feel more relaxed

(181), most women admitted to feeling guilty towards their partners about not being able to give them a desired child (182, 221, 222)

3.3.2.2.1.4. 'It is not all bad'

In contrast to the negative emotions, some women focused on the positive consequences brought about by the treatments they underwent and as a consequence, by the loss of fertility. They mentioned feeling relieved that hysterectomy would prevent cancer from recurring and also put a halt to any menstrual symptoms (221). Women who completed their families and those nearing menopause before cancer diagnosis accepted their infertility (179, 228) and some perceived it as liberation of their sexuality (223). Finally, women who did not know to what extent cancer treatments affected their fertility and hence whose fertility status was uncertain, were hopeful that their fertility may still recover (192).

3.3.2.2.2. Being different/Comparisons with other women

The negative consequences of cancer-related infertility as well as challenges women diagnosed with cancer meet in existing relationships or when trying to enter new ones could be explained by the way they perceive themselves compared to women who have not had cancer. Those comparisons take place at two levels – the local level where cancer patients compare themselves with their healthy peers and the broad level where the comparisons are made with healthy women in general.

When comparing themselves to peers, women took into account the life stage they and their peers were at. Being in line with peers with regards to family-planning was important and made women feel as part of a group (191, 220). Where friends were not at the age to immediately have children and cancer survivors were not constantly reminded of their cancer-related fertility loss, they felt they could still keep up with their peers in terms of developmental milestones (191). However, when friends started to have children of their own, many women felt they did not quite fit in their peer group any more (191) and were being left behind (229). They blamed cancer for cutting short their life plans sometimes even before they had a chance to enter a life stage where they would be able to consider having a family (222). Many women expressed mixed feelings about their friends having children, being torn between happiness for their peers and sadness for themselves knowing they might not be able to ever achieve this

important developmental milestone in their adult life (191, 220, 222). Some also admitted they were jealous (221) or even angry at not being able to have the same experiences that came so easily to their friends (180).

Those reactions extended to a broader level of comparison with healthy women in general. Cancer survivors thought it unfair not to be able to share the common experience of pregnancy, childbirth, and motherhood that were available to healthy women but did not extend to them (191). They felt as if they could not be part of the normal lifestyle involving finding love, settling down, and becoming a parent (191). The pain and sadness of this situation was highlighted by the fact that some women considered reproduction to be a matter of choice and therefore, they questioned whether there was something wrong with them and worried about what other people would think if they remained childless (229). As much as reproduction was seen in terms of exercising one's right to choose a lifestyle, cancer was considered something outwith one's control. However, women perceived cancer-related fertility loss as a constant reminder of their disease and found it difficult to move on with their lives (179). Particularly women who were uncertain of whether their cancer treatments rendered them definitely infertile found this uncertainty difficult to deal with. They felt as if they were unable to go back to normal life and felt stuck in limbo (179, 191, 192). But, also those who knew they were infertile believed they were 'marked' (182, p.144) by both cancer and their loss of fertility and found it difficult go on living this way. Halliday, L.E. et al. (191) suggested a term 'self-othering' (p. 259) to describe the process through which survivors compared themselves to healthy women and categorised themselves as different, not quite fitting or defective.

3.3.2.2.3. Identity as a social construct

Zooming out from where cancer survivors compare themselves to their healthy friends and even women in general lays the concept of female identity that is constructed within a socio-cultural context. Three subthemes were identified within the *Identity as social construct* theme*: Motherhood central to identity; Threatened femininity;* and *Redefining identity* (see Figure 3.3).

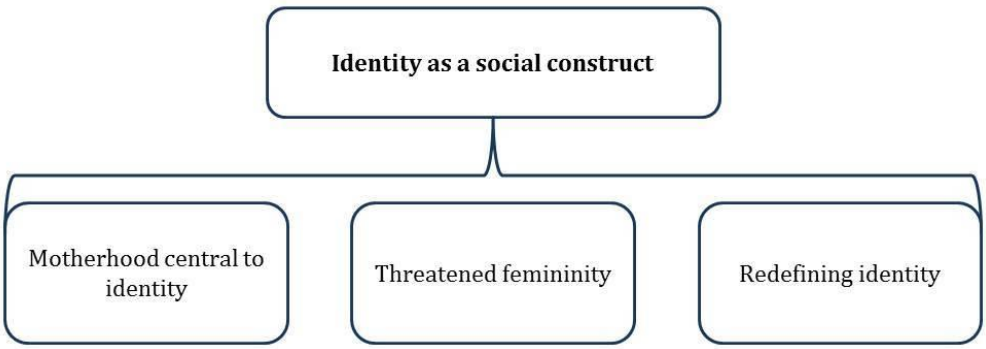


Figure 3.3. Visual representation of the subthemes identified within the theme *Identity as a social construct*

3.3.2.2.3.1. Motherhood central to identity

Many women indicated that being able to have children was central to their female identity which resulted from the fact that from a very early age they were taught what was normal for women and which social roles they should endorse. This is best illustrated by a quote from one of the participants in a study by Kirkman, M. et al. (194) who described it this way: '*You are taught that you grow up, and you go through school, and then you go to university, and then you meet your life partner, buy a house with a car, and have 2.5 children, and then live happily ever after*.' (p. 505)

Normal lifestyle which for women included the expectation to become a mother one day was created on a socio-cultural level (191). Women perceived having children as important in defining who they were (221) and something that gave life its meaning (191). Therefore, loss of fertility for many of them meant loss of identity (179) and equalled with failure (229). This was especially difficult in the context of cancer. Before diagnosis, female identity was defined by external factors such as physical health, body confidence, and potential to be a mother (194). Diagnosis and treatment stripped women of all those things (194) and left them without any indication of who they were after treatments had finished (192). One of the survivors reflected on it saying: '*My whole currency as a human being was forever changed as a result.*' (194, p. 508)

3.3.2.2.3.2. Threatened femininity

Being able to become pregnant and bear children not only allowed women to fulfil the social role of a parent but were also important markers of differences between women and men. Without them, women felt unable to perform in accordance with gender norms (229). Losing fertility due to cancer treatment made survivors feel incomplete and as if they failed as women (179, 182, 221, 229). They referred to themselves as 'barren' (220) and 'useless' (182). Not only were their breasts diseased but their childbearing potential was taken away from them (229). Reproductive organs that did not work were perceived as something that could destroy a woman's image of herself (180). Infertility along with other side-effects of cancer treatments threatened women's femininity and their status as women in society (223).

3.3.2.2.3.3. Redefining identity

For some women, motherhood was not the most important component of their female identity (229) and they self-identified as childfree (194). Other survivors, who did consider motherhood to be an important part of their life, had to redefine their identity as a result of cancer. They did that by shifting their priorities and finding meaning in their relationships, religion, or professional development (229). Some engaged in physically demanding activities or travelled to regain control over their lives (194). Finally, a lot of women focused on alternative ways to parenting such as adoption, egg donation, or surrogacy. For some, having biological children was the only legitimate way of becoming a parent, however, many women considered social parenting a good alternative and thus were able to find new meaning in their lives by exploring and pursuing those options (180, 229).

3.3.3. Objective 3: To explore how women diagnosed with cancer during their reproductive years make cancer treatment-related decisions that can affect their reproductive potential and outcomes in the future

Forty original studies meeting all the eligibility criteria and two studies missing one of the criteria (177, 183) investigated the process and consequences of treatment-related decisions that could affect reproductive potential and outcomes of young women diagnosed with cancer (for details of included studies see Table in Appendix 7). The two studies that missed one of the criteria, and specifically the criterion missed were

discussed in sections 3.2.4.1 and 3.2.4.2. Quantitative data from 23 original studies and qualitative data from 19 studies are summarised for the purpose of this review. Qualitative and quantitative findings are presented separately. The results of quantitative studies are organised according to the outcome they pertained to. Since objective 3 of this review explores treatment related decision-making the results are systematised based on the following types of treatment-related decisions:

1. Unspecified decisions, where authors failed to specify which decisions they were referring to;
2. Decisions about initial potentially fertility reducing treatments (e.g., surgery; chemotherapy; full body irradiation; bone marrow transplant);
3. Decisions about endocrine therapy (tamoxifen for breast cancer);
4. Decisions about FP (e.g., egg or embryo cryopreservation; ovarian tissue cryopreservation; the use of gonadotropin-releasing hormone agonists).

The results of qualitative studies are summarised under themes that were identified in the process of thematic synthesis.

3.3.3.1. Quantitative findings

3.3.3.1.1. Unspecified decisions

Three quantitative studies provided information about treatment decisions without specifying what type of decision they were referring to. Scanlon, M. *et al.* (231) investigated a group of women with various cancer diagnoses and reported that the risk of infertility affected treatment-related decisions in 13% of participants. Partridge, A.H. et al. (210) as well as Ruddy, K.J. et al. (211) focused on young women with breast cancer and noted that fertility concerns influenced treatment decisions for 29% and 26% of their participants, respectively. Younger and unmarried women with no prior successful pregnancies (231) as well as those who wanted to have (more) children, had prior difficulty conceiving and recalled depressive symptoms prior to diagnosis (210) were more likely to make their choices based on fertility concerns. Partridge, A.H. et al. (210) additionally investigated to what extent women questioned their breast cancer treatment decisions and found that 45% of all participants questioned their decisions at least a little bit. Although having more concerns about fertility was not associated with

being more likely to question treatment decisions, 33% of women who reported being more concerned about fertility at diagnosis admitted that the questioning of treatment decisions stemmed from fertility issues at least to some extent (210).

3.3.3.1.2. Decisions about initial potentially fertility reducing treatments

Five quantitative studies explored how decisions about potentially fertility reducing treatments were made by young cancer patients. Two of them (197, 198, 232) focused on decisions to undergo surgery and the other three (210, 211, 233) investigated decisions about chemotherapy. No studies were found to examine decisions about the full body irradiation or bone marrow transplant.

3.3.3.1.2.1. Surgery

Campos, S.M. et al. (232) examined a group of young women diagnosed with early-stage ovarian cancer or borderline tumours who underwent fertility-sparing surgery. They asked their participants whether undergoing fertility-sparing treatment was important to them and found that for 87.5% of participants it was ‘extremely’ or ‘very important’. The remaining 12.5% indicated that that sparing fertility was only a ’somewhat important’ feature of their treatment.

Two articles published by Carter et al. (197, 198) based on the same dataset investigated young cervical cancer patients’ reasons to undergo a radical trachelectomy (type of surgery to remove only part of the cervix). The following reasons were given by participants who chose trachelectomy as treatment modality: preservation of fertility [97% of participants in the preliminary report (197) and 98% of participants in the final report (198)] and not having had enough time to complete childbearing [74% (198)], followed by discussions with physicians and their recommendations [41 and 36% in the preliminary (197) and full (198) report respectively], wanting a family or preserving future fertility options [41% (197)], personal initiative (28%) and research (17%) (198). The full report (198) also investigated the reasons to undergo a radical hysterectomy (a type of surgery to remove the entire uterus, including the ovaries) and the authors reported that for approximately half of the women, fertility and childbearing potential played a role in making this decision. Additionally, 46% of participants decided to have this type of treatment based on doctor’s recommendations, 25% cited concerns about survival as a reason and another 25% felt it was the best or the only available option.

3.3.3.1.2.2. Chemotherapy

As mentioned in section 3.3.3.1.1, Ruddy, K.J. et al. (211) reported that for 26% of young women with breast cancer who participated in their study, fertility concerns played a role in treatment-related decision-making. Of those who provided specific details, 2% chose one chemotherapy regimen over another and 1% reported to have decided to refuse chemotherapy in hope to preserve fertility. Similarly, Senkus, E. et al. (233) analysed data collected from an international sample of young women with breast cancer and found that 8% of their participants would have decided against chemotherapy had they known it could be detrimental to their fertility.

The same study further examined the likelihood of accepting chemotherapy among its participants and concluded that women were significantly more likely to accept chemotherapy if they already had children, did not want children in the future, were diagnosed with higher disease stage, were from Western Europe, and had chemotherapy planned as part of their regimen according to both univariate and multivariate analyses (233).

Both Senkus, E. et al. (233) and Partridge, A.H. et al. (210) also investigated the risks and benefits young women with breast cancer were willing to accept given that chemotherapy could affect their fertility. In terms of the maximal risk of infertility associated with chemotherapy, 57.5% to 65% of women respectively were ready to accept a risk higher than 50% (210, 233). Still, according to Senkus, E. et al. (233), 25.6% of women would only agree to chemotherapy if it posed no more than 25% risk to fertility.

Several factors were found to affect the acceptance of chemotherapy-related infertility risk. Partridge, A.H. et al. (210) reported that women who were more concerned about fertility at diagnosis were less likely to accept higher risk of infertility from chemotherapy. The study by Senkus, E. et al. (233) suggested that higher acceptance of infertility risk was significantly associated with already having children, no desire for children in the future, younger age, being from Western Europe, and planned chemotherapy. They also found an interaction between a wish to have children and already having children. Compared to women who wanted children but did not have any, women who neither wanted nor had children, women who had children and did not

want any more, and women who both had and wanted children were respectively 26.58 (95 CI 7.21, 98.1; $p < 0.0001$), 5.3 (95 CI 3.22, 8.7; $p < 0.0001$) and 2.9 (95 CI 1.76, 4.77; $p < 0.0001$) times more likely to accept a higher risk of infertility due to chemotherapy.

In terms of the minimal survival benefit associated with chemotherapy, approximately 30% of participants in both studies (210, 233) were inclined to accept the benefit of less than 5%, however, for 32% and 47.6% of participants, respectively, this benefit would have to amount to at least 20%. Women experiencing greater concern about fertility at diagnosis also required a greater survival benefit to accept chemotherapy ($p < 0.05$) compared to those who were less concerned about fertility (210).

3.3.3.1.3. Decisions about endocrine therapy

Seven quantitative studies (184, 195, 196, 211, 234-236) examined decisions about either initiation or discontinuation of endocrine therapy among young women diagnosed with breast cancer. Desire for pregnancy was mentioned as a reason to discontinue tamoxifen in several studies. Some of them have not provided exact the numbers (184, 234) whereas in others these ranged from 3.6 to 16% (235, 236). Referring to participants who admitted that their treatment decisions were affected by reproductive concerns, Ruddy, K.J. et al. (211) reported that 1% of women considered refusing endocrine therapy and 3% actually did refuse to take tamoxifen. Further 11% considered cutting taking tamoxifen for five years (as per recommendations) short (211).

Bramwell, V.H. et al. (234) also identified several other factors that played a role in tamoxifen discontinuation among 30-49 year old patients. These included lack of motivation, resistance against drug intake or wish to stop (28%), intolerance (12%), weight gain (8%), hot flushes (20%), dermatologic symptoms (4%) and mental health issues (4%).

Finally, two articles described the findings drawn from the ELIPPSE40 cohort which was established to explore the impact of breast cancer on QoL and survival of young women (195, 196). In a study by Huiart, L. et al. (196), 39.5% of women discontinued tamoxifen over a 3-year period and discontinuation was significantly associated with

lower social support and self-reported non-compliance at 10 months after diagnosis. According to Cluze, C. et al. (195), 7% of women never initiated taking tamoxifen and 42% interrupted the treatment. The authors concentrated on early (between tamoxifen initiation and 16 months post-diagnosis) and late (more than 16 months post-diagnosis) interruption of tamoxifen. They concluded that early interruption was more likely among women with less social support and those who considered information provided to them about tamoxifen difficult to understand. Late interruption was positively associated with lower social support, lower fear of cancer recurrence, two or fewer treatment modalities, more menopausal symptoms and no opportunity to ask questions and have them answered at the time of diagnosis (195).

3.3.3.1.4. Decisions about FP

Thirteen quantitative studies (183, 185, 186, 228, 237-245) investigated how young women diagnosed with cancer made decisions about FP. These studies described factors associated with the uptake or the intentions to pursue FP (183, 185, 186, 228, 237-240, 242-245) and the consequences of undergoing FP in terms of decision-specific outcomes (183, 185, 239, 241).

Several socio-demographic and medical factors were examined in relation to pursuing FP among young women. One of the reports by Letourneau, J.M. et al. (186) suggested that higher education level was associated with higher odds of pursuing FP in a large group of young women with various cancer diagnoses. This (186) and another report by Letourneau et al. (185) also found that parity at diagnosis and younger age were significantly related to the uptake of FP. The latter results, however, were not supported by a study by Kim, J. et al. (240) which focused on breast cancer patients and found that neither parity nor age were associated with FP. Somewhat surprisingly, studies that examined whether having a partner was associated with pursuit or the intention to pursue FP did not find any significant relationship between the two (186, 240, 242) despite relationship status being mentioned as a factor in decision-making in free-response section of a survey in a study by Bastings, L. et al. (183).

Kim, J. et al. (240) found that the lower body mass index, lower cancer stage, and higher income were related to pursuing FP in univariate analyses yet, the insurance coverage was not. Letourneau, J.M. et al. (186) did not find a relationship between

household income and FP. Nonetheless, cost was an issue that appeared in the US-based studies. Huyghe, E. et al. (238) surveyed young patients with various cancer diagnoses about the potential use of FP services and noted that having to self-pay for FP services reduced the willingness to use them. In a study by Hill, K.A. et al. (237), 67% of breast cancer patients offered FP reported that the cost of treatment had an impact on their FP decision. Kim, J. et al. (239) evaluated the actual FP decisions among young women with cancer who were referred to the University-based clinic and cost consistently came up as one of the most influential factors to affect women's choices. It was also a second-most important factor to be reported by women who did not receive FP. Overall, according to Kim, J. et al. (239) women's decisions about FP were most influenced by the desire to have children after cancer treatment (65% of participants), cost (46% of participants), and amount of time for FP (42% of participants). The group who preserved fertility listed desire for future children (63%) and partner's wish (11%) as the most important factors, whereas the group who did not pursue FP considered desire for future children (27%), cost (21%) and the amount of time needed for treatment (12%) the most influential (239).

Desire for a child in the future transpired to be an important motivation to undergo FP (186, 239). Reh, A.E. et al. (244) investigated young women diagnosed with different types of cancer who were referred to FP clinic and found that for 52% of their participants having a child was the most important life event and 62% were most concerned about the impact cancer could have on their fertility. Treves, R. et al. (245) cited the desire to be able to conceive a child and prevent future regret as primary motivations for women to undergo FP. Pursuing FP was seen by some of the participants as a 'life insurance' in the sense that should they want to have children in the future but could not conceive naturally, their frozen embryos or oocytes would be at their disposal/still available to them as an option (243, 245). On the other hand, a study among a group of Australian breast cancer survivors showed that desire to have children was not associated with intentions to pursue FP (242).

In a study by Razzano, A. et al. (243), young women also referred to FP as being an important part of cancer therapy (54.2%) and an option not to be wasted (70.8%). As suggested by Peate, M. et al. (242), breast cancer patients who regarded information

about fertility to be important were more likely to consider FP (OR = 2.14, $p = 0.004$). However, women who had more negative attitudes towards FP were less likely to do so (OR = 0.84, $p < 0.001$) (242). Those negative attitudes could result from the fact that FP is not a completely innocuous procedure as well as from the timing of the decision-making. A short period of time within which a decision about FP had to be made (183, 245); the fear that the harvested material could be altered while being frozen/thawed; the uncertainty about being able to obtain a future pregnancy; the fear of not surviving and thus not being able to use the harvested material; the fear of worsening cancer prognosis as a consequence of FP (243); young age and a recent start of a relationship (183) all complicated FP decisions.

Tschudin, S. et al. (228) explored attitudes towards FP among an international group of survivors with various cancer diagnoses and concluded that while positive attitudes towards FP were more pronounced than the negative ones (M= 4.4 (SD= 0.62); M= 2.75 (SD= 0.61) on a scale from 1 to 5, respectively), willingness to consider FP if there were risks involved was not as high (2.32 on a scale from 1 to 5 where 5 indicated the highest willingness to pursue FP). In a study by Reh, A.E. et al. (244), 54% of participants were unsure of the risks they were willing to take to pursue FP while 38% were willing to take minimal to moderate risks and only 8% claimed they would do whatever it takes to preserve fertility.

Studies that explored the consequences of FP in terms of decision-specific outcomes focused on two indicators – decision regret and decisional conflict. According to Letourneau, J.M. et al. (185), women who were counselled by their oncologist regarding fertility options and who pursued FP had significantly lower decision regret compared to those who did not pursue FP (6.6 vs. 11.0; $p < 0.0001$). Decision regret was also closely related to decisional conflict about FP (183). Three studies directly explored the relationship between the decisional conflict and FP (183, 239, 241). Two of them found that women who underwent FP treatment had significantly less decisional conflict about FP choices than those who did not (26.6 vs. 50.0, $p < 0.001$ and 18.8 vs. 37.5, $p = 0.0006$) (239, 241) while one did not find a significant association between decisional conflict and FP (183).

3.3.3.2. Qualitative findings

Thematic synthesis (201) of the nineteen qualitative studies resulted in four broad themes summarising how young women who were diagnosed with cancer made treatment-related decisions that could affect their future reproductive potential. Those themes were:

1. Finding a balance between survival and fertility (quantity vs. quality of life)
2. I need to know… otherwise I can't make a decision
3. The decisions are complex and multifactorial
4. There are positive and negative consequences to every decision (see Figure 3.4).

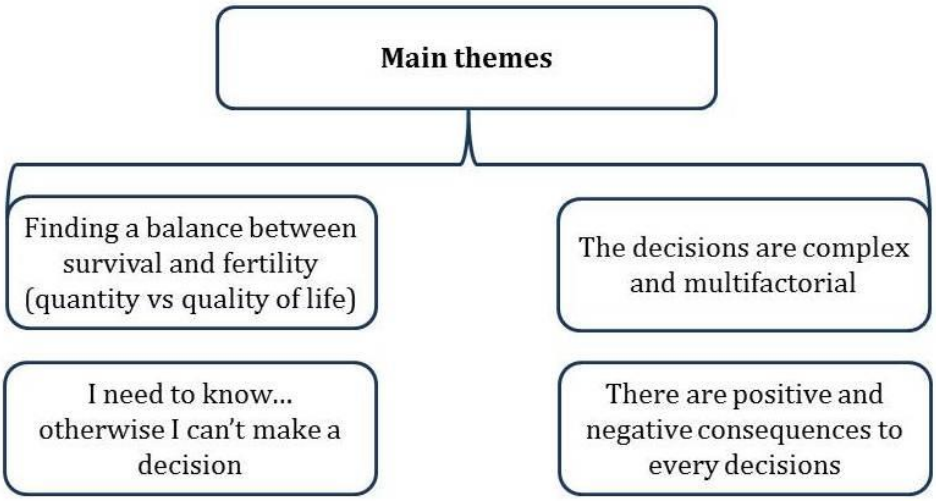


Figure 3.4. Visual representation of the main themes identified within the qualitative literature addressing objective 3 of the review

The term 'fertility preservation' in this section, if not specified otherwise, is used to refer to both procedures to spare fertility (radical trachelectomy and ARTs including oocyte or embryo cryopreservation) and declining treatments that could potentially impair fertility (such as chemotherapy, radiotherapy or surgical procedures to remove reproductive organs).

3.3.3.2.1. Finding a balance between survival and fertility (quantity vs. quality of life)

When confronted with a cancer diagnosis, young women attempted to find balance between doing everything to give themselves the best chance of surviving the disease and preserving the aspect of their post-cancer QoL that is fertility.

For some women, survival and prevention of recurrence were of paramount importance (188, 193, 219, 246-248). While knowing about the effect of cancer treatment on fertility was considered important, some women were adamant that this information would not change their decisions regarding treatments (219, 246). Their priority was to get rid of the cancer as soon as possible, to get it over with, and be able to move on with their lives (219). They were willing to take the risk of losing their fertility and becoming menopausal in exchange for the peace of mind that everything possible was done to cure the disease (219). Women emphasised how important it was to them to receive the most aggressive treatments to ensure that they would stay healthy and would not have to deal with cancer again in the future (219). As one of the participants in the study by Gorman, J.R. et al. (219) said: *'All I remember saying is tell me what I have to do to survive'* (p. 35). These women were also reluctant to take any steps that could possibly interfere with their prognosis (for example inject hormones to stimulate the oocyte growth for egg harvesting when their cancer was already hormone positive) (248). This was seen as an additional risk and many women were not willing to take any such risks, particularly if they had a young family to think about (193, 219, 247). Already having children, sometimes even if women had plans to have more, prevented them from looking into any of the FP options and made them concentrate on survival to ensure they would get better and be there for their existing children for as long as possible (193, 247, 248). Similarly, teenagers and young adults who had not yet reached the developmental stage in their life where they would consider starting a family (249) and women who simply did not want to have children (193) reported that FP was not something they were thinking about at the time of their diagnosis.

On the other hand, for women who were at the time of their diagnosis trying for or contemplating having children, maintaining their fertility was an important issue (188, 247, 250). As one of the participants in the study by Gorman, J.R. et al. (219) said: *'I*

made it very very clear to everybody that fertility was extremely important to me. I was two months away from my wedding, and we were talking about getting pregnant right away…' (p. 36). Some women in this group decided that they would not risk undergoing certain treatments that could result in fertility loss such as chemotherapy (190, 219, 224) and radiotherapy (229), or take tamoxifen that would necessitate that they postpone their childbearing plans (219, 250). One young woman very proactively arranged to check whether she was still fertile after having received her first line treatment and decided to decline further treatment to protect her fertility (251). Another one said that had she known that there were different chemotherapy regimens available, she would have asked for the one that would have been the least threatening to her fertility (219).

Women for whom fertility constituted an important issue were inclined to take their chances with treatments and see what would happen (229, 247) as they wanted to make sure they did everything they could to protect their fertility (188, 190, 246). This attitude, although not shared, was appreciated by women who already completed their families. While they were not willing to take risks to preserve their fertility throughout cancer treatments, they admitted that had they not had the desired children, they might have been more inclined to pursue FP (247).

Women who found fertility of paramount importance needed to balance their desire to have children after cancer against their own survival. Some stated that decisions regarding refusing treatments or pursuing some sort of FP were one of the hardest they ever had to make (188, 193). Some found the survival vs fertility trade-off very difficult to accept with one of the participants in a study by Corney, R.H. and A.J. Swinglehurst (190) saying: *'Right from the start she's [the oncologist] been very much 'it's about saving my life and nothing else' so in the early days that was very, very difficult for both David and I to accept'* (p. 23). Yet, women appreciated the fact that keeping fertility only made sense if one day they were well enough to have children and then be there for them (188, 219). This is illustrated by a quote from a participant from the study by Hershberger, P.E. et al. (188): *'Honestly, you look at it [cryopreservation] like, well... you kind of have to focus on living and treating your disease because if you're not*

gonna be here in five years to take care of your child – what's the point of trying to have one?' (p. 64).

3.3.3.2.2. I need to know… otherwise I can't make a decision

To be able to decide whether they wanted to act upon preserving their fertility, women stressed the importance of getting the right information (subtheme *Information*) and ultimately knowing what their real options were (subtheme *Options*). They also spoke about how being informed and able to make decisions contributed to their feelings of being in control over the situation they found themselves in whereas being deprived of information and options led to the loss of control and feeling excluded from what women considered very important life decisions (subtheme *Being involved vs. feeling excluded*) (see Figure 3.5).

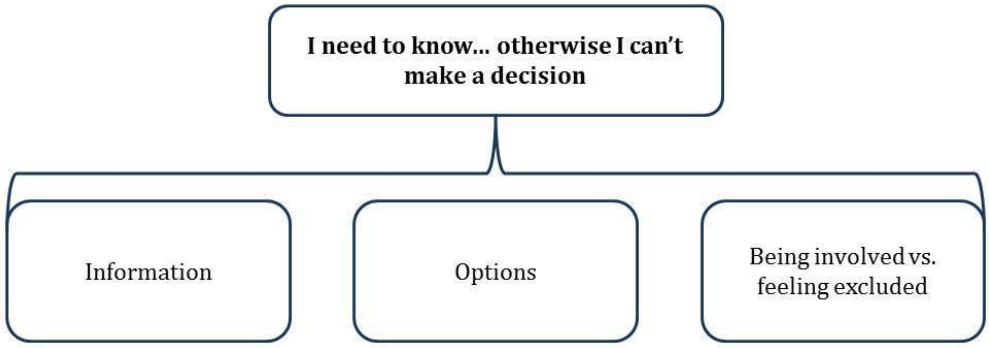


Figure 3.5. Visual representation of the subthemes identified within the theme *I need to know… otherwise I can't make a decision*

3.3.3.2.2.1. Information

Women considered their clinical team as a primary source of information about cancer treatment and its impact on fertility. They particularly valued practical information about what preserving fertility would entail (187) and they thought that it was the medical professionals' responsibility to broach the topic since faced with a cancer diagnosis many women did not think about their life afterwards and therefore did not ask questions about fertility (193). Some women had a positive experience of obtaining fertility-related information from their team (177, 229). Where the adequate information was provided, women were able to build a trusting relationship with their physicians

which additionally helped them guide their decisions (219, 229) (for further details see section 3.3.3.2.3).

Not all women however had good experience with obtaining information about fertility from their team. Some received conflicting information which made it difficult for them to navigate through the decision-making process (187). In those cases, help from a fertility specialist could have been particularly helpful. Women considered a referral to a reproductive medicine specialist to be a fundamental part of care provided to young women with cancer (193, 224, 247). This is reflected in a quote from one of the participants from the study by Kirkman, M. et al. (193) who said: '*My concern is, if you just talk to your cancer specialist, they care about cancer. And they do, they do obviously care about the other stuff as well, but their number one thing is cancer, and for some women their number one priority is having a baby'* (p. 60).

While some women relied solely on the fertility-related information provided by medical professionals (187), others considered it also their responsibility to stay informed (187, 188, 219, 224, 229). They mostly searched the internet for additional information about cancer and fertility (187, 188, 224). While some women deemed it to be an invaluable source of information that could later be discussed with their physicians (219), others found it rather confusing and were not sure of the quality of information they accessed (187). In those cases having a receptive clinical team was particularly important.

Yet, not all physicians were willing to discuss fertility with their patients. Sometimes fertility was either poorly addressed or not acknowledged at all by the medical professionals (187, 193, 247, 249) and women had to bring the topic up themselves suspecting that it would not have been addressed at all otherwise (190, 193, 224). Their impression was that a degree of assertiveness was needed to obtain necessary information from their physicians (193, 246, 251). One participant in a study by Dryden, A. et al. (229) described how she pressed for additional information about fertility but her concerns were ignored by her physician which discouraged her from asking any further questions. She described it in the following way: *'I've been asking him if I'm still able to have a baby, because I'm still young (...). He said, you know, "It's not important. Let's focus on you right now" (...) I actually gathered the courage*

to ask him, then when he answered me, I felt a bit, kind of, like, okay, he doesn't want to talk about it (…) It made me feel really uncomfortable, and sad, and embarrassed.' (229, p.1353)

Women felt that when the physicians did not offer to discuss fertility it was because they felt uncomfortable about the topic (177, 249) or because they did not care about it (177). They were particuarly dissatisfied when physicians simply communicated that fertility would be impaired due to treatments without suggesting any available options to preserve it (249, 251) or when medical professionals did not provide any explanation for the unavailability of FP options (190, 249, 251, 252). This was succinctly summarised by one of the participants from the study by Corney, R.H. and A.J. Swinglehurst (190) who stated: *'Because I still don't know whether I was told I couldn't have it (ARTs) because I really, really couldn't have it, or was it I couldn't have it because she wanted to start my treatment straight away?' and to this day I still don't know the reason why I couldn't have it'* (p. 23).

Another problem identified by women was the untimeliness of information provision. Some of them pointed out the fact that fertility was discussed too late for them to be able to take any steps towards preserving it (219, 247). They suggested that it should have been broached early (224, 247) which would have given them enough time to explore their options and make an informed decision.

3.3.3.2.2.2. Options

Women stressed the importance of knowing their FP options, including the option of doing nothing (193). Knowing one's options and being able to make a decision about whether to pursue any of them was sometimes important to a degree where women threatened to delay the whole treatment if they did not get referred to a fertility specialist to explore those options (190). Women considered it as 'good care' when physicians took time to explain FP options and made sure that women understood them (187, 193, 224).

Having reproductive options available evoked positive emotions such as hope (224, 249), relief, and feeling good about trying to preserve fertility (249). Yet, not all women felt they had options available to them to spare their fertility (190, 246, 247, 253). This

was the case when physicians decided that no options were feasible (177, 190, 251, 252). This situation evoked frustration and distress (177, 246), however, some women coped with it using what has been named in the literature as the 'illusion of choice' (254). This means that while describing decisions regarding the course of their treatment they presented the situation as if they had a choice while in reality they followed closely the advice of their physicians (219). This is best illustrated by the following quote from Gorman, J.R. et al. (219): *'I mean the decisions were mine, not that I always made them, but… we got three opinions from different doctors, and did some research, and talked to some survivors… Ultimately I went with my oncologist's recommendations'* (p. 35).

3.3.3.2.2.3. Being involved vs. feeling excluded

Being well informed and knowing one's options allowed women to make FP decisions that were appropriate for their particular circumstances (224, 229, 246, 247). Women valued the possibility of making those choices, especially since in the whirlwind of all the cancer treatments, deciding about whether to pursue ARTs was one of the few decisions that women felt they could truly make (246). Being in charge of FP decisions gave women the sense of agency and some control over their lives in the midst of their cancer experience (248).

On the other hand, when choices were taken away from women either by cancer itself (194, 247) or by the healthcare professionals (221, 247), they felt 'robbed' (194) and powerless. Women described the healthcare professionals as being in control by dictating women's choices (193, 194) and not providing enough information for women to make their own informed choices (249, 252). This led women to believe that they were excluded from the decision-making about fertility. Ultimately this situation evoked a profound sense of loss of control over one's own life (193, 249). As one of the participants in the study by Niemasik, E.E. et al. (249) said: *'After the first round of chemo, I asked the oncology fellow why I had not been given the option and she told me I should be happy that I had a healthy set of twins and to not worry about more children. Her tone made me feel like I was stupid and selfish to even consider more children when I was trying to survive the cancer. The pain and emotional strains of cancer are significant. I think that providing a woman with her options would give back*

some of the control in this situation and provide her with a bit of much needed respect and dignity in a process that after takes those things from her' (p. 328).

3.3.3.2.3. The decisions are complex and multifactorial

Decisions about whether to take steps to preserve fertility proved to be complex and where women were provided with information and options, there were many factors that influenced their decisions. Three groups of factors were identified in the literature: the moderators, barriers, and facilitators of fertility-related decisions (see Figure 3.6).

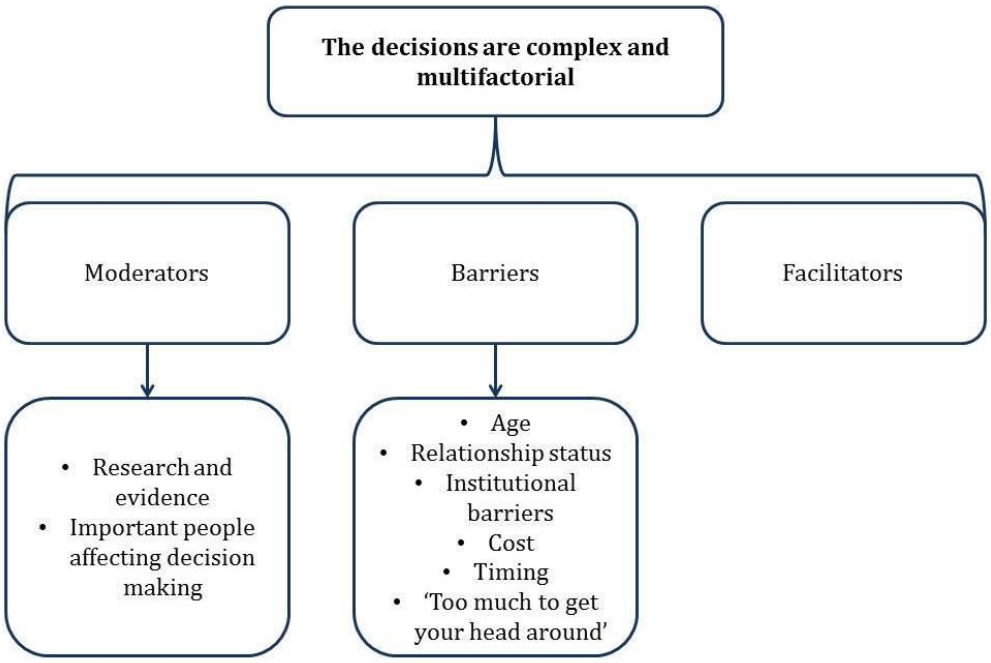


Figure 3.6. Visual representation of the subthemes identified within the theme *The decisions are complex and multifactorial*

3.3.3.2.3.1. Moderators

3.3.3.2.3.1.1. Research and evidence

After receiving some initial information from their physicians, women often went away and did their own research to decide over the course of action they wished to take with regards to preserving fertility (219). They looked for evidence that would help them choose a suitable option.

When deciding about cancer treatments such as undergoing chemotherapy (219) or choosing between a hysterectomy and a trachelectomy (255), women were interested in

survival and recurrence rates in the first place to assure that regardless of the choice their long term prognosis would not be compromised. Some were adamant that even a slight increase in survival would convince them to undergo a more aggressive treatment (219).

While deciding about pursuing ARTs, women were interested in knowing the success rates (189, 246, 248). Embryo cryopreservation was seen as a standard option for women keen to pursue ARTs (248), yet not all of them were convinced by the procedure's success rates. Some declined the procedure because it did not give a 100% guarantee of a future pregnancy (248). Oocyte cryopreservation was considered to be even less reliable, however, unpartnered women found it to be an acceptable alternative to embryo cryopreservation (189). What complicated those choices even further was the uncertainty surrounding the necessity of pursuing ARTs in case natural fertility stayed intact during and after treatments (246, 248, 253).

3.3.3.2.3.1.2. Important people affecting decision-making

Women involved other people in their decision-making process, the most important being their physicians, but also significant others, and people who had experienced cancer themselves.

Women often spoke about how their treatment-related decisions were influenced by the recommendations and advice given by their physicians (190, 219, 248). They described their doctors as the 'guiding force' for their decisions (219, p. 36).

When referring to the decisions involving undergoing ARTs women mostly reported that their physicians were more on the negative side, presenting disadvantages and risks of ARTs rather than the benefits (190, 248, 249). This might not have affected women for whom fertility was very important and who were adamant they wanted to preserve it from the very beginning, yet the advice did affect the decision-making of women who were not entirely sure about ARTs. The latter cited their doctor's opinion as influential in not going forward with FP (248).

While chemotherapy regimens might have been questioned and challenged by some women, they usually relied on their physicians' recommendations (219) although some took the risk of foregoing chemotherapy to preserve their natural fertility (190, 224).

Women also interrogated their physicians about having to take tamoxifen – a hormonal drug that is known to prevent hormone receptor positive breast cancer recurrence but also to be teratogenic and therefore, contraindicated during pregnancy. Compared to first line treatments, physicians seemed to be more open to discussing the options and allowing women to shorten their tamoxifen treatment in order to restore their fertility (190).

Whatever advice was given by the healthcare professionals, it was embedded in the broader context of the relationship that women had built with their doctors. The literature suggests that women either felt supported in their decisions by their physicians or thought that their and their doctors' priorities differed to the extent where reaching a consensual decision proved extremely difficult.

In a supportive relationship, women could trust their physicians and this trust was built upon good communication. This was the case when women felt that they were told the truth about what was happening inside their bodies, when that no information was withheld from them (187), and when they could take time to ask questions and make sure that they understood everything (219). Listening to patients, picking up on subtle cues (187, 193), and then tailoring consultations to one's particular needs (219) were highly valued. Women were grateful when doctors respected their priorities, particularly those regarding childbearing plans, regardless of whether they had them or not (193). They also appreciated when their doctors stayed calm in the uncertain times of cancer diagnosis and were confident about what was going to happen to the patient (187, 219) which provided reassurance and hope (229). At the same time, women valued being empowered by their doctors to make their own decisions during difficult period of cancer diagnosis (187). All those qualities contributed to a supportive and trustworthy doctor-patient relationship which enabled women to exercise their choice over FP. Sometimes trustworthy relationship was built upon doctor's reputation (as a good and respected specialist in the field), however, that was not always enough and women reported changing doctors if they did not find their relationship satisfactory (193).

Unsatisfactory patient-doctor relationship could make exercising treatment choices difficult for young women. Some women felt as if they were not treated as fellow human beings but rather cases that need to be treated. They reported their doctors' lack

of communication skills and insensitivity (193, 229) as barriers to building a good patient-doctor relationship. The barrier women most often referred to, however, was the conflict between their and their physicians' priorities regarding fertility. Women gave examples of situations where physicians withheld fertility-related information (251) or ignored the topic entirely (177, 187, 229). These were interpreted as physicians' unwillingness to acknowledge patients' priorities.

Women also spoke about their doctors' unwarranted assumptions about patients' childbearing plans. They felt that healthcare professionals assessed their patients' needs based on sociodemographic indicators without asking the person about those needs. Thus, older women, the unpartnered ones (187, 193), and those who already had children at the time of diagnosis (247, 249) were more likely to miss out on FP opportunities, even if they wished to pursue them, because of doctors' assumptions. This is how one of the participants in a study by Hershberger, P.E. et al. (187) described it: *'Because when I got the answer [from clinicians], "Well we don't see many patients like you" -- meaning that even if they are pre-menopausal the chances being thirty- six is "We assume you've already had a child or two -- it's not going to be a big deal if we take away your fertility." Knock, Knock, Ding, Ding, Ding … This is not acceptable. I have some concerns here and I want them addressed! Um, can you please help me? [pauses] And they didn't'* (p. 268). On the other hand, some women reported that their doctors assumed they would want to have children after cancer while that was not the case (193). Those differences between patients' and physicians' values made it more difficult for women to choose a fertility option that was best suited to their situation.

While some women admitted that they preferred to make their FP decisions on their own (246, 248), others involved their significant others including partners or parents in the decision-making process (188, 246, 248). Talking to partners and parents gave patients perspective (188) and also allowed women to take their partners' parenting desires into account while making decisions (248). On the other hand, especially regarding parents' involvement in fertility-related decisions, some women felt under pressure to pursue ARTs with one participant in the study by Snyder, K.A. and A.L. Tate (248) poignantly saying: 'Dad said, *'Here's the credit card, go get it. I want to make sure I'll have insurance on a grandchild'* (p. 176).

Some women also turned to other cancer survivors, either their friends or people they had met online, for advice regarding FP (177, 188). They were interested in how other people with cancer navigated through the decision-making process and were keen to take their experiences and stories into account while making their own choices (188). Some women recounted stories of their friends who were not offered FP when diagnosed with cancer and made it clear that they did not wish to be faced with that same situation (188).

Finally, women also drew on their own pre-cancer fertility related experience with those who experienced fertility issues prior to cancer more often declining FP (188, 248) and explaining that they had already become used to the fact that they might remain childless (248).

3.3.3.2.3.2. Barriers

3.3.3.2.3.2.1. Age

Being at either end of the reproductive age spectrum was perceived as a barrier to FP. Very young women were told that their fertility would spontaneously recover after cancer treatment and therefore, they did not need to preserve fertility (249). In the case of women at the other end of the spectrum, approaching their forties, physicians usually assumed they were not interested in childbearing (193, 246). These women were faced with a paradox of being perceived as too young to be having cancer but too old to be thinking about having children (193).

3.3.3.2.3.2.2. Relationship status

Relationship status played a role in FP decisions with single women being less likely to be offered ARTs (189, 190) or pursue them (224). Women identified several reasons that they thought contributed to that.

Some single women believed that they were not offered FP because of doctors' assumption that having children was not important to them (189). They also suspected that physicians did not want to suggest oocyte cryopreservation because it was less successful than embryo cryopreservation (190).

Those women who were offered ARTs, found their relationship status added complexity to an already difficult decision. If they wanted to give themselves the best chance to preserve fertility, they were advised to choose embryo cryopreservation over oocyte storage. This meant, however, that they needed to ask their ex-partner to provide sperm (187-189, 246) or use sperm from an anonymous sperm donor (188, 189, 224).

Some women found asking an ex-partner or a partner they were unsure was ready to commit to a long-term relationship to provide sperm difficult (188, 189, 246) or even unacceptable (187). They also identified ethical issues with using embryos created with a partner they did or might, in the future, separate from. They did not want to be 'stuck with' the embryos created with somebody they would not be in a relationship with (246). Another issue related to the ownership of the embryos. Women did not want to find themselves in a situation where they would have embryos stored but would be unable to use them in case the sperm donor changed his mind and was unwilling to consent to the ultimate use of the embryos to conceive (189).

Women who were contemplating using an anonymous sperm donor found it difficult to make such a decision in the very short time they had to preserve fertility (188, 189). They were also aware of possible implications of using a sperm donor on their future relationships in case their new partner wanted to have biological children. Women pointed to the fact that had they become infertile after cancer treatment but stored the embryos fertilised with a donor's sperm instead of oocytes, they would be unable to provide their potential future partner with a biological child (189). Therefore, some single women decided to pursue the less successful route of oocyte storage (248).

3.3.3.2.3.2.3. Institutional barriers

Some women reported institutional barriers such as being outwith the government or healthcare system guidelines for provision of ARTs (189, 190, 247). The availability of ARTs differed between regions and, therefore, was easier for some women and more difficult for others (190). These issues were mentioned in two UK-based studies where ARTs are provided to cancer patients free of charge. However, cost was a frequently mentioned barrier to pursuing ARTs and is discussed below. Women in a Dutch study also mentioned the inconvenience of cancer and fertility clinics being in different hospitals and the way it affected the coordination of their care (246).

3.3.3.2.3.2.4. Cost

Cost was mentioned as a deterrent to FP in six studies, four of which were conducted in the US (188, 248, 249, 253), one in the Netherlands (246) and one in Canada (224). Some women said they had no other choice than to decline fertility treatment. Sometimes ARTs were not covered by the insurance scheme women were part of (188, 253) and patients could not afford an out-of-pocket expense. Also, the uncertainty about whether cancer treatment would affect fertility led some women to question whether paying for ARTs was a waste of money since they may prove not to be necessary in the future (248).

3.3.3.2.3.2.5. Timing

Many women found the timing of FP decisions difficult (193, 246, 248, 256). For women who were not considering having children at the time of their diagnosis, cancer precipitated decisions they would otherwise be making much later in their lives (188, 253). Those in new relationships had to speak to their partners about having children a lot earlier in the course of the relationship than they would have wanted to (193, 194). They also needed to decide whether a partner they were with at the time of diagnosis was the person they wanted to build a family with (188).

Women also found it uncomfortable to think about their future fertility while being faced with their own mortality (248). One woman described it as being 'in a rotating mill' (246, p. 8) and many stated they did not have enough time to consider their options properly and make a truly informed choice (188, 190, 193, 194, 248). A participant in a study by Hershberger, P.E. et al. (188) summarised this: *'It's tough to make this decision under the gun... feeling like you don't have enough time to think about it'* (p. 64).

Such a short time to make FP decisions resulted from the fact that women did not want to delay their cancer treatments (177, 190, 224, 248, 249, 251-253, 256). The delays women wanted to avoid stemmed from long waits for fertility consultations (177, 190) and a lengthy process of hormonal stimulation to harvest eggs (224, 246-248). The fear that cancer could spread further while they were waiting for treatments (248) and the unfavourable characteristics of their cancer (251) were given as reasons for the urgent need of treatment. Many women, however, were under the impression that their cancer

therapy could not wait because their physicians wanted them to get on with the treatments as soon as possible (177, 190, 194, 247, 249, 252). When reasons for this were not provided (252), women reported feeling as if their reproductive choices were taken away from them (247).

3.3.3.2.3.2.6. 'Too much to get your head around'

Many women described FP decisions as overwhelming both emotionally (188, 224, 247, 248, 253) and physically (224). When talking about their emotional experience they referred to it as if being on a constant 'rollercoaster' having to undergo cancer treatment and decide about ARTs at the same time (247). They found it challenging to make such decisions at this very difficult time (253).

With regards to the physical demands, some women indicated that in the midst of their cancer treatments they were not willing to undergo additional medical procedures that were not immediately necessary to rid them of the cancer (224, 246). In case of ovarian tissue cryopreservation, women were also aware it was still an experimental procedure that might not increase their chances of successful pregnancy (246). Finally, the uncertainty whether these additional and experimental treatments were actually necessary given that fertility might stay intact during cancer therapy further hindered women from pursuing ARTs (246, 253).

3.3.3.2.3.3. Facilitators

One reason why women decided to pursue ARTs was that having embryos, eggs, or ovarian tissue stored gave them not only a sense of hope for future motherhood but also for recovery and a chance for normal life after cancer (224, 246). Cryopreserving gametes served as a back-up plan and constituted something they could fall back on in case cancer treatments destroyed their fertility (248).

Some women saw it as an 'insurance policy' for the future (248). Other women also mentioned that their main concern was the health of their future children. They decided to cryopreserve embryos that were created using younger eggs harvested at the time of diagnosis to use them after they had finished their tamoxifen treatment a couple of years later (248).

3.3.3.2.4. There are positive and negative consequences to every decision

Women acknowledged that making decisions about either pursuing FP or leaving it to chance both had positive and negative consequences.

Women who pursued treatments to preserve their fertility were generally happy with the decision they made (246) and did not regret it (190). In fact, anticipated future regret about not taking steps to preserve fertility was one of the reasons to undergo ARTs (224). Women described their decision as the 'right' (246, 255) or the 'best' one (255) given their circumstances. Yet, not all women who preserved fertility shared those views. One woman in the study by Garvelink, M.M. et al. (246) had mixed feelings about her decision since she felt that ARTs did not guarantee a future pregnancy. Other women in the same study were dissatisfied with their decision to pursue FP because some of them remained fertile after finishing cancer treatments, one was bothered by the side effects of FP, and one knew that she would be too old to take advantage of her cryopreserved material after having finished all her treatments (246).

Negative consequences were, however, more pronounced in women who did not take steps to preserve their fertility. Many women who decided against or could not pursue FP at the time of diagnosis regretted their decision (190, 219, 221, 224, 257). The feeling of regret developed over time (257) and particularly when peers were having children which reminded women that they could not have their own (221). This prompted women to think that maybe they should have decided differently as illustrated by this quote from one of the participants in the study by Gorman, J.R. et al. (219) who said: *'The only thing I would do would probably… freeze my eggs, because at the time I didn't even think about doing that'* (p. 38).

3.4. Discussion

3.4.1. Summary of evidence

The aim of this review was to investigate fertility-related issues experienced by young women diagnosed with cancer.

3.4.1.1. Objective 1

The first objective of this review was to establish the determinants of the psychological experience of fertility issues in women who were diagnosed with cancer during their

reproductive years. A close analysis of the included studies resulted in the identification of multiple factors which were grouped into the following four categories: socio-demographic characteristics, childbearing/parenthood status, desire to have children, and medical factors. However, the extent to which these determinants were related to fertility issues varied and often was far from clear.

Multiple sociodemographic factors were investigated in relationship to fertility issues. Some contradicting evidence exists for the association between fertility issues and age, education level, employment status, income level/financial comfort, and race (178, 208-211). The only factor that seemed to be consistently related to reproductive concerns was relationship status, with unmarried or unpartnered women experiencing more fertility issues (178, 210, 211).

According to the reviewed literature, childbearing status was related to fertility issues with women who did not have children being more likely to experience more reproductive concerns (178, 211). The type of relationship to the child (e. g., biological or social such as being an adoptive- or a step-parent) was also associated with fertility concerns: women who did not have any children had the most reproductive concerns and reported the highest levels of infertility-related distress whereas those with biological children had the lowest levels of both fertility concerns and distress related to infertility compared to other women in the study (208). This could potentially be associated with a degree of importance women attach to a biological link with a child (178). Finally, the desire to have (more) children was consistently related to higher reproductive concerns (178, 208, 209, 211).

The association between medical factors and fertility issues seems unclear at best. Among general medical characteristics, only having a first degree relative with any type of cancer was correlated with more reproductive concerns (210).

The relationship with gynaecological and obstetric medical history appears particularly compex with studies reporting contradicting results, especially concerning the association of fertility issues with the history of miscarriages (209-211), history of difficulty conceiving or fertility treatments prior to cancer (210, 211), menstrual pattern during and after treatment (178, 209, 210), or the number or live births before the

diagnosis (178, 210). The two factors for which somewhat consistent results were obtained across the studies were: having had fewer pregnancies before the diagnosis (which was associated with more fertility issues) and history of abortions (which was not associated with reproductive concerns at all) (210, 211).

Most of the explored cancer characteristics (stage, grade, hormone receptor and HER2 status, and time since cancer diagnosis) were not associated with fertility concerns with only one study suggesting that cancer recurrence and second primary cancer could be related to reproductive issues (208). Among cancer treatment characteristics, receipt of chemotherapy which can result in ovarian damage was associated with more fertility concerns in two studies (209, 211) whereas one suggested an inverse relationship (208). Both lumpectomy and mastectomy were related to more reproductive issues (210, 211).

The literature suggests that several factors may contribute to higher reproductive concerns in young women diagnosed with cancer. Being single, not having children, a wish to have a child or more children, fewer pregnancies prior to cancer, and possibly receiving gonadotoxic treatments were all consistently associated with fertility issues across the included studies. This is in line with the results of another systematic review by Howard-Anderson, J. et al. (56) who investigated QoL, fertility concerns and behavioural health outcomes in young breast cancer survivors. Howard-Anderson, J. et al. (56) conclude that not having children, a desire to have children, and fewer pregnancies prior to cancer were all related to more fertility issues. The findings of this review also resonate with the evidence regarding fertility-related information needs among young female cancer patients. Both Peate, M. et al. (14) and Holton, S. et al. (13) who reviewed the literature regarding fertility-related concerns, needs and preferences among young women with breast cancer and chronic, non-communicable conditions, respectively reported that fertility information was particularly important to women without children and those who desired children in the future.

Some similarities can also be seen in terms of the relationship between cancer-related medical factors and post-cancer fertility concerns, and the association between the objective disease characteristic and another psychological consequence of cancer, namely fear of cancer recurrence. The systematic review of fear of cancer recurrence in adult cancer survivors by Simard, S. et al. (50) concluded that the link between fear of

recurrence and the objective characteristics of cancer or its treatment remained unclear. The same stands for the psychological experience of fertility issues as reflected by the findings of this review. Indeed, studies including cancer patients have confirmed that the objective disease status was not a good predictor of patients' emotional response to cancer (258, 259). Leventhal and colleagues suggested that it was not the objective characteristics of a particular illness but the way individuals conceptualised them that may affect the way they psychologically respond to an illness (62, 64). Neither of the studies included in this review, however, investigated such an association.

3.4.1.2. Objective 2

The second objective of this review was to investigate the association between fertility concerns and psychological well-being in young women diagnosed with cancer. Both qualitative and quantitative literature were reviewed. Quantitative studies were searched for particular measures of psychological well-being including QoL, relationship functioning/dating experience, sexual functioning, depression, anxiety, and fear of cancer recurrence, while qualitative studies were analysed using thematic synthesis.

3.4.1.2.1. QoL and depression

Higher levels of reproductive concerns were consistently and significantly associated with lower QoL (208, 212, 213), particularly its emotional component. This is in line with the findings from a review exploring childbearing concerns and needs among women with non-communicable diseases (13). Holton, S. et al. (13) reported that childbearing concerns contributed to patients' poorer QoL.

Evidence regarding the relationship between fertility issues and depression and anxiety remains somewhat unclear, with two studies linking more reproductive concerns with more depressive symptoms (209, 218), and two others showing no relationship between the two variables (210, 211).

Qualitative literature provides a more in-depth understanding of the impact of impaired fertility on young women diagnosed with cancer. Survivors described their cancer diagnosis and the threat it posed to their fertility as a 'double blow'. They reported a variety of negative emotional responses to becoming infertile following treatment such as feelings of grief, sadness or anger. These could be explained by the fact that

survivors compared themselves to their peers and other women who, if they so desired, could fulfil their goal of having a family. This made cancer survivors feel different and not quite fitting in since they were not able to share a common experience of pregnancy, childbirth and motherhood.

On a broader scale, the feminine identity of many of the survivors was tightly related to fulfilling a social role of being a mother. When that possibility was taken away from them, they felt incomplete and as if they failed as women. They perceived cancer-related infertility as a threat to their femininity and something that could destroy a woman's image of herself. On the other hand, there were survivors who accepted infertility as a consequence of cancer. They mentioned feeling relieved as a result of having undergone fertility impairing treatment and reassured that radical treatment would prevent their cancer from recurring. Other women, for whom infertility was initially devastating, found ways to cope with their situation and succeeded in redefining their identity. They shifted their priorities and concentrated on other spheres of their lives such as relationships or professional development, or pursued alternative ways to parenting such as adoption, egg donation, or surrogacy. These findings are in line with the meta-ethnography by Adams, E. et al. (162) investigating the experiences, needs and concerns of young women with breast cancer. The authors of this review concluded that women engaged in normalising processes subsequently to their cancer treatment to cope with the disruption that cancer caused to their lives (162).

The inconsistency in the results of the quantitative studies could at least partially be explained by the insight gained through the qualitative synthesis. As described above, women might respond to fertility issues related to cancer differently. They might also find ways to move on from them with time. Therefore, large scale, quantitative studies including women in different points in their survivorship might not capture some of the nuances of the relationship between fertility issues and the indicators of psychological well-being.

Also, unlike in the case of QoL, studies investigating depressive symptoms among young women with cancer used different instruments to measure them with one using the CES-D scale (209) and the other two using the HADS (210, 253). The CES-D scale includes items measuring somatic symptoms of depression such as insomnia or fatigue

which overlap with the side effects of cancer treatment. This could result in cancer patients scoring high on this scale (67). The HADS was devised to resolve this problem by eliminating the items surveying physical symptoms of depression. This, however, resulted in the scale measuring anhedonia rather than depression (67). These differences in the conceptualisation of the measurement of depression by the two instruments make direct comparisons of the studies problematic.

Finally, as suggested by Greil, A.L. et al. (47) in their extensive review of the experiences of infertility, women facing infertility might experience distress to a certain extent but are not more likely to exhibit psychopathology compared to other women. The same stands for people with chronic illnesses such as cancer, diabetes, or cardiovascular disease for whom the evidence does not support the notion of the increased prevalence of major depression or severe distress compared to matched controls without chronic illness (67). Hence, although impaired fertility might be an issue for young women with cancer, it does not necessarily mean that it contributes to higher psychopathology in this group.

3.4.1.2.2. Fear of recurrence

One study that explored the relationship between fear of recurrence and fertility concerns (210) found a negative association between the two. Research showed that fear of cancer recurrence can hinder patients' ability to move on with their lives – to make plans for the future and go back to normal life as they knew it before cancer (260-262). It is possible that patients who are constantly concerned about their survival might not see the point of worrying about fertility. On the other hand, women who experience less of fear of recurrence might be more inclined to be anxious about fertility and having children. For some women, having children was what motivated them to stay healthy and alive as well as gave them back their sense of normality (163). This process of balancing between one's own health and survival on the one hand and fertility on the other was described as one of the phases young women with cancer went through after their diagnosis (162).

3.4.1.2.3. Sexual and relationship functioning

Findings regarding sexual functioning among female cancer survivors consistently indicated that more reproductive concerns were associated with worse sexual

functioning (208, 212, 213, 217). Yet, at the same time, studies exploring the relationship between fertility issues and relationship functioning or dating experience suggested that these two variables were unrelated (208, 212).

Again, the evidence from the qualitative studies provides a more in-depth understanding of the reason for that. Single women felt that building a new relationship could be complicated by the fact that they had cancer which led to loss of fertility. Some of them perceived fertility as a necessary part of a healthy romantic relationship and feared telling potential partners about their reproductive issues. They were concerned about going through fertility treatment or adoption with a partner that had not been through the experience of cancer treatment with them. Similarly, partnered women admitted to feeling guilty towards their partners about not being able to give them a desired child. It is, however, important to remember that women voiced these concerns when interviewed individually. While neither the scores on the CARES dating subscale, nor the ones on A-DAS measuring relationship quality were associated with fertility issues, these instruments were not designed to account specifically for the impact of post-cancer infertility. This means that when filling out questionnaires asking about the quality of their relationships or dating experience, women could have been considering how their overall cancer experience, and not specifically the fertility issues, affected these domains of their lives.

Furthermore, cancer experience was found to bring couples together (263). Greil, A.L. et al. (47) who reviewed the literature on the psychological experience of infertility suggested that, similar to cancer diagnosis, infertility tended to unify couples through a shared experience rather than have a deleterious effect on relationships. Nonetheless, he advised that this effect might depend on the sociocultural context. For example, societies which associate a woman's role more closely with having children, and where having children is defined in terms of marital obligation, infertility could potentially exert a greater negative effect on couple relationships (47).

In relation to women's sexual functioning which was consistently and negatively associated with fertility issues, the qualitative evidence indicates that women felt as if they were letting their partners down and that their partners were missing on an important part of a relationship, namely a healthy sexual life that leads to having a

family. Although this contradicts the findings reported by Greil, A.L. et al. (47) who concluded that infertility in otherwise healthy people did not lead to sexual problems, women who were diagnosed with cancer might not fully fit in the 'healthy' criterion. Lower levels of sexual satisfaction among women with cancer can be additionally explained by the effects of cancer treatments which may, at the same time, lead to infertility and early menopause. The evidence indicates that young women experiencing menopausal symptoms or amenorrhea following chemotherapy for breast cancer were sexually worse-off than women who did not have these symptoms (56, 264, 265). Similarly, women who underwent unilateral salpingo-oophorectomy for ovarian cancer functioned better sexually compared to women who had a combination of treatments that could lead to premature menopause (266). Premature menopause induced by chemotherapy or oophorectomy results in decreased oestrogen levels which can in turn lead to vaginal dryness (267-269). This, together with the psychological effect of not being able to have a child could contribute to sexual dysfunction among young women with cancer.

3.4.1.3. Objective 3

The third objective of this review was to explore how women diagnosed with cancer during their reproductive years made cancer treatment-related decisions given that these decisions could affect their reproductive potential and outcomes in the future. Similarly to objective 2, both the quantitative and the qualitative literature addressing this objective was reviewed and summarised.

3.4.1.3.1. The importance of fertility in treatment-related decision-making

The quantitative evidence suggests that for 13-29% of women fertility was an important factor that affected their treatment decisions (210, 211, 231). More specifically 1-8% of women across the studies refused or would consider refusing chemotherapy (211, 233), 2% opted for a less gonadotoxic chemotherapy regimen (211), 3.6-16% discontinued their endocrine therapy (184, 234-236), and almost all cited fertility as a reason to undergo radical trachelectomy for cervical cancer (197, 198). Women with more reproductive concerns were also less likely to accept chemotherapy that posed higher risks to their fertility and needed a bigger survival benefit from chemotherapy to accept it than women who were less concerned about fertility (210). Although these numbers

cited do not represent the majority of patients, it is important to recognise that a substantial minority of women do consider fertility a critical issue which guides their treatment decisions.

The qualitative evidence sheds some light on the processes involved in considering fertility a factor in the decision-making. It suggests that while engaging in the treatment decision-making process women first tried to find a balance between survival and fertility. And while for some eradicating cancer was the main driving force behind their decisions, others emphasised the importance of fertility at the same time acknowledging that any means to preserve their reproductive potential needed to be balanced against their chances of surviving the diagnosis. Clarifying those values might be extremely challenging for some women and this is where decisions aids could be of help to women who have a difficult time making a decision whether or not to take steps to preserve their fertility (63, 270). This is also where the physician-patient relationship comes into play.

3.4.1.3.2. The role of patient-physician relationship, information, and personal treatment preferences in the decision-making process

Across the qualitative studies, but also in some of the quantitative studies, women stressed the importance their relationship with the clinical team played in the treatment decision-making process. Physicians were seen as primary providers of information about how cancer treatments could impair fertility and about available FP options including the option to do nothing. Having a physician who was attuned to patients' fertility-related information needs and willing to discuss reproductive issues made women feel included in the decision-making process and hence gave them back some of the control over their lives. On the other hand, when women were not provided with the desired fertility-related information, they felt excluded from the decision-making process. This added to the sense of loss of control over their lives that cancer had inflicted on them in the first place. These findings suggest that fertility-related information was crucial to female cancer patients. However, according to a recent systematic review of cancer patients' and professional caregivers' needs and preferences for providing fertility-related information (4), 66-100% of young cancer patients report

the need for information about the impact of cancer treatment on their fertility, yet only 0 to 85% of patients receive it and 11 to 90% find it sufficient.

The review by Goossens, J. et al. (4) also emphasises the importance of the timing of information provision. It suggests that fertility-related information should be delivered after the initial cancer diagnosis but prior to any treatments to allow the patients enough time to act upon it (4). Time, understood as both the timing of decisions and the amount of time given to make them, was one of the barriers to treatment decision-making which emerged as a result of the qualitative literature synthesis. Although it would be impossible to change the timing of the decision-making regarding FP, it should be possible to give women more time to make their decisions without substantially delaying primary cancer treatment. A recent study by Kim, J. and J.E. Mersereau (271) exploring differences in the decisional conflict among two groups of cancer patients – those who were referred for fertility consultation within two weeks of diagnosis (early referral) and those who were referred more than two weeks after diagnosis (late referral), suggested that women in the late referral group were more likely to have high decisional conflict compared to women in the early referral group (OR 4.8, CI 95% 1.5, 21.6). These findings indicate that giving women more time to process information about fertility is feasible and might facilitate treatment decision-making.

Many women across the studies included in this review complained about receiving crucial information about fertility too late which prevented them from making truly informed choices (219, 247). Such a delay, or at times even a complete lack of information provision might stem from healthcare professionals' barriers to discussing fertility-related issues with their patients. Goossens, J. et al. (4) describe four factors that prevent physicians from providing fertility related information to their patients:

1. lack of knowledge and training related to FP;
2. negative attitudes of healthcare professionals towards fertility-related discussions stemming from the low priority attached to fertility-related information, lack of comfort in discussing fertility, perception of having no role in fertility discussions, impression that fertility was not an important topic for the patients, and negative attitudes towards delaying treatment to pursue FP;

3. institutional barriers involving the lack of coverage for FP, lack of practical guidelines regarding fertility referral pathways and time pressure during consultations; and
4. patient-related barriers such as being female, having a poor health status and prognosis, as well as cultural, religious, and financial barriers (4).

The importance of patient-related barriers as seen by healthcare professionals became apparent in a study by Snyder, K.A. and W. Pearse (272). They interviewed 67 women diagnosed with breast cancer under the age of 40 and identified five trajectories of fertility-related communication between healthcare providers and their patients:

1. fertility not being discussed at all (11.9%);
2. oncologist taking initiative to discuss fertility but without providing FP options (20.9%);
3. oncologist taking initiative to discuss fertility and provide FP options (26.9%);
4. patient taking initiative to discuss fertility but FP options not provided (17.9%); and
5. patient taking initiative to discuss fertility and FP options provided (22.4%).

Women in those various trajectories differed in terms of their educational level, occupation, and ethnicity with women in trajectories 1, 2, and 4 tending to have lower educational attainment, hold jobs outside healthcare, and be non-Caucasian. On the other hand, women in trajectories 3 and 5 were more likely to be well-educated and knowledgeable about cancer's impact on fertility, hence able to initiate discussions and make decisions with regard to fertility. Snyder, K.A. and W. Pearse (272) suggested that status differences between the physician and the patient shaped their relationship and affected the presence of fertility-related discussions.

This review proposes that patient-physician relationship should not be based on healthcare professionals' assumptions regarding their patients wishes but on clear and open communication as this appears to facilitate women's treatment choices. Physicians' unwillingness to discuss and incorporate women's values into the treatment decision-making process precluded women from building a satisfactory relationship with their physicians and hence acted as a barrier to treatment decision-making.

The importance of the physician-patient relationship and its impact on the decision-making process has been widely emphasised in the literature (117). With the shift from the paternalistic model, patients, and especially young women (113), expect their physicians to involve them in the treatment decision-making process (see section 2.2.2.2).

Patient's involvement in treatment decisions is at the very core of the Shared Decision Making model. Described by Charles and colleagues (115, 116), the Shared Decision Making model assumes that (1) there needs to be at least two participants in the decision-making process – the physician and the patient; (2) both parties need to be willing to participate in the decision-making; (3) information needs to be exchanged between the physician and the patient and this process needs to be reciprocal; and (4) the decision agreed by both parties needs to be made at the end of the process.

Relating the results of this review to the theory it becomes apparent that the majority of women wished to make their treatment decision in a shared manner. They stressed the importance of information provision during the physician-patient interaction as well as put emphasis on early establishment and communication of treatment priorities of both the patient and the physician. Finally, not only did they want to include their physicians in their treatment decision-making process, but also others such as their partners, parents, and other cancer survivors they knew personally or met online.

While most young women might want to participate in treatment decisions, some would rather leave the responsibility for treatment choices to their physicians. However, even this group could benefit from receiving information about their treatments. Information was found to act as a source of reassurance, to allow patients to retain control over what was happening to them, and to improve the physician-patient relationship by contributing to building trust and understanding between them (104).

Most importantly, it was the match between patient's expectations and the physician's consultation style that proved to be associated with patient satisfaction (127). Therefore, even in situations where shared decision-making is not possible or the patient does not want to be involved in treatment decisions, physicians should still attempt to tailor their consultation style to the particular patient. This individual approach to each patient

seems crucial as the evidence often remains inconclusive as to which groups of young female cancer patients might be particularly interested in preserving their fertility.

3.4.1.3.3. Fertility-specific considerations in the decision-making process

Desire for children was cited across the studies as a factor determining the extent to which women were likely to accept the risk of infertility related to chemotherapy (210, 233) as well as whether they would pursue FP (185, 186). Additionally, some quantitative studies reported that sociodemographic factors such as younger age, being single as well as difficulty conceiving prior to cancer diagnosis were indicators of making one's treatment choices based on fertility concerns (210, 231). Yet, the evidence from studies specifically investigating decisions about FP understood as ARTs has not been consistent with regards to characteristics such as age or relationship status. Qualitative literature suggests that being on either end of the reproductive age spectrum acted as a barrier to FP in that very young women were assured their natural fertility would recover subsequently to treatments whereas older women were considered too old to be interested in childbearing. Relationship status was mentioned as a factor complicating FP since some single women reported that they had to ask their ex-partners or use donated sperm to create embryos.

Being on either end of the reproductive age spectrum as well as being single may prevent physicians from addressing fertility issues with patients. Physicians may wrongly assume that these patients are not interested in childbearing (age), or are not in a situation to pursue FP (single patients). To avoid the situation whereby women are excluded from making informed choices that might influence their future reproductive potential, physicians need to remain impartial and provide fertility-related information to all their patients as suggested in section 3.4.1.3.2.

This does not guarantee that treatment decisions will be straightforward. This review identified further factors complicating women's decisions. These include additional physical (e. g., additional medical procedures not immediately needed to treat cancer) and psychological (e. g., difficulty deciding about FP in the midst of cancer diagnosis and treatment) burdens as well as cost and institutional barriers to FP.

Although physical demands of ARTs are likely to be similar for women whose fertility is threatened by cancer and other infertile women, the psychological burden of infertility might be different. A study by Carter, J. *et al.* (273) investigating the differences between women who suffered from infertility due to cancer treatments and other infertile women reported that the two populations were similar in terms of reproductive concerns, mood, distress levels, QoL and relationship functioning. However, qualitative studies found that patients who faced both cancer and a threat to fertility at the same time were likely to be subject to a 'double trauma'. In women's words, the added burden of infertility while receiving cancer diagnosis was 'confronting on top of everything else' (179, p. 516) (for details see section 3.3.2.2.1.1). The difference between women who lost their fertility to cancer and these whose infertility is due to other reasons might therefore lie in the quality of the experience.

Unlike other infertile women, who are usually able to take time and do extensive research about ARTs, cancer patients are often not afforded the opportunity to do the same. The short period between cancer diagnosis and the need to make decisions about FP means that cancer patients lack the time to prepare themselves for the cost demands of the procedure (224) or read the guidelines that apply to fertility treatment provision (189, 190, 247). Literature suggests that before fertility consultation, cancer patients were often unaware of the costs of fertility treatments (274) and therefore, taken by surprise by the financial commitments associated with the procedure (224). This often led women to decline FP.

While financial reasons have been shown to influence the decisions about pursuing fertility treatments even among otherwise healthy infertile women (275), cancer patients also face other concerns. The uncertainty about whether fertility treatments were absolutely necessary (248) or whether their health would ever allow them to use the cryopreserved gametes after the primary cancer treatment had finished (243) constituted additional factors that cancer patients but not otherwise healthy infertile women were confronted with. These further complicate their decisions about pursuing FP.

Finally, the reason why women did pursue FP involved a sense of hope for future motherhood and a chance for a normal life after cancer. This is in line with two systematic reviews concentrating on the experiences of young breast cancer patients

(162, 163). Adams, E. et al. (162) suggested that being able to conceive after cancer was part of the normalising process allowing women to continue with their everyday lives after diagnosis. Gonçalves, V. et al. (163) also emphasised the beneficial effects of having children after cancer such as regaining hope about the future, being motivated to stay healthy and alive and reconnecting with peers.

On the other hand, Adams, E. et al. (162), Gonçalves, V. et al. (163), and Peate, M. et al. (14) also pointed to the fact that many women changed their reproductive decisions and preferred to abandon their childbearing desires because of multiple fears experienced with regard to their own health and the health of future children. The medical literature provides evidence for pregnancy after breast cancer to be safe in terms of mortality or cancer recurrence rates (276-278), as well as foetal outcomes (279, 280), yet pregnancy rates in cancer survivors remain consistently lower than expected (281-286).

According to a recent review by Moffat, R. and U. Güth (287), cancer survivors use only approximately 2 to 4% of the gametes they cryopreserved. Newer studies estimate the utilisation rate for frozen embryos to be 23-33% (288-290) and replantation rate for cryopreserved ovarian tissue 3.5-8% (289). However, the evidence shows that women who preserved their fertility prior to cancer treatment were even less likely to try for pregnancy than women who did not pursue ARTs (291). Authors speculate that this might stem from the false sense of security due to the lack of patients' understanding that the efficacy of IVF procedures is age dependent (291). This might necessitate further patient education to ensure that patients understand how ARTs work. This could prevent future regret due to not taking the opportunity to use cryopreserved gametes when the time was right. It could also prevent possible regret with regard to financial resources spent on a procedure that women could not effectively use which was mentioned as one of the consequences of pursuing FP (246).

3.4.1.3.4. Consequences of decisions implicating fertility

Although most women who decided to preserve fertility were satisfied with their decision and reported less decisional regret and conflict than women who did not take steps to preserve their reproductive potential, some felt that pursuing ARTs was an unnecessary burden. Among infertile women, satisfaction with IVF treatments is often

related to the achievement of a desired outcome, notably having a baby (292, 293). Women with cancer have to postpone fulfilling their wish for a child until after the end of their cancer treatment and are usually advised to start trying for children later on in their survivorship to avoid the risk of cancer recurrence (294, 295). The lack of immediate positive outcome of FP might constitute a factor contributing to their dissatisfaction with treatment experience.

Nonetheless, regret was more pronounced in women who did not pursue FP. Even if fertility did not seem to be important at the time of diagnosis, for some women it became a major concern later on in survivorship (226) as they discovered that their desire for a child did not disappear after treatment (257). The evidence suggests that for the majority of female cancer patients the disease does not change the desire to be a parent (63). Fertility stays a crucial issue in survivorship with women wanting information about reproductive life planning and risks to a potential child in the follow-up stage of cancer trajectory (4). Unfortunately for some, it might be too late to give them a chance for a biological child. Therefore, it is important to inform women about the risks and benefits of FP at the time of diagnosis and enable them to make informed choices particularly since research shows that with the new protocols for ovarian stimulation, FP does not necessarily increase the recurrence rates nor does it compromise patients' survival (296).

3.4.2. Limitations of the review

The findings of this literature review should be interpreted accounting for both the limitations of the included studies and those of the review itself.

Across the quantitative studies, several limitations were identified including: (1) issues related to study samples (e.g., small sample sizes, homogeneity of the samples within studies as well as homogeneity of locations across studies, and single-centre recruitment), (2) methodological issues (e.g., predominantly cross-sectional design, use of non-validated instruments), and (3) issues related to data analysis (e. g., lack of sample size estimation calculations). Some of these limitations such as sampling issues (e .g., predominantly convenience sampling and homogeneity of participants within and across studies) were also prevalent across the qualitative studies. Additionally, those studies often lacked the elaboration of the theoretical framework used to analyse the

data. Although some discussed their inherent limitations related to the qualitative design, none reflected on how authors themselves could have influenced the data analysis process.

I used quality checklists (206) to formally assess the quality of the included studies. The quality scores ranged from 56 to 100% for quantitative studies (81.8 to 100%, 59.09 to 100%, and 56% to 95% for studies related to objective 1, 2, and 3, respectively) and from 50 to 95% for qualitative studies (50 to 95% and 56 to 95% for studies related to objective 2 and 3, respectively). The median quality scores for quantitative studies pertaining to objective 1, 2, and 3 were 95.45, 84.1 and 82% respectively while the median quality scores for qualitative studies pertaining to objective 2 and 3 both equalled 75%.

3.4.2.1. Quantitative studies

Studies pertaining to objective 1 were overall of good quality with the number of participants across the studies ranging from 131 to 657 (median 240) amounting to 1852 participants in total. The majority of the studies had appropriate sample sizes and their results are likely to be reliable. However, since all of the studies related to objective 1 were conducted in the US their generalisability might be restricted to this region.

There was variability in the quality of quantitative studies pertaining to objectives 2 and 3. The number of participants across the studies related to objective 2 ranged from 20 to 657 (median 106) and amounted to 2139 in total. For objective 3, the number of participants varied from 16 to 1370 (median 137) and summed up to 8029. Yet, five out of 10 (50%) studies related to objective 2 and 11 out of 26 (42.3%) studies related to objective 3 had less than 100 participants. Since most of the studies looked at large numbers of predictors and outcomes, it is possible that they were underpowered to detect significant associations or changes in outcomes. Additionally, the vast majority of the studies did not provide the information about the estimated sample size needed to power the calculations. This might have biased the results of the individual studies and thus the conclusions of this review.

Many studies used a single-centre recruitment strategy and some provided only basic descriptive statistical analysis of the data. Additionally, the majority of the studies

concentrated on well-educated, predominantly white, affluent women, which is an issue in this type of research in general. These aspects somewhat undermine the generalisability of the results of this review. In a similar vein to objective 1, generalisability of the results related to objectives 2 and 3 might also be restricted due to the fact that most of the included studies have been conducted in the US (60% and 50% for objective 2 and 3, respectively).

The majority of quantitative studies related to all three objectives used cross-sectional design. Although this allows for drawing conclusions with regard to associations between fertility issues and other variables, it precludes from inferring about the causality of these relationships.

The heterogeneity of outcome measures made comparisons between the results of the individual studies problematic. This is because different instruments, even if measuring similar constructs, might refer to different definitions of this construct (e. g., QoL or depression, for details see section 3.4.1.2.1). Additionally, some studies used non-validated instruments which made it difficult to ascertain which constructs these instruments truly measured and hence make accurate comparisons between the studies.

Even though it was specified that this review would concentrate only on psychological experience of fertility issues, the conceptualisation of reproductive issues differed across the quantitative studies. This means that comparisons between studies that employed various definitions of fertility concerns might not have yielded valid results.

3.4.2.2. Qualitative studies

The variability in the quality of the qualitative studies pertaining to objectives 2 and 3 stemmed mostly from the sampling strategies they used, poor reporting of theoretical frameworks underpinning data analysis, as well as the lack of acknowledgement as to how the authors' backgrounds could have influenced data analysis and interpretation.

A lot of the studies used convenience sampling where the selection of subjects is based on their accessibility (297). This strategy is easier to implement than purposeful or theoretical sampling, however, it might preclude the recruitment of subjects with a wide variety of opinions on the topic of interest which can in turn lead to biased results and restrict their transferability (297).

Other issues limiting the transferability of qualitative findings, similar to the ones already mentioned while discussing the generalisability of the quantitative studies, include the homogeneity of participant samples within the studies as well as locations across the studies. Most of the women who participated in the qualitative studies were white, well-educated, and affluent. Therefore the results of this review need to be applied with caution to minorities or women from lower socioeconomic backgrounds since their representation of fertility issues might differ from what has been presented in this synthesis. Also, although the diversity of locations where the qualitative studies were conducted was greater than the quantitative studies used, most of them took place in the US (36%), Australia (24%), and UK (21%) which again constrains the transferability of the findings to other social contexts. This is particularly important in the case of research into fertility since the construct of fertility depends strongly on socio-cultural norms (47, 136, see also section 2.2.3).

An issue that undermined the credibility of the included studies was a frequent lack of detailed reporting regarding data analysis methods. Although the majority of the studies used some variation of thematic analysis, only the minority described an exact theoretical framework that guided data analysis. Validity was also weakened due to the fact that authors often failed to perform or report procedures to verify their findings such as data triangulation, member checking or negative case analysis. Only 39% of the included studies described the verification procedures used to assure their credibility.

Finally, even though the majority of the studies described the limitations of qualitative design, none has accounted for the researcher effect which stems from the preconceptions that every researcher brings into the project. Researcher's background influences all aspects of his or her research starting with the topic he or she chooses to investigate and ending with the findings he or she chooses to report and the way these are framed and communicated (298). It has long been acknowledged that the neutral observer does not exist and that objectivity in qualitative research relies on accounting for researcher's position (298). Failing to reflect on one's own preconceptions and how they influenced the research process can introduce bias into the research findings and undermine their credibility.

3.4.2.3. General limitations of the review

This review only looked at published literature which due to publication bias might have led to the omission of studies that presented non-significant results. Due to the lack of resources this review was also limited to the literature published in English, French, and Polish and grey literature was omitted from the search strategy due to time constraints. For all these reasons, there is a risk that this review did not capture all the existing evidence and its conclusions should therefore be treated with caution.

Also, this review was conducted by one researcher only and failing to acknowledge the researcher's background, especially with regard to the qualitative synthesis, could bias the results. Being mindful of that, a reflexivity statement accounting for the researcher's preconceptions and how they could have influenced this analysis is presented below.

3.4.3. Reflexivity statement

It has been long acknowledged that qualitative inquiry involves a degree of subjectivity and a neutral observer as such does not exist (298), it is therefore important to outline the researcher's own effect on the process of data collection and analysis. This is known as reflexivity. This section applies to both the thematic synthesis of the qualitative literature being part of the systematic review and to the qualitative study conducted as part of this PhD project.

I have approached this project bringing in multiple perspectives and identities. First of all, I approached it from a personal perspective, yet, I also brought in my multiple professional identities including my identity as a junior doctor, a trained psychologist, and a researcher. They have all contributed to how this project was conducted and are discussed below.

Personally, I have never been in a position where I would have to decide whether or when to have children. My attitude towards motherhood is rather ambivalent, however, I have found myself thinking about it more and more often since my friends started having children. I am still unsure as to whether I wish to have children. Nonetheless, I believe that motherhood is an important experience which I might regret missing on if it comes to that. I approached my literature review and the qualitative part of this PhD project with this in mind. Particularly with respect to the interviews I have conducted, I

found myself quite emotionally affected by my participants' stories. In terms of age I was very close to some of these women. I imagined myself being in their situation and anticipated that I would have been under enormous stress had I had to make decisions they needed to make. Perhaps I have projected some of these emotions on the way the interviews were conducted and the data subsequently analysed. This might have also affected the way I read and synthesised the existing evidence.

On the other hand, from my perspective of a junior doctor which often prevailed over my identity as a psychologist, I approached this research project with a practical focus in mind trying to pinpoint issues that could be changed and improved rather than look for psychological constructs in the data. I have used theoretical frameworks while working with the data, however, this was to facilitate future practical application of the findings.

Finally, as a researcher, when I first approached the project, I was relatively inexperienced in qualitative inquiry. This possibly influenced the way interviews were conducted, particularly in the early stages of the study. Someone with more experience in qualitative research, and specifically in research into sensitive topics might have handled the interviews differently. I needed some time to gain confidence in my own skills and feel comfortable probing participants about more personal issues. Therefore, some of the initial interviews might have been not be as in depth as the latter ones.

In conclusion, a number of factors may have influenced the way the questions in the interviews were asked, how women responded to them, and how the original data as well as the literature have been analysed.

3.4.4. Conclusions

Overall, fertility issues play an important role in young female cancer patients' lives. Specifically, the evidence suggests that:

1. The psychological experience of fertility issues is associated with women's childbearing status and their desire to have children, however, the findings regarding other factors such as sociodemographic and medical characteristics remain inconclusive.

2. Fertility issues can have a profound impact on young women's post-cancer lives in terms of their QoL and ability to regain normality after cancer treatment.
3. While making treatment decisions which can affect their reproductive potential, women engage in a process of balancing survival and fertility and subsequently pursue treatments in line with their values. Although the process of decision-making is a complex one, it can be facilitated by the physician's involvement in information provision and support through the process. The importance of involving physicians, being provided with information, and having one's preferences taken into account throughout the decision-making process suggest that women's preferred way of making treatment decisions is best reflected by the Shared Decision Making model.

Current literature, although relatively extensive, is by no means comprehensive. First of all, as the evidence remains inconclusive, more focused research is needed into factors associated with the psychological experience of fertility issues to enable healthcare professionals to better recognise patients' fertility-related needs. This gap is addressed by the quantitative study where research question 1 specifically investigates predictors of the distress related to reproductive issues among young women diagnosed with breast or gynaecological cancer.

Also, research involving more diverse locations and cross-cultural comparisons is warranted since the field of cancer-related fertility seems to be dominated by research from the US. This gap is addressed throughout the quantitative study which was designed to examine fertility-related distress, fear of recurrence, and QoL among young breast or gynaecological cancer survivors recruited from two different countries, namely the United Kingdom and Poland. This recruitment strategy not only allows for expanding the evidence base in the field of oncofertility in the UK, and addressing issues that have never been studied in the Polish setting before, but also for comparisons between the two countries. The reasons behind choosing these two particular European populations stem from studies in cross-cultural psychology conducted by the Hofstede Centre and also some scarce evidence from the field of oncofertility. As indicated by cross-cultural research by The Hofstede Centre (149), the UK, as opposed to Poland, is considered to be a particularly individualistic society. Greil, A.L. et al. (47) in turn

suggest that the role of reproductive health varies between egocentric (or individualistic) and sociocentric societies. Although according to The Hofstede Centre (299), Poland cannot be considered a purely sociocentric society, it would be expected that because of the cultural differences between the UK and Poland (see section 2.2.3.2.1), the perceived importance of fertility might also differ. Indeed, the only international study that examined fertility issues among young breast cancer patients (233) found notable differences between women from Western and Eastern Europe in terms of how much importance they attached to their fertility. Following up on these findings, including British and Polish women in an oncofertility study allows for further exploration and potentially clarification of these differences.

Finally, more theoretically guided studies which could provide insight into how cancer-related fertility issues are conceptualised by women and how they can affect their lives are needed. This gap is addressed by the qualitative and quantitative study both of which, to a varying extent, are driven by the CSM (quantitative and qualitative study) and the Shared Decision Making model (qualitative study). This allows not only for describing the studied phenomena but also for uncovering the mechanisms behind them (300). This in turn, is a pre-requisite to designing interventions to tackle the problematic issues. The detailed discussion of how the qualitative and quantitative studies address the gaps in the existing literature are provided in sections 4.1 and 5.1, respectively.

Chapter 4 Treatment decision-making in the context of fertility – a qualitative study

This chapter focuses on the qualitative study conducted as part of this PhD project. First, the rationale for the study, with reference to the systematic review of literature and the gaps identified within the existing evidence, is presented (section 4.1). Second, the aims of the study and the research questions it attempts to answer established based on the gaps in the knowledge are outlined (sections 4.1.1 and 4.1.2). The methodology of the study is summarised explaining the choice of the qualitative method (section 4.2.1), inclusion criteria for the study (section 4.2.1.1), recruitment strategy (section 4.2.1.2), ethical considerations (section 4.2.2) as well as data collection (section 4.2.3) and analysis (section 4.2.4). The results are then presented as themes in a manner reflecting the chronological order of events from diagnosis through treatment to the survivorship phase (section 4.3). The conceptualisation of themes reflects the components of the CSM and the Shared Decision Making model which served as a framework to organise the data. The findings of the study are discussed in the context of the two models as well as compared and contrasted with the existing literature (section 4.4.1). Its limitations are presented and their influence on the conclusions that can be drawn from the study is described (section 4.4.2). Since the study uses two different types of recruitment – the face-to-face and online strategy – a separate section is dedicated to discussing the potential advantages and disadvantages of this approach and how these can be used to guide future studies in oncofertility (section 4.4.3). The chapter concludes with a brief description of the main study findings and highlights the results that are novel in the field (section 4.4.4).

4.1. Introduction

Cancer treatments have the potential to affect young women's fertility and this in turn can have an effect on their psychological well-being in survivorship (see section 3.3.2). Decisions regarding treatments can be the first step for women to try and preserve their fertility should they find it important, and prevent potential negative effects related to reproductive issues occurring later on in survivorship.

Research exploring how reproductive age women make their cancer-treatment decisions in the context of fertility has been growing for the past 10 years. The systematic review

I conducted (see section 3.3.3) identified a breadth of both quantitative and qualitative literature pertaining to this topic. The evidence suggests that for a substantial minority of women fertility is a significant factor influencing their cancer-treatment decisions. Women engage in a process of value clarification and balance fertility against survival and prognosis to decide whether they wish to take steps to preserve their fertility in the context of cancer treatment. Their decisions are constrained by multiple factors including their age, institutional and cost issues, their relationship status and psychological burden of making such a decision. Despite the many barriers, provision of information and relationship with the clinical team can act as facilitators to decision-making. While this evidence gives quite a comprehensive image of women's experiences of treatment-related decision-making, it is not free of limitations.

The existing research has been predominantly conducted in the US (36%) and Australia (24%) with some of it in the UK (21%). The evidence from studies concentrating on the experience of infertility suggests that it is conceptually based on two components – the medical and the socio-cultural one (47). The latter means that culture-specific and cross-cultural studies need to be conducted into the subject. Although nine UK-based studies (seven of which were qualitative) were identified in the systematic review, most of these investigate the experiences of fertility issues raised alongside cancer diagnosis or later in survivorship (189, 190, 255, 256) and fertility-related information needs (251). Whilst these studies provide decision-related data, they do not concentrate specifically on exploring the decision-making process. The two studies that do, focus on breast cancer patients exclusively (247, 252). The UK-based evidence regarding decisions about endocrine therapy is limited to one study (236). These gaps in the existing literature are addressed in this study by explicitly targeting treatment decision-making processes and including both breast and gynaecological cancer patients.

Another limitation of the literature is a methodological one, namely the lack of studies investigating treatment decision processes over time. To date, the only study to use longitudinal qualitative methodology is Connell, S. et al. (257). This PhD study was primarily designed to address this gap and explore the change in decision-making processes over time (see section 4.2.1). However, the difficulties in recruitment required

a change in methodology and the project was conducted as a cross-sectional qualitative study instead.

Although the use of this methodology is not novel in the field, a particular strength of this study is its theoretical underpinnings. Of all the qualitative studies included in the systematic review, none were guided by a particular theory or model. Whilst this does not preclude studies from producing valid and meaningful results, the lack of theoretical framework may prevent the researchers from uncovering important concepts or processes, and their explanations in the data (300). This study is informed by two theoretical models: the Common Sense and Shared Decision Making models.

The CSM was chosen from the outset and guided both the design and the analysis of the data. This is because the evidence shows that in egocentric cultures, such as the European and the Northern American ones, individuals tend to cope with medical issues by seeking medical help (75). Although physicians are responsible for accurately diagnosing and treating the condition the patient presents with, it is the patient who will live with the consequences of an illness. Many cancer patients refer to information-seeking and treatment-related decision-making to cope with the possible consequences of their disease (104-107). Additionally, it has been shown that patients' treatment decision-making processes are frequently driven by their own lay perceptions of illness and treatment (126). This study specifically sought to examine whether the CSM was applicable to young women diagnosed with cancer for whom fertility might be an important issue at the time of their diagnosis.

The Shared Decision Making model was selected to guide the data analysis based on the findings of the systematic review which suggest that the main components of women's decisions regarding treatment coincided with those of the model. Therefore, using this framework allowed for comparing and contrasting the results of this study with the existing evidence.

4.1.1. Aims

The primary aim of this study is to gain insight into how young women diagnosed with breast or gynaecological cancer make their cancer treatment-related decisions and to what extent these decisions are affected by fertility issues and fear of cancer recurrence.

The secondary objective was to investigate the change of perspective on treatment decisions over time, however, because of the difficulties with the recruitment process this line of inquiry was discontinued (for details see section 4.2.1)

4.1.2. Research questions

The following research questions exploring treatment-related decision-making in detail were established in order to achieve the primary aim of the study:

1. How do young women make their cancer treatment-related decisions?
2. To what extent do illness perceptions (particularly the consequences including fertility issues and fear of cancer recurrence) play a role in women's cancer treatment-related decisions?
3. How do women perceive their treatment-related decisions from the post-treatment perspective?

The last research question reflects the longitudinal component of the study:

4. What is the interplay of fertility issues and fear of cancer recurrence at the time of the decision-making and over time?

This study addresses the first three research questions. As mentioned above, due to the difficulties recruiting appropriate participants, research question 4, referring to the time component of the decision-making process, could not be answered and was discarded (see section 4.2.1).

4.2. Materials and methods

4.2.1. Study design

Maxwell, J.A. (301) identified five types of study goals where qualitative methodology is particularly useful and has advantage over a quantitative approach. He suggested it should be used when one wants to (1) understand how people make sense of the experience they are involved in; (2) understand the context of a particular experience; (3) understand the process underlying the experience; (4) identify phenomena based on which new theories could be generated; and (5) explore causal relationships between phenomena (301). Although this study was not designed to generate a new theory, its aims comply with the other four of Maxwell's suggestions. It addresses women's

experiences of treatment-related decision-making in the broader context of maintaining fertility, explores how women make sense of this experience and focuses on the personal meaning of fertility concerns as well as possible societal influences that may both play a role in the process of decision-making. According to the previously mentioned review by Greil, A.L. et al. (47) and the review of literature investigating cancer-related fertility concerns (see Chapter 3), the experience of infertility is shaped within a social context and qualitative inquiry enables us to investigate this aspect in a more detailed way as opposed to quantitative methodology.

The study also aimed to describe the process of cancer treatment-related decision-making and how women's experiences might change over time. Evidence from the literature suggests that fertility concerns reported by young women with cancer change along the cancer treatment trajectory (114, 226). Therefore, to explore this change and how it might affect the process of cancer treatment-related decision-making, I chose to conduct a longitudinal qualitative study. According to Miller, R.L. (302) 'the ideal method for monitoring an individual's experience of change across time would be a proper longitudinal study where the person is followed across a lengthy span of time' (p. 109). Although longitudinal qualitative design has become increasingly popular in health research (303) to date only one study has explored reproductive issues in young women with breast cancer using this method (257). None have investigated treatment-related decision-making processes in the context of fertility in a population of young women with cancer. Therefore, the initial design of this study included two in-depth telephone interviews. I planned to interview newly diagnosed cervical and uterine cancer patients before their initial treatment (surgery or radio-chemotherapy) and after the treatment and newly diagnosed breast and ovarian cancer patients before and after the course of adjuvant or neo-adjuvant chemotherapy. An interview schedule was designed for that purpose (see Appendix 8). An attempt was made to recruit participants to this study, and although five potential participants were approached, none of them chose to participate.

Since recruitment for the longitudinal qualitative study proved difficult and yielded no results, the study design was changed to a retrospective one-off telephone interview with women who had been treated for breast or gynaecological cancer within five years

prior to this study. The five year threshold was chosen to minimise participants' recollection bias. The previous interview schedule was adapted for the cross-sectional, retrospective study (see Appendix 9). The aims of the project and the research questions were also altered to reflect the change in the study methodology (see sections 4.1.1. and 4.1.2).

4.2.1.1. Participants

Participants for the study were identified and deemed eligible to participate if they:

- were diagnosed with gynaecological or breast cancer;
- were diagnosed between the ages of 18-45 years old;
- were menstruating at the time of diagnosis;
- had chemotherapy (neo-adjuvant or adjuvant) as part of their treatment if they were diagnosed with breast cancer;
- finished active treatment (with the exception of endocrine therapy for breast cancer) within five years prior to study enrolment;
- had no known evidence of cancer recurrence at the time of participation;
- spoke English or Polish

Women who were diagnosed with types of cancer other than gynaecological or breast; were diagnosed outwith the specified age range; did not undergo chemotherapy as part of breast cancer treatment; were undergoing treatment or having a recurrence at the time of invitation to participate in the study; finished treatment more than five years prior to study enrolment; were menopausal prior to diagnosis or had psychiatric comorbidities were excluded from the study.

4.2.1.2. Recruitment strategy

This study only recruited participants via the two following UK-based outlets:

- The NHS oncology clinics in Edinburgh (Western General Hospital and Royal Infirmary of Edinburgh), Dundee (Ninewells Hospital), and Kirkcaldy (Victoria Hospital)
- The online outlets of cancer charities and support organisations.

Although the recruitment process varied depending on the oncology clinics, all the participants were provided with a standard research pack including a cover letter, a participant information sheet, an opt-in form, two copies of the consent form, an interview schedule, a debriefing form and two stamped-addressed envelopes. Participants recruited online received the same standard research pack, however, it did not contain an opt-in form. Contacting the researcher via email to express interest in participating was considered equivalent to the opt-in form.

4.2.1.2.1. Gynaecology/oncology clinics (Edinburgh, Dundee, and Kirkcaldy)

Potential participants were initially informed about the study by one of the collaborating consultants or nurses and if interested in participating, I then approached them after their oncology consultation. I explained the study to the potential participants and handed them the research pack which they were encouraged to take home and consider in their own time whether they would want to take part in the study. They were advised to familiarise themselves with the study information and the interview schedule prior to filling out the opt-in form and sending it back to the researcher should they wish to participate. The interview schedule was included in the research pack so that participants were fully aware of the content of the interview and could make an informed decision as to whether they felt comfortable participating in a discussion that touched upon sensitive topics. Although women were advised to take the research pack with them and send the opt-in form via post, five participants decided to fill out the opt-in form in the clinic. The opt-in form asked for participant's name and contact details. Up to two weeks after receiving the opt-in form, I called potential participants to discuss the project, answer any questions the participants had, and solicit consent. During that first phone call, the date for the interview was scheduled. Participants were asked to sign both copies of the consent form and send it back using one of the stamped-addressed envelopes. Consent forms were then counter signed by the researcher and one copy was sent back to the participant for her own record (one participant only sent back one copy of the consent form, in this case the form was counter signed and retained for audit purposes). Interviews took place after the consent forms were obtained from participants. Eight participants were recruited in total through gynaecology and oncology clinics (for recruitment details see Table 4.1).

4.2.1.2.2. Breast clinic (Dundee)

Potential participants were initially identified through the case notes screening. The Caldicott Approval from the NHS Tayside was obtained to make this process possible. I screened the case notes against a screening chart and where the patient met all the eligibility criteria, I inserted the research pack into the case notes to let the clinician (a consultant or a nurse) treating the patient during consultation know that the patient was eligible for the study. The clinician then informed the patient about the study during the consultation and if the woman was interested in participating, I then approached her after the consultation to explain the study to her. From this point on, the procedure followed the steps outlined in section 4.2.1.2.1. Out of the two participants recruited in this site, both decided to fill out the opt-in form in the clinic (for recruitment details see Table 4.1).

Table 4.1. Participant recruitment details for NHS clinics

Site	Clinic	Recruitment dates	Research packs given out	Opt-in forms returned (recruitment rate)	Participated in interviews (participation rate)
Dundee, Ninewells Hospital	gynaecology outpatients	Jan 2015 – May 2015	1	0	0
Dundee, Ninewells Hospital	oncology outpatients	Apr 2015 – May 2015	5	1 (20%)	1 (20%)
Edinburgh, Western General Hospital	oncology outpatients	Oct 2014 – May 2015	24	7 (29.17%)	6 (25%)
Edinburgh, Royal Infirmary	gynaecology outpatients	Oct 2014 – May 2015	1	0	0
Kirkcaldy, Victoria Hospital	gynaecology outpatients	Oct 2014 – May2015	3	2 (66.67%)	1 (33.33%)
Dundee, Ninewells Hospital	breast outpatients	Oct 2014 – May 2015	5	2 (40%)	2 (40%)
Overall			**39**	**12 (30.77%)**	**10 (25.64%)**

4.2.1.2.3. Online outlets

Information about the study was also distributed online by British cancer charities and cancer support organisations. They were first approached via email or private message on Facebook to inquire whether they would be willing to disseminate information about the study. Organisations that agreed to facilitate the recruitment did so in their own capacity using different online outlets (for details see Table in Appendix 10). The most frequently used Twitter-based strategy involved the researcher tweeting about the study and the organisations retweeting the information. In the process, tweets were not only retweeted by the charities but also by anybody on Twitter who wished to do so. Overall, I tweeted the information about the study 18 times and it was retweeted 38 times over a period of eight months. Information posted online included a link to an advertisement designed for the purpose of this study (see Appendix 11) which outlined the study inclusion criteria and advised the women who were interested in participating to contact the researcher via email providing their name and contact details (postal address and phone number). This was equivalent to sending back the opt-in form in the clinic-based recruitment. Women who contacted the researcher were then sent the research pack and from this point on the procedure followed the steps outlined in section 4.2.1.2.1.

The online recruitment took place between October 2014 and May 2015. During this time 17 women expressed interest in participating in the project. Two of them were ineligible to participate (one was still undergoing treatment at the time of the study and one was treated more than five years prior to the study). Fifteen research packs were sent out and 14 women consented to and participated in the interviews for a participation rate of 93.33%. Although they were all advised to sign two copies of the consent form five of them only retrned one copy. In those cases the form was counter signed and retained by the researcher for audit purposes.

The recruitment strategy yielded a sample of 24 participants in total. Because of the sensitive nature of the study, I relied on convenience sampling. This means that although women with various socio-demographic and disease-related characteristics were approached for participation, none were targeted specifically through purposive sampling. This was to decrease the pressure to participate in the study. Nonetheless, the convenience sampling strategy yielded participants with a wide range of characteristics

in terms of cancer diagnoses and treatments received, age, relationship status (at the time of diagnosis and at the time of interview), childbearing status, and the use of FP (for details see Table 4.2 in section 4.3.1).

While the inclusion criteria indicate that Polish-speaking women would be included in the study, these participants were not actively sought. Although two were approached for participation, they decided not to participate.

4.2.2. Ethical consideration

The ethical approval for the project was sought and received from the East of Scotland Research Ethics Service (REC1) as well as from the School Ethics Committee at the School of Medicine, University of St Andrews (for approvals see Appendix 12).

The following issues were taken into account when designing the study:

4.2.2.1. Psychological harm

Although the participant information sheet explained potential risks to participants including distress due to the sensitive nature of the study, additional support was offered to those participants who needed it and contact details to a clinical psychologist working with cancer patients were provided on the debriefing form.

The interview schedule was included in the research pack for every participant to familiarise herself with the questions prior to consenting to participate in the study. This was to enable each woman to make an informed decision as to whether she felt comfortable discussing potentially sensitive and distressing topics.

4.2.2.2. Pressure to participate

To prevent the pressure to participate, no time constraints to opt-in were imposed on participants. The researcher only contacted those women who:

- sent back the opt-in form (gynaecology/oncology clinics)
- left the opt-in form in a sealed box or sent it back (breast cancer clinic)
- contacted the researcher directly and provided her contact information (through online outlets)

This prevented the use of purposive sampling, however, as mentioned above, the convenience sampling strategy produced a group of participants with various socio-demographic and disease characteristics.

4.2.2.3. Confidentiality and anonymity

To protect participants' confidentiality, paper data including opt-in forms, consent forms, notes and reflexive diary were kept in a locked cabinet in an interviewing room with swipe card access. Computer data including audio-recordings and interview transcripts were stored on an encrypted memory stick kept locked in the cabinet with the paper data. To assure anonymity, identifiers were removed from the transcripts and numeric codes were assigned to link the interview data with the respective notes.

4.2.2.4. Inconvenience to participants

The researcher tried to keep any inconvenience of participating in the study to a minimum by choosing to conduct phone interviews at a time that suited the participant.

4.2.3. Data collection

Despite face-to-face interviews being described as the "gold standard" in qualitative research (304, p. 389), I chose telephone interviews primarily to facilitate data collection from women who were recruited via online outlets and thus could potentially live in any part of the United Kingdom.

However, telephone interviews also possess other merits that were important in the context of this study. A systematic review of literature investigating the use of telephone interviews in qualitative research suggests that this mode of interviewing allows the participant to remain anonymous, permits privacy, diminishes social pressure, and thus enables participants to disclose sensitive or intimate information more freely (305). This was of paramount importance in this study since the topic of fertility might be considered a sensitive issue.

The interviews were guided by an interview schedule designed for the purpose of the study. The questions aimed at exploring women's experiences of cancer treatment-related decision-making, the importance of fertility in this process and also their illness perceptions (for the interview schedule see Appendix 9). Each interview started with an opening question asking the participant to describe the circumstances of her cancer

diagnosis and the treatment process she underwent. Every interview followed the interview schedule, however, questions were asked in different order depending on the flow of the conversation and participants' answers. Each interview ended with a question asking whether the participant had anything else to add and this is where participants had a chance to speak about other issues they faced because of their cancer diagnosis at a young age. Answers to this question yielded additional themes that were not directly related to the research questions yet enriched the understanding of the participants' cancer experiences. Participants were also asked to provide basic socio-demographic details (current age, country of origin, relationship status, childbearing status, monthly income before tax, and the highest education level) as well as disease characteristics (type of cancer, stage of cancer at diagnosis, types of cancer treatment received and date of diagnosis) if these were not mentioned during the interview. The interviews lasted on average 55 minutes, ranging from 22 to 121 minutes.

All the interviews were digitally recorded and transcribed verbatim. Identifying details were removed from the transcripts and each transcript was assigned a numeric code. I took notes during interviews and wrote a reflexive statement after each interview. The notes and the reflexive statement were assigned the same numeric code as the interview transcript to link all the relevant participant data.

4.2.4. Data analysis

The data were analysed using the principles of thematic analysis outlined by Braun, V. and V. Clarke (306). They present thematic analysis as a standalone qualitative data analysis method for 'identifying, analysing, and reporting patterns (themes) within data' (306, p. 79) and describe six phases of data analysis:

1. Familiarisation with data
2. Generation of initial codes
3. Searching for themes
4. Reviewing themes
5. Defining and naming themes
6. Producing the report

One of the important advantages of thematic analysis is its flexibility. As opposed to other methods of qualitative analysis [e. g., interpretative phenomenological analysis (307), grounded theory (308) or narrative analysis (309)] it is not tied to any particular epistemological or theoretical approach (306). It can, therefore, be adapted to the researcher's needs in terms of epistemological or theoretical framework. Another benefit of thematic analysis lies in the fact that, while many qualitative methods are purely inductive, thematic analysis can be used in both an inductive and deductive manner (306). These two characteristics of thematic analysis guided the choice of the analytical method for this study. A method that would allow for a deductive approach and application of a specific theoretical framework to the data (CSM and Shared Decision Making model) was essential for this project and thematic analysis fulfilled these criteria.

The stages outlined by Braun, V. and V. Clarke (306) were followed throughout the data analysis process. First, the interview transcripts were read and reread for a thorough familiarisation with the data. Next, all the transcripts were uploaded to QSR International's NVivo 10 Software (199) and the first cycle coding method – the descriptive coding – was applied to the data. Descriptive coding uses short phrases to summarise topics reoccurring in the data (310). Once all the data were coded, the second cycle coding method – the pattern coding – was applied. The pattern coding allows for grouping of the descriptive codes and making sense of the relationships among them (310). Through further reading and rereading of the interviews, secondary codes were refined to better reflect the data. Up to this point the data analysis was conducted by one researcher. In the next step, the map of secondary codes was applied to three out of 24 interviews by the second researcher (GO) – the project supervisor. Where discrepancies in coding between the researchers occurred, these were discussed until a consensus was reached and codes were clarified and reorganised to better fit the data.

The analysis up to this point was carried out in an inductive manner. However, since this study focused particularly on the experiences of treatment-related decision-making and was driven by the CSM as well as the Shared Decision Making model, once the secondary codes were obtained, the rest of the analysis was conducted in deductive

manner. In other words, the process of searching for themes among the codes was guided by the two underlying theoretical models (see Figure 4.1).

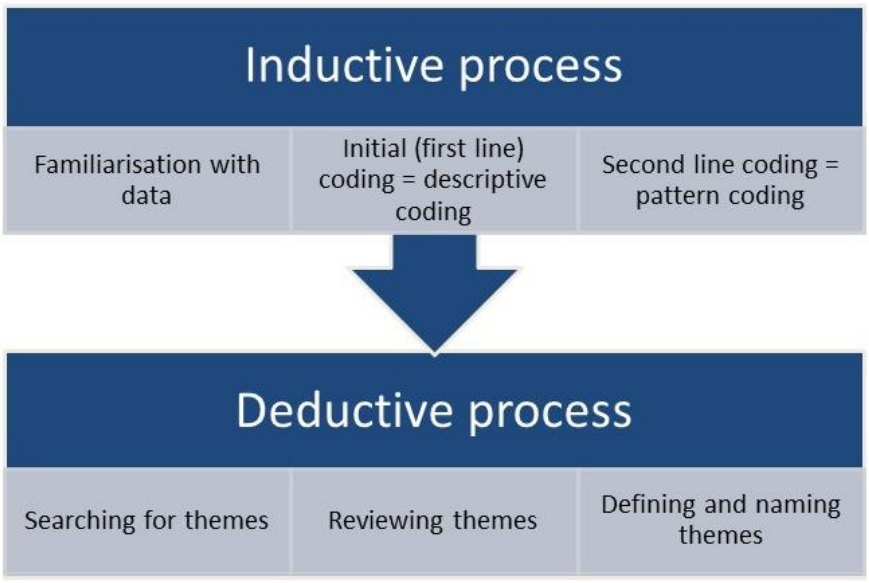


Figure 4.1. Application of thematic analysis to study data

This type of analysis, as suggested by Braun, V. and V. Clarke (306), focuses on answering a particular research question and exploring the theory, rather than on providing the description of the whole dataset (understood as all the data collected for the particular project). This approach results in a more detailed analysis of certain aspect of the dataset – in this case the data related to treatment decision-making in the context of fertility. Therefore, at this point of analysis, all the codes were reviewed again and those that did not contribute directly to answering any of the research questions were moved to a separate folder. These codes included for example, 'the side effects of treatments' (code encompassing descriptions of physical side effects of cancer treatments, as opposed to the measures women took to cope with these side effects), or 'raising awareness' (code encompassing women's efforts to get involved in raising awareness about cancer among young people). Some of the excluded codes also included those which were only mentioned by the minority of the participants (i.e., one to four women mentioned a particular concept).

The remaining codes were iteratively reread and arranged according to the main concepts involved in the CSM and Shared Decision Making model. Codes categorised as belonging to the same concepts within the theoretical models were then conceptualised into internally homogenous and externally heterogeneous themes. These themes were subsequently discussed within the research team to assure the credibility and the rigour of the analysis. Also, because the data were primarily analysed by one researcher, the reflexivity statement is included (section 3.4.3) to account for any bias that could have been introduced to the analysis.

A table compiling participant characteristics was also prepared (see Table 4.2). It presents a summary of participant characteristics rather than outlines them case by case. This way of presentation facilitates thinking about the data as a whole rather than in terms of each participant's account separately and was used because the interviews were analysed using thematic analysis which aims to identify patterns across data as opposed to other methods (e.g., interpretative phenomenological analysis) which concentrate more on individual participants' stories.

4.3. Results

4.3.1. Participant characteristics

Ten participants were recruited via the NHS clinics and 14 participants through the online outlets. The average age at the time of the interview and at the time of diagnosis was 36.7 (range 28-45) and 34.4 years (range 26-43), respectively. Participants included 11 women diagnosed with breast cancer, five with cervical cancer, four with ovarian cancer or borderline tumour, and four with uterine cancer. Most were diagnosed within two years prior to the study (67%). Five of the women who had breast cancer underwent a mastectomy and three chose to have a contralateral prophylactic procedure later on. Six women had breast conserving surgery – a lumpectomy or a local wide excision. All participants who had breast cancer received radiotherapy and chemotherapy (five received neoadjuvant and six received adjuvant chemotherapy). Ten of them did or were still undergoing endocrine therapy (tamoxifen). Three of the cervical cancer patients underwent radical trachelectomy, however, one required a simple hysterectomy later due to cancer histological characteristics. Two other patients had radical hysterectomy as first line treatment and both also underwent chemo-radiation. All participants who

had uterine cancer required radical hysterectomy. Additionally, two of them underwent radiotherapy and one also had chemotherapy. Two women who were diagnosed with borderline ovarian tumour received radical hysterectomy and one also required chemotherapy. One participant who had epithelial ovarian cancer initially refused a hysterectomy and underwent bilateral salpingo-oophorectomy. However, due to cancer spread she underwent hysterectomy and received chemotherapy later on. Finally, one woman with borderline ovarian tumour initially underwent unilateral salpingo-oophorectomy and had a contralateral procedure done a year later.

At the time of diagnosis, 18 participants were in a partnered relationship. Two participants who were single at diagnosis had a partner at the time of the interview and one participant who had a partner at the time of diagnosis was single at the time of the interview therefore, 19 participants were in a relationship at the time of interview. The majority of participants did not have any children at the time of the interview (63%). Seven women had children prior to cancer diagnosis, one participant who had no children prior to cancer had a child after diagnosis via surrogacy and one participant who had one child prior to cancer had a healthy pregnancy and gave birth to a child after her diagnosis. The majority of participants (67%) could not or decided not to take measures to preserve their fertility. Among those who did, four women cryopreserved embryos, two received GnRH agonist injections during chemotherapy, and three underwent radical trachelectomy, however, as mentioned above one of them required a completion hysterectomy later. Finally, the majority of participants spoke English as their first language (96%) and had at least some university education (79%) (see Table 4.2).

Table 4.2. Participant characteristics

Characteristic	Number (%)
Current age (years)	
≤ 30	1 (4%)
31-35	11 (46%)
36-40	6 (25%)
41-45	6 (25%)
Cancer diagnosis	
Breast	11 (46%)
Cervical	6 (21%)
Ovarian	4 (17%)
Uterine	4 (17%)
Time since diagnosis (years)	
0-2	16 (67%)
3-5	8 (33%)
Partnership status at diagnosis	
Partnered	18 (75%)
Unpartnered	6 (25%)
Partnership status at interview	
Partnered	19 (79%)
Unpartnered	5 (21%)
Education	
Less than university education	5 (21%)
At least some university education	19 (79%)
First language	
English	23 (96%)
Other	1 (4%)
FP	
Yes	8 (33%)
ARTs	4 (17%)
GnRH agonist injections	2 (8%)
Trachelectomy	2 (8%)
No	16 (67%)
Childbearing status	
No children	15 (63%)
Child(ren) before diagnosis but not after diagnosis	7 (29%)
No child(ren) before but child(ren) after diagnosis	1 (4%)
Child(ren) before and after diagnosis	1 (4%)

4.3.2. Themes

Six main themes pertaining to treatment-related decision-making experiences among young women diagnosed with breast or gynaecological cancer were identified throughout the data. These themes include: *Cancer diagnosis as a surprise because of*

age and perception of symptoms; Becoming aware of infertility as a potential consequence of cancer treatment; Attitudes towards fertility as a factor affecting cancer perceptions; Decisions about treatments; Evaluation of treatment decisions; and *The consequences of treatments*. Subthemes that were identified within the themes are described in detail under the appropriate themes.

The themes were first organised around the four components of the CSM: 'appraisal of health threat,' 'perceptions of illness,' 'strategies to cope with illness,' and 'appraisal of these strategies' (see Figure 2.2).

The appraisal of health threat and perceptions of illness are represented throughout the following themes: *Cancer diagnosis as a surprise because of age and lack of symptoms; Becoming aware of infertility as a potential consequence of cancer treatment;* and *Attitudes towards fertility as a factor affecting cancer perceptions* (see Figure 4.2).

Treatment decision-making processes were conceptualised as a strategy to cope with the illness and are represented in the theme *Decisions about treatments* (see Figure 4.2). The subthemes that were identified within this theme reflect the concepts of the Shared Decision Making model as it pertains to the clinical settings (see section 2.2.2.2).

Finally, the themes *Evaluation of treatment decisions* and *The consequences of treatments* represent the last component of the CSM – the appraisal of coping strategies (see Figure 4.2). Traditionally, in the CSM, the information gained through the appraisal process feeds back into the coping strategies and allows for their modification as appropriate to a specific situation. In the case of treatment decisions, however, that would be impossible since once treatments had been administered one cannot take back one's decision (e.g., to pursue FP or not) and opt for a different regimen. One can only cope with the consequences of these decisions made at the time under difficult circumstances. The last theme describes these consequences as well as women's attempts to cope with them in a situation where the change of treatment decisions is impossible.

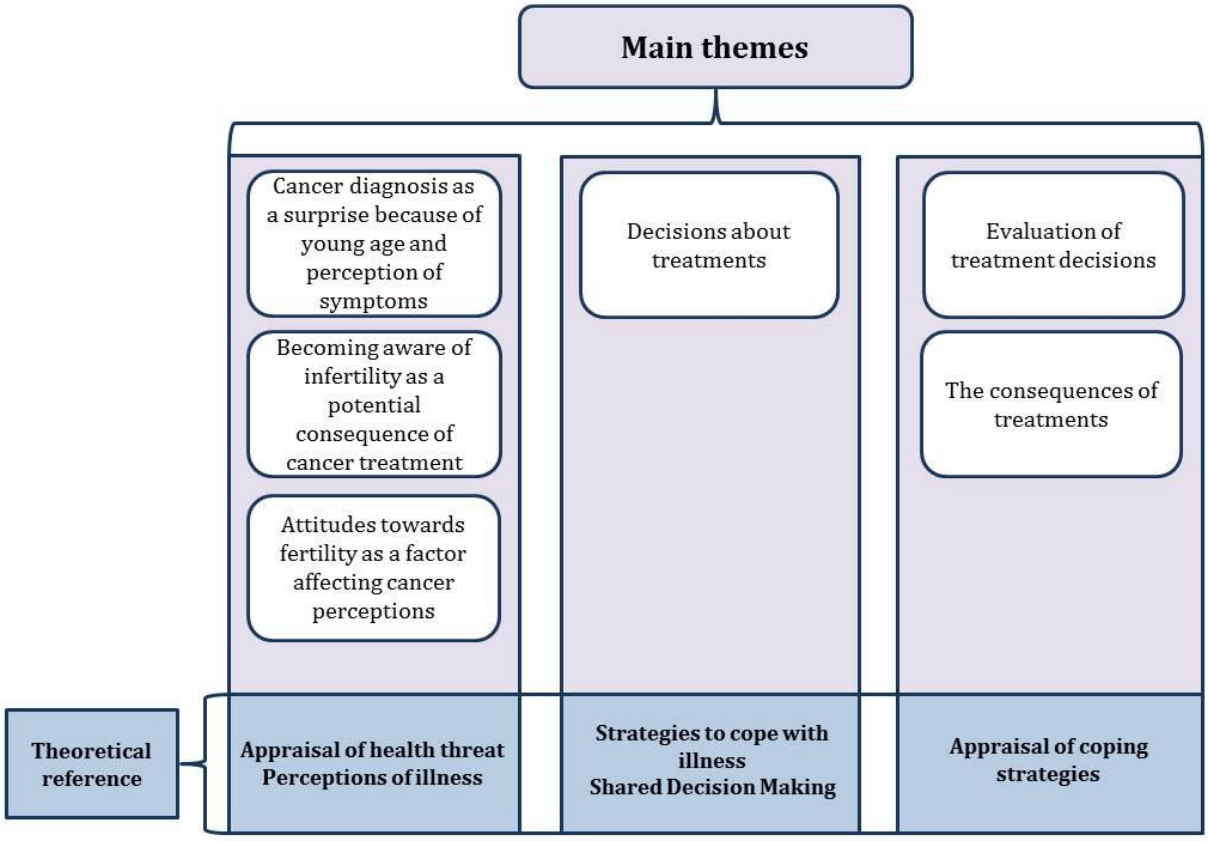


Figure 4.2. Main themes with their references to theory

4.3.2.1. Cancer diagnosis as a surprise because of young age and perception of symptoms

The circumstances in which women were diagnosed with cancer differed among the participants. For women with breast cancer, it was most often the event of finding a lump, sometimes in the context of breastfeeding. Symptomatic diagnosis was also the most frequent route to diagnosis for women with ovarian or womb cancer. Those who had cervical cancer were all diagnosed through the screening programme. The occurrence of symptoms, or the first contact with the healthcare professionals where the participant had no symptoms prompted the process of initial conceptualisation of the health threat women were facing. Women's illness perceptions were based on their symptoms (or lack of thereof), their pre-existing knowledge about cancer, and also their interactions with physicians.

Many women recounted that they did not have any initial symptoms or the symptoms they did have did not seem to be indicative of a serious illness. Women who

experienced gynaecological problems tended to minimise them and associate them with their menstrual cycles or taking oral contraceptives. Women with breast cancer generally assumed their lumps were harmless and those who were diagnosed in the context of breastfeeding thought their lumps were related to the physiological changes to their breasts or breastfeeding complications. Women's perception that their symptoms were benign was also reinforced by the attitudes of their physicians. Several women mentioned that their GPs, who were their first point of call to enquire about these symptoms, told them that they had nothing to worry about.

My GP kept telling me not to be silly, if they thought it was cancer… basically stop… stop dwelling on that and thinking about it.

P18, borderline ovarian tumour diagnosed at 31, 2 children before diagnosis

Women also perceived their young age to be a factor that protected them from cancer. Many of them were unaware of the fact that cancer could be diagnosed at any age. This assumption in women's views was also reinforced by some of the physicians. Several women described how their GPs reassured them that because of their age, the symptoms they were experiencing were unlikely to be related to a serious illness.

Even my own GP, you know, well 'you're only young'. You know, 'It can't be cancer', and then they did this… a swab… or a smear, whatever and that came back clear and they said, you know, 'See, it's not cancer'. And… obviously, you know, it was cancer.

P05, womb cancer diagnosed at 31, 1 child before diagnosis

Although most women were promptly referred by their GPs for further investigations in specialist centres, they thought it was standard practice and did not expect to be diagnosed with cancer. The diagnosis, therefore, came as a shock and a surprise to many women. They found it hard to believe that after being reassured every step of the way that their condition was most probably innocent they would have to face the cancer and all its consequences.

And then a week later I went in for my results and sort of imagine my surprise, shock and horror that I actually found out that I had stage III, invasive breast cancer in both lumps. […] Because I've sort of been assured by them the whole way over the 6 weeks'

process that it… it wasn't anything to worry about and in my mind I thought 'Of course it's nothing to worry about because otherwise they would have hurried this up'.

P01, breast cancer diagnosed at 32, no children

4.3.2.2. Becoming aware of infertility as a potential consequence of cancer treatment

Alongside the initial shock of transitioning from being a healthy individual to being a cancer patient, women also became aware of what that meant for their fertility. Whether they were diagnosed with gynaecological or breast cancer, most of them had a perception that treatments could be detrimental to their reproductive potential. While for some that was not an issue, others wanted to know what could possibly be done to spare or preserve their fertility. Two scenarios became apparent in women's accounts: fertility discussions were either part of the consultation and initiated by the physicians or they needed to be broached by the women themselves.

For some women, a member of their clinical team, either a consultant or a nurse, brought the topic of fertility up during one of the consultations. Most women appreciated this, irrespective of whether they were interested in preserving their fertility. They welcomed the opportunity to receive the relevant information and be able to consider what it meant for them.

I mean when the… gynaecologist I had was fantastic. Honestly, absolutely fantastic. And he talked through everything. He also said that if I didn't want to go through a hyst… a hysterectomy just now he could monitor it over a period of time, they could try and give me… oestrogen I think it was and to see if I would… if I could conceive over a period of time and they would help me… but he then told me the consequences of doing that, which is the cancer could grow quicker, you know it might be that I could conceive but I couldn't carry a child, loads of different things. He explained everything fully, gave me the pros and cons and then you know, sent me away to think about it.

P06, womb cancer diagnosed at 35, no children

When fertility discussions constituted a standard part of a consultation, women had a chance to express their preferences without having to broach the topic themselves.

However, that was not always the case. When fertility was not standard part of the consultation, the onus of initiating the discussion about was on women or their relatives.

So when I was first diagnosed my husband just happened to… say… 'Will it affect our chances of having children?' and I'm so glad he thought of asking that 'cause I… I just wouldn't have asked it. 'Cause… 'cause obviously I had lots of other things going on in my head.

P15, breast cancer diagnosed at 32, no children

On occasion, women had to assume the responsibility for getting informed regarding FP. They had to be the ones to start the conversation and at times even force their consultants to engage in the discussion about the fertility aspect of their treatment.

Yeah, it was Dr [name] who was my first oncologist [inaudible], but that was only like I said after I… stood up and said 'Is there anything we could do to preserve the fertility?' […] He wasn't willing to discuss it. It was only when I approached it… and then he said he would go away and think about it and look at my case. And it was only when he looked at my case notes and realised I was young and not like 50 – 40 and was only… like a… grade I and grade Ia that he decided to send me for the clinical trial.

P02, womb cancer diagnosed at 32, no children

In those cases, women often felt that fertility was not important to their physicians and was treated as an '*add-on'* or something extra and not part of standard care. Some even questioned whether fertility would have been discussed at all had they not broached the subject themselves.

4.3.2.3. Attitudes towards fertility as a factor affecting cancer perceptions

Although women held personal ideas and beliefs about fertility, when faced with a threatening illness, these often needed to be re-evaluated. The concept of fertility that transpired from women's accounts was bi-level. All women had certain pre-cancer expectations regarding fertility, including factors that facilitated or acted as barriers to fulfilling fertility-related plans. These, in turn, fed into women's perceptions of fertility in the context of cancer along with the life stage women were in at the time of cancer diagnosis. Faced with a threatening illness women weighed the importance of fertility

against the desire to survive the diagnosis. Through this process they formulated their priorities which were subsequently used to guide their treatment decisions. These concepts are discussed in depth in the following subthemes: *Pre-cancer attitudes towards fertility; Life stage affects the importance of fertility in the context of cancer;* and *Balancing – prioritising cancer and fertility* (see Figure 4.3).

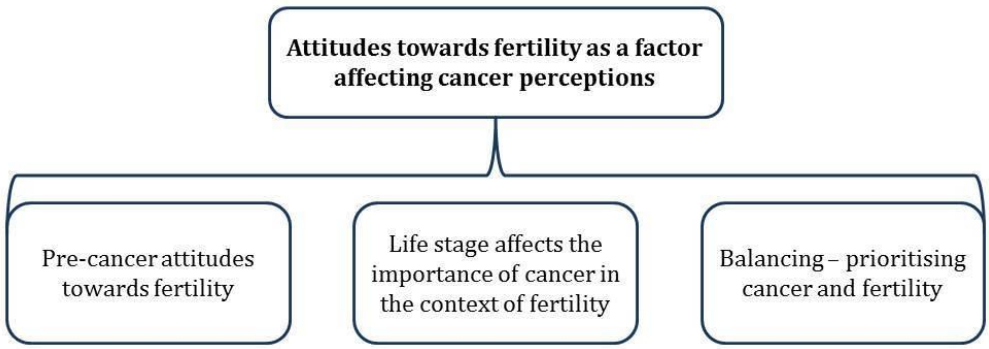


Figure 4.3. Visual representation of the theme *Attitudes towards fertility as a factor affecting cancer perceptions*

4.3.2.3.1. Pre-cancer attitudes towards fertility

Women's pre-cancer attitudes towards fertility fell into one of two distinct groups. For some, fertility was of particular importance which manifested itself in the way women described their longstanding dreams and plans regarding having children. They recounted how they always knew they wanted to have a family and imagined themselves as mothers.

I have always seen myself having a… having a family. A large family and… therefore I suppose… yeah, I'd have to say that my fertility meant every… absolutely everything to me.

P20, cervical cancer diagnosed at 31, no children

Fertility in a biological sense pertains to one's ability to have children, however, in their narratives women also extended it to building a family, in general. While for some it was crucial to be able to conceive and carry a child that had a biological link to

themselves, others were more concerned about becoming mothers '*in some shape or form'*, not necessarily through pregnancy and childbirth.

The bit that hurts and upsets me more is that I will never have a biological child… I'll never… I will never give birth to my own child, and I can't give my husband… a child, I can't give birth to part of him and part of me and… you know, have our genes living on. That's… that's the thing that hurts so much.

P06, womb cancer diagnosed at 35, no children

I would as much be happy to adopt and have a child and complete our family that way as I would be to go through the whole process myself. For me it isn't just about the having a biological child and having it myself but I don't… that isn't how I feel about it.

P16, breast cancer diagnosed at 32, 1 child before diagnosis

For those who did not have children, the importance of their fertility was highlighted once their peers started having children. Those who were already mothers reflected on the value of providing siblings for their existing children and the joy that accompanied having their first child.

Although these women admitted that fertility was something that in a way defined who they were, some of them also pointed to the fact that they might have taken it for granted. The perception that fertility was a natural given led women to believe that when the time was right they would be able to have children or complete their families.

I didn't really… I didn't really give it a second thought, I just thought, that, you know, I'd fall pregnant and, you know, there'd not really be any sort of hassle I guess. You know in… in doing so.

P11, ovarian cancer diagnosed at 31, 1 child through surrogacy after cancer

On the other hand, some women adopted a *'if it happens, it happens'* approach, accepting that they might or might not have children. Most of them did not have a pre-defined plan regarding childbearing and, as opposed to women for whom fertility was extremely important, they stressed that they had never been particularly '*broody*' or with '*a burning desire'* to have children.

I've never been broody so I didn't have that kind of, 'by this age I would like to have this many children' approach to it, if I had had children it would have been a nice surprise rather that something I'd set out to do.

P09, cervical cancer diagnosed at 40, no children

Some of them explained that, while they did not completely rule out the possibility of having children, their lifestyle did not concur with having a family. They treated fertility as an option that was available to them should they ever want to use it. For some, this was compatible with how their peers lived their lives and therefore did not feel as if they would be missing on something important had they decided not to have children at all.

I'd never really, you know, at 31 well a lot of people maybe have had a family but certainly my friends, my social circle, you know, how I live my life at 31 it'd never really been an issue.

P08, cervical cancer diagnosed at 31, no children

Regardless of whether women considered their fertility important or simply treated it as an option should they wish to have children, they all felt that in order to fulfil their fertility-related plans, certain factors needed to fall into place. Finding the right partner was one issue they touched upon. Although they might have wanted children, they did not wish to have them with just anybody or be a single parent. They would have preferred to be in a stable relationship or even get married before planning for children.

I didn't really want to do it [have children] on my own. So I'd always assumed that if I was in a long term relationship I would consider having children.

P09, cervical cancer diagnosed at 40, no children

Women, particularly in relationships, also noted that some degree of stability and security was required before they could plan for children or expand their families. Stable financial and housing situation were mentioned as preferable to fulfil fertility-related desires.

We just reached that point in our lives where… we wanted that [become parents] to be the next step. As I said, we were fairly recently married, we've been settled in the same

place for a number of years now and… […] But with [inaudible] commitments and now other things and work commitments, you know, it wasn't… it wasn't ever the right time.

P14, breast cancer diagnosed at 27, no children

4.3.2.3.2. Life stage affects the importance of fertility in the context of cancer

It appears that women needed it to be the right moment for them to settle and realise their childbearing plans. Their attitude towards fertility and hence desire to have children combined with their life circumstances contributed to the life stage they were in at the time of their cancer diagnosis. For some, cancer occurred when they were actively planning or about to plan to have (more) children.

Well, before I was diagnosed as I said, my husband and I had decided that the time was right to start trying to have children and so it was very much part of our plan at that point. So if you'd asked me 2 years ago what I'd be doing now, I'd just hopefully be a parent… but obviously that's not… not the case but… but yeah it was… it was very much on the cards for us or we hoped at that time.

P14, breast cancer diagnosed at 27, no children

Before I was diagnosed we probably would have waited another… probably 6 months and then… tried to have our second… second child. That would have been the plan.

P16, breast cancer diagnosed at 32, 1 child before diagnosis

Being in this life stage meant that fertility was very much on women's minds even before they were diagnosed with cancer. The diagnosis had the effect of bringing this issue forward. The importance they attached to fertility was reflected through their immediate questions and enquiries regarding what could be done to minimise cancer's impact on their reproductive potential as well as their emotional reactions to the situation. Some of them found receiving the news about cancer and learning about the treatment's impact on fertility equally devastating and referred to it as a '*double blow'*. Some expected that inability to have children after cancer would *'put them in therapy'*. Others found the threat to their fertility more difficult to deal with than cancer itself.

So, I was devastated… when they told me that I had the cancer I wasn't really bothered

and just said 'All right, ok then.' And then when they said 'We have to remove your womb' that's when I... that's when I fell into pieces.

P05, womb cancer diagnosed at 31, 1 child before cancer

On the other hand, for some women the diagnosis occurred at the time when they were not thinking or did not consider themselves to be in a position to have children, or they had already completed their families.

I think because I didn't… I wasn't in a lifestyle position where I wanted to do something about that [fertility] instantly. And at 40 I just didn't think it was potentially worth harvesting the eggs.

P09, cervical cancer diagnosed at 40, no children

Well, she obviously started off by asking if I had a partner at the time, if I was sexually act… active, if I was planning to have children in the near future… and at the time obviously all questions she asked… or to all those questions the answer gave her was no.

P22, borderline ovarian tumour diagnosed at 39, no children

For them, although fertility might have been generally important, in the context of cancer other issues took priority ahead of fertility. In this group, women who had already completed their families admitted however that had they not had children, fertility could have been more of an issue for them.

I kind of… the fertility would have been an option… would have been a concern had I wanted more kids.

P21, borderline ovarian tumour diagnosed at 39, 2 children before diagnosis

4.3.2.3.3. Balancing – prioritising cancer and fertility

Regardless of how important fertility was at the time of diagnosis, most women admitted that their concern was primarily for their own health and they wanted to give themselves the best chance at surviving the cancer and prevent any future recurrence.

It's more… well I mean, for… for us the main thing for us was for me to get better that was first and foremost.

P12, breast cancer diagnosed at 38, 1 child before diagnosis

Because I was worried maybe if it was gonna be growing to something… more serious. And I was worried it was gonna turn into cancer so I just wanted everything cleared out.

P22, borderline ovarian tumour diagnosed at 39, no children

Some of them were ready to suffer through the most aggressive treatments to make sure that no stray cancer cells were left behind even if that meant having to deal with the treatment side-effects and increasing the risk of losing fertility to cancer.

Women who already had children, whether they considered their family complete or not, felt responsible for their existing children and their primary concern was to get better for them. Even if it was presented as an option, they felt they could not afford an attempt at preserving their fertility at the potential cost of worsening their prognosis.

We were very much of the mind, that we have to try our best to… for me to stay alive for my son, for my child and, you know, then not… so that kind of meant that… we said that preserving fertility just wasn't an opt… you know, getting… doing an IVF effectively wasn't an option.

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Women who did not have children were willing to take more risks to try and preserve their fertility. In terms of the balancing-prioritising process, they were the ones for whom finding this balance between preserving their fertility and the desire to survive cancer diagnosis was the most difficult since the two were often valued as equally important. However, even this group of participants admitted that it would only make sense to preserve fertility if they were at some point well enough to actually become pregnant and have a child. This shows the importance they too attached to receiving appropriate and even aggressive treatments to manage their disease successfully.

And he's [the oncologist]… he's always said, which I agree, it's a balance of… it's alright having a baby but you've got to be there, to be around to bring it up (laughter). … It's quite a stark way of saying it.

P01, breast cancer diagnosed at 32, no children

The balancing-prioritising process certainly differed between women who considered fertility important at the time of their cancer diagnosis and those who did not. However, within the group of women for whom fertility was important, this process also differed between women diagnosed with breast and those diagnosed with gynaecological cancers. The difference appeared to be related to the distinct consequences that treatment decisions had for the two groups of patients.

For women with breast cancer, receiving chemotherapy did not automatically equate to becoming infertile after treatment. It rather meant that their post-cancer fertility status would remain uncertain. Although chemotherapy could hasten the menopause, if their menstrual cycles returned after chemotherapy they could still have a window of opportunity to conceive naturally. Therefore, even without FP, there was hope that their fertility would remain unaffected by cancer treatments. Additionally, in the case of breast cancer, FP was a process separate from cancer treatments. Women could choose to undergo FP as an additional procedure which involved a separate decision-making process to the one about cancer treatments. Although potentially not neutral to their cancer prognosis, FP for women with breast cancer was not directly related to their cancer treatments.

For women with gynaecological cancers, on the other hand, the two were intrinsically intertwined and therefore the desire to preserve fertility and potentially forgo some of the cancer treatments could have a much bigger impact on their prognosis and survival. There was also no element of uncertainty – once they had radical treatment, their chance at having their own child was taken away forever.

These differences could potentially explain why women diagnosed with gynaecological cancers were much more hesitant and reluctant while progressing through the balancing-prioritising process. Despite these difficulties however, most of them did choose to go forward with treatments, even at the cost of fertility.

I actually asked… when I was diagnosed, was, 'Can… can you get eggs out to, you know, preserve them? Can I keep my womb so I could, you know, at least carry a child?' And… first off, you know… I was… I was told… basically I was kind of, 'No that's… that's not sort of gold standard practice', the best thing to do increase my … my chances of survival would be to have everything removed. But I was really quite adamant I didn't want that to happen. […] I mean, I was … advised that if I did, for example, if they could get my own eggs out, that could stimulate the cancer but at that point I thought, well… I know I've got cancer already… and I'm going to get treatment for it. I'm at this point to be, you know, within the next, you know, like couple of weeks, so I thought it was worth a chance, to take that chance. I've had this cancer, I've probably had it for maybe up to a year anyway… but for the actual… for the uterus… then again I was advised that it wouldn't be a good idea… but I… I just… I really wanted to be able to carry a baby myself. And I mean… at that point I didn't… we didn't know if there was cancer… you know, I mean, at that point. It wasn't until they did… they did an r… kind of a small procedure, they did the… a D&C and that's when it appeared that was after… just to check to see, you know, if there is any cancer there. And they put a… I mean, a coil in as well to try and dampen down the… the cancerous cells that were in there. And it didn't make any difference. And that's when… after that I went on to have the hysterectomy. But yeah… if… if that was clear of cancer I would have continued, you know, to pursue the donor egg route and you know, go down that way.

P11, ovarian cancer diagnosed at 31, 1 child through surrogacy after cancer

Only one woman positioned herself in opposition to other participants and clearly stated that her priority was not to lose her fertility to cancer and save it if at all possible, even at the cost of her longer term prognosis. After weighing the pros and cons she eventually decided to opt in for a radical trachelectomy instead of a hysterectomy.

The long-term survival wasn't… my longer term prognosis didn't really ever enter my mind. I would say it did for my family, it did for my partner. I think it may have been there vaguely in the background for me but all I wanted to do was that my fertility

wasn't taken away and that my desire to carry a child wasn't taken away. And I didn't want it taken away by cancer if I could at all help it.

P13, cervical cancer diagnosed at 31, no children

4.3.2.4. Decisions about treatments

Having established their fertility and survival-related priorities, women needed to make choices regarding their treatments. Some of these decisions had to be made at the time of diagnosis (e.g., decisions about first-line treatments, opting in for fertility-sparing surgery or pursuing artificial reproductive technologies) while others later on, after the first-line treatments for cancer had finished (e.g., continuing or interrupting the tamoxifen among women diagnosed with oestrogen-receptor positive breast cancer).

Although women might have prioritised their fertility and survival in different ways, there were similarities in terms of the main processes that all of them went through. Also, even though some of the decisions needed to be made at the time of diagnosis and others later on and hence they differed in terms of timing, again the processes involved in both were very much alike. Henceforth, these main processes are presented for all the participants and all the decisions together under the following subthemes: *Perceptions of choice*; *Following the consultant's lead, Knowledge as a double edged sword, Informing vs. involving others;* and *Alignment of treatment preferences between women and their physicians, and its consequences.* Where differences occurred between treatment decisions and decisions relating specifically to FP or between decisions made at the time of diagnosis and those made later on, these are discussed within the subthemes. Factors specific to FP and interrupting the tamoxifen treatment are summarised separately under the subtheme *Specific considerations related to immediate fertility preservation and tamoxifen.* Figure 4.4 represents the visualisation of the all subthemes within this theme.

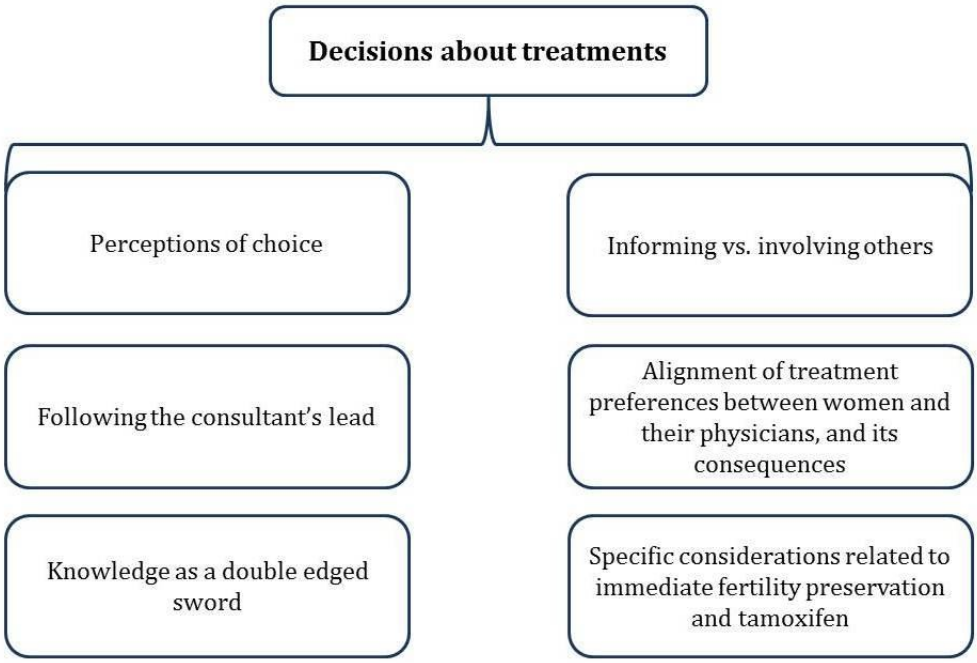


Figure 4.4. Visual representation of the theme *Decisions about treatments*

4.3.2.4.1. Perceptions of choice

Being faced with a threatening illness that could have fatal consequences if not managed appropriately and in a timely manner made women reflect on whether they were truly in control of making the decisions regarding their treatment process. Some women perceived that the choices were theirs in terms of selecting a treatment modality to spare fertility (in the case of gynaecological cancers) or deciding to pursue ARTs (to preserve fertility in the case of breast cancer). These women, however, were diagnosed with cancer at the stage where they could be presented with real options to choose from. They could weigh the pros and cons of the treatments that were available to them and actually make a decision in line with their preferences.

Actually I was told in the same 20 minute consultation of being told, yes it's cancer of my cervix and the details of that, I was then told, 'Well we need to now think about what we're gonna do'. And I was given two options. One was to have a hysterectomy and the other option was to have the radical trachelectomy. […] And it just… to me it was always everything that I wanted to do, to keep fertility. Yeah and we agreed that that would be what we would do. So I was given a choice.

P13, cervical cancer diagnose at 31, no children

For women with breast cancer specifically, pursuing FP was perceived as the only aspect of their treatment regimen where they were given leeway and could make a decision themselves. The other components of their treatment plan were seen as non-negotiable and administered to them rather than chosen by them.

The only option… the only options I was given was obviously about… was about fertility and about delaying treatment. But other than that, the treatment, she gave me.

P16, diagnosed with breast cancer at 32, 1 child before diagnosis

The lack of choice regarding the treatment regimen was by some women considered to be reassuring. They described how the treatment they were offered was a golden standard for their condition and since it had already worked for others in the same situation there were no reasons to try and change it. However, women who were happy to accept this standard treatment were more often than not, not concerned about fertility. On the other hand, women for whom fertility was an important issue described the situation of the lack of choice with respect to treatments or pursuing FP as rather upsetting and disappointing. They felt that the choices were taken away from them. Some of them placed the responsibility on the services, while others thought it was the cancer that denied them their choices.

It was mentioned that some people have… kind of the same IVF type process to preserve their eggs or… but it… I was advised against it because of the extra delays that I'd had with the diagnosis and then because of the spots they'd found on the liver… the oncologist really felt there wasn't the time to wait which is… another… kind of upset really that the doctor [GP] had waited so long to refer me that I'd lost that opportunity really.

P04, breast cancer diagnosed at 29, no children

But I'm not saying that in a way that I feel like the… the consultants left me with no choice. I just felt like the situation left me with no choice.

P20, cervical cancer diagnosed at 31, no children

4.3.2.4.2. Following the consultant's lead

Irrespective of the type of treatment women were referring to, the vast majority considered their consultants' opinion to be the most important factor that swayed or even dictated their treatment-related decisions entirely.

But I think if I was thinking about stopping the tamoxifen I would talk to… you know, go and see my… I'd discuss it with my consultant instead of just stopping and trying on my own.

P19, breast cancer diagnosed at 40, no children

One reason for that was that women felt that where health and life were at stake, one had to be guided by somebody with appropriate professional background and experience. They considered their physicians to be the experts, able to recognise whether somebody was a candidate for a particular treatment and hence recommend the most appropriate regimen.

There… there was always an element through… through seeing all of the medical people, all the way through of sort of having to trust them because of course they know a lot more than, than we did about… what treatment was best for me etc.

P01, breast cancer diagnosed at 32, no children

The faith women had in the healthcare professionals and their skills was reinforced if a physician in charge of their care was nationally or internationally renowned and had a good reputation. This made them feel as if the treatment decisions they were making or that were made on their behalf were best suited for their particular situation.

I trusted, even though I… I had a good debate with my surgeon and questioned him a lot, I do trust him… trust him and I quite soon learnt… learnt I was quite lucky that he is kind of internationally renowned, he's quite high up in his profession…

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Women talked at length about the trust they had in healthcare professionals in general and in their respective physicians, in particular. Some women perceived the medical profession as trustworthy and referred to physicians' responsibility to act in the patients'

best interest. They, therefore, admitted that regardless of the situation they would always follow physicians' advice. Although they recognised that healthcare professionals did not know everything, they thought that entrusting them with medical decisions was the best option they had.

I'm sure I could have said, you know, 'No I don't want it' but… I… I would never have said that… I would just always kind of go with and trust what I'm told really.

P15, breast cancer diagnosed at 33, no children

Others reflected on the process of building a personal relationship with their treating physician. Where this relationship was based on trust and mutual respect which for the patients involved mainly being listened to and heard, it acted as a facilitator in the treatment decision-making process.

Because I'd built up such… such a good relationship with her by then, I just kind of knew… I had to follow her instructions. And I knew it was gonna be the best option for me.

P02, womb cancer diagnosed at 32, no children

Previous negative experiences with healthcare professionals, however, could impede this process and hence make the treatment decision-making more complicated.

4.3.2.4.3. Knowledge as a double edged sword

While expert opinion of physicians was what all women found very important when navigating through the treatment decision-making process, the importance they attached to additional information regarding their treatments varied. There were women who felt that knowing everything about their treatments was not necessary. Yet, most of the participants did not want to believe blindly in what their physicians were saying. They needed to have an understanding of why certain treatments were recommended to them while others were not. They also thought it important to know what undergoing those treatments meant in terms of short and long-term consequences and side effects.

In terms of the sources of information, the clinical team and the Internet were the two most frequently mentioned by women. For some of the participants, the information

given to them by their clinical team, including their consultant and cancer nurse, were sufficient and they did not feel the need to search for additional information. The informational support provided by the cancer nurses was particularly valued by women. They appreciated the fact that they could call and ask any questions they had, whenever they had them. Some women preferred that to going online and actively looking for information, acknowledging that online information was not always credible and that it was easy to get *'sucked in'* the process of constantly looking up information that was not necessarily useful. Some women also admitted that they preferred not to know everything to avoid sowing doubt in their minds regarding their treatments and the prognosis it gave them.

I think I was too scared to Google anything because you… as mum always said, that angry people shout the loudest. And so I think, I didn't want to go and Google any of the treatments because I didn't want to read what people saying 'Oh this… this didn't work' or 'This did work'. I just wanted to have blind faith in the fact that she was… she's a qualified medical person…

P16, breast cancer diagnosed at 32, 1 child before diagnosis

On the other hand, many women wanted to know everything that related to their treatment plan. These women mostly took the responsibility for informing themselves and actively sought the information they felt they needed using the Internet as their first point of call. There were two types of information that women searched for. The vast majority was interested in facts regarding treatments, whereas some found other people's accounts and experiences of cancer treatments shared on forums and chatrooms more valuable. These women, too, were aware that the quality of online information available could be variable and explained that they mostly consulted websites run by the well-known cancer charities or read peer-reviewed literature, especially when looking for factual information regarding treatments.

For some women, the process of searching for information and educating themselves was a way of reassuring themselves with regards to what had been proposed by their clinical team. By reading more about their treatments and understanding why they were

offered to them, women built trust in their clinical team. They gained confidence that their physicians really did have their best interest at heart and advised them well.

I mean it's hard especially 'cause I'd had the… the bad experience of the doctor who didn't refer me. It's then hard to just trust what anyone said. So that's why I read as much as I could but… about what had been suggested. And I did… I was confident in the… the team, that they'd suggest what was the best option for me.

P04, breast cancer diagnosed at 29, no children

For some women still the factual information that was provided to them by their physicians or which they found online played an active role in their decision-making process. Although women attached great importance to their physicians' opinions, some of them also needed to retrace the physicians' steps of reasoning and understand the evidence which guided their recommendations. They needed to make sense of it and form their own opinions, even if more often than not, these were exactly in line with the physicians' suggestions.

I remember having this debate about, 'cause he said to me that chemotherapy would give me a 13% better chance and kind of drew me a graph and stuff, still got the piece of paper somewhere. And I remember saying '13% that's nothing, that's just awful' and we had this like hour long debate about whether… whether I would have chemotherapy because I was like 'With 13% you… is that really worth it?' And… having learnt a bit more and having discussed it with other people, I came to realise that 13% was actually quite an amazing well… quite a big response to the, you know, expected… response to chemotherapy when some people are kind of given 3 or 4% kind of increase in survival from chemo.

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

This process was of particular importance in the case of decisions that could bear weight on future fertility, especially for women whose cancer stage allowed them to consider FP. These women described their need to understand what the current evidence suggested regarding their treatment options and outcomes in order to make decisions congruent with their childbearing priorities.

Once we've been given the statistics of chances of me not regaining… any ovarian function after chemotherapy etc. etc. we both decided that because having children meant so much to both of us, we had to do it [fertility preservation].

P14, breast cancer diagnosed at 27, no children

Sometimes the research and clear guidelines were missing – for example regarding the consequences of interrupting tamoxifen with a view to becoming pregnant and the risks that such a situation carried. This led to uncertainty regarding what decision should be made and women described how they wished there was more information available to them to guide their decisions.

I… it's all you know, the main thing for me now, of course is the whole, whether I go on and have a baby and whether, you know, do… I don't know… I said that… take a risk or… and trying to weigh all up in my head. But if there was any, you know, anything more out there that would be able to help me, that would be, you know, that would be good.

P12, breast cancer diagnosed at 38, 1 child before diagnosis

4.3.2.4.4. Informing vs. involving others

Because of their expertise to advise women regarding treatments physicians were somewhat automatically involved in the decision-making process. Yet, there were also other people such as partners and parents whose opinions women wanted to take into consideration while making treatment-related decisions.

There was a clear difference between the degree of involvement of the significant others in the decisions that concerned only cancer treatments and the ones that could also potentially impact on fertility.

Treatment decisions, in general, were made between the patient and her clinical team. Women informed their families including parents and partners about what was going to happen rather than sought their advice about what they should do. Although family members lent their support to patients' decisions they rarely played an active role in them.

I… come from a medical family so of course I spoke to… family members and discussed what my consultants were talking to me about […] but I was solely… guided by my consultants.

P14, breast cancer diagnosed at 27, no children

On the other hand, decisions that involved the fertility aspect were more often consulted and discussed with the significant others. Partnered women often described these decisions as joint decisions. Since fertility was something that couples negotiated between themselves, women considered it important for their partners to partake in making the decisions which could potentially affect that aspect of their relationship. For some women, this involvement meant discussing their childbearing plans without engaging the partner directly in the treatment process as in the case of gynaecological surgery (e.g., hysterectomy or trachelectomy). Others, who wished to cryopreserve embryos, needed their partners to consent to the procedure which made them directly implicated in the process. Negotiating when to stop the tamoxifen in order to conceive was also described as a joint decision. Partnered women wanted to establish their priorities as a couple and make a decision in line with those priorities, regardless of its final outcome.

We di… sort of decided between us that, yes, we did want a family, we wanted that chance. So rather than it being sort of completely taken away from us… at least we'd have the opportunity.

P15, breast cancer diagnosed at 33, no children

My husband was just wanting me better. You know, he was ok about not being able to have any more kids. He was… you know, he was quite happy with his two sons and he just wanted me to get better basically so… I didn't really… the fertility… we… that didn't really bother him.

P18, borderline ovarian tumour diagnosed at 31, 2 children before diagnosis

With respect to interrupting the tamoxifen, women specifically emphasised the importance of partner's involvement because of the consequences (e.g., increased risk of cancer recurrence) that such a decision could carry.

I think he [partner] would have been happy for me to just go and make a decision but I so much felt like I needed that to be a joint decision. If… the shit hits the fan basically… I couldn't ever have him saying 'You kind of… you wanted this, you went off and did it' kind of… to me that wasn't… I wasn't comfortable with that… it had to be what we kind of all wanted.

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Women who were in the early stages of their relationships felt that cancer brought forward the discussions and decisions about having children together with their new partners and they did not necessarily feel comfortable with that. Yet, they still did prefer to make decisions about treatments potentially affecting fertility jointly with their partners.

Not only was it kind of absorbing the fact that I had cancer, it was also putting my partner and I in a position of, well we haven't really spoken about this because we haven't been together a great deal of time… to suddenly, do we want to have children? I know I did and we had spoken about it briefly but not to the point of well am I gonna lose my fertility or keep my fertility. So we did have some time to think about it. And it just… to me it was always everything that I wanted to do, to keep fertility. Yeah and we agreed that that would be what we would do.

P13, cervical cancer diagnosed at 31, no children

Single women often consulted their decisions with their parents and sought their advice regarding the treatment options that were available to them.

I spoke to my dad and he obviously then… said to me… he said 'I'd rather you still be with me that having kids. I want you to be healthy.' And he kind of reassured me… and said to me, you know 'Have the full operation and… you… you can always adopt, you can always do fostering and stuff like that.'

P22, borderline ovarian tumour diagnosed at 39, no children

4.3.2.4.5. Alignment of treatment preferences between women and their physicians, and its consequences

The final factor women wished to account for throughout their treatment decision-making to achieve the desired post-treatment outcomes were their own preferences and priorities. Some of them were related to fertility, while others were not.

With respect to fertility, women engaged in the prioritising-balancing process described in the subtheme *Balancing-prioritising cancer and fertility.* This process enabled women to clarify the value fertility had for them at the time of diagnosis and incorporate it into the decision-making processes about treatments involving the fertility aspect accordingly. Women's preferences, however, were not sufficient to guide treatment decisions. The priority their doctors gave to fertility and patients' childbearing desires equally played a role in the treatment decision-making process. The extent to which the priorities of these two parties involved in the process were in line with each other affected the decision-making.

For women for whom fertility was not an issue, the situation was fairly straightforward since neither they nor their physicians had to factor it into the treatment plan.

I said 'Look, it's [fertility] not a problem as such' because… at my age and… to… we didn't really know if we could have… children either cause my partner had some issues as well, he'd had [type of] cancer, so that impacted on him anyway so… as I say we'd resigned ourselves to the fact that we weren't… we weren't going to have any children anyway so it wasn't… you know, so once I'd explained all of that, she was like 'Well, that's behind us, as long as you know, that if you…' you know, if… if… I did want to then we would have discussed it further.

P24, cervical cancer diagnosed at 40, no children

For women who wished to consider fertility while making treatment decisions and who were under the care of physicians who acknowledged their priorities, the situation was similarly straightforward and boiled down to discussing the available options and drawing the treatment plan around them.

My oncologist was very, very proactive in organising an appointment for me and my husband to go and see assisted conception before I started chemotherapy.

P14, breast cancer diagnosed at 27, no children

The situation became more complicated for women who wished to consider fertility while making treatment decisions and who were under the care of the physicians whose priorities differed from theirs. Some women clearly considered preserving their fertility equally important to treating cancer whereas physicians treated it as an '*add-on'*. This created a confusing situation for women who, on the one hand, wanted to follow their consultants' lead and accept the treatments that were suggested to them and on the other, prioritised their fertility differently from their physicians. While many women in this situation ended up accepting treatments suggested by their physicians, some went against the advice they received or consulted another physician.

So within the first week of me being diagnosed I was referred by my oncologist to a gynaecologist at the hospital. And I went to see him and it was, it was quite an awful meeting really because he basically said he wasn't happy doing anything with me because I had oestrogen-positive breast cancer… which, it was just a really awkward meeting, my partner was there with me and we thought it felt like a bit, like we're being interviewed about our relationship and he was very down on it all and said that he would not do anything at all until after I had chemo and I was sort of trying to explain 'Well, I've been told that actually… the chemo is going to affect my eggs and my ovaries possibly and my fertility so shouldn't we try and do it before and…' And anyway he just wasn't, he wasn't interested and wasn't going to help me at all. […] A friend of… of the family went to a consultant [fertility specialist] so my partner and me went to see him, I think this was like the day before my surgery… so it was all like a real mad rush to get it done. And he said 'Yeah don't worry at all'. He was brilliant actually… he'd said that he'd treated other women with tumours and there was a pill I could take during the IVF process that would keep my oestrogen levels down and he was just really good and really sympathetic and just sort of gelled with him very quickly.

P01, breast cancer diagnosed at 32, no children

Aside from preserving fertility, women had other preferences regarding their treatments. Some of them wanted to receive the minimal amount or the least invasive treatments because they wished to preserve their short- and long-term QoL as well as body image.

My sort of concern was that at… 31 I didn't want the side effects of the alternative treatments, I didn't want to… you know, I didn't want to be on HRT at 31 or be infertile or have a poorer sex life or anything else that I associate with the kind of hysterectomy type side of things.

P08, cervical cancer diagnosed at 31, no children

On the other side of the spectrum were women who opted in for the most aggressive treatments. Some of them saw this as the only way to restore their QoL which deteriorated because of the symptoms they had prior to diagnosis. However, the most frequent reason for wanting radical treatments was the fear that by doing less, some of the cancer cells would be left behind and the cancer could eventually recur.

If I hadn't had chemotherapy… there would be a higher risk of recurrence so I think, I think everything that was thrown at me and everything that was on offer… it can only be positive because you want to throw everything at it.

P07, breast cancer diagnosed at 39, no children

The physicians acquiesced to patients' preferences regarding treatments as long as they thought these were reasonable. Women's preferences and their realisation were therefore tempered by their physicians' perception of need for treatment.

4.3.2.4.6. Specific considerations related to immediate fertility preservation and tamoxifen

Physician's advice, cancer treatment and fertility-related information, significant others, and personal preferences, although to varying extents, all played a role in treatment decisions in general, and decisions involving fertility aspect in particular. However, there were certain factors women spoke about that related specifically to fertility-related decisions. These included institutional issues, the timing of the initial treatment decisions, and the length of time participants needed to be on the tamoxifen before they could try for a pregnancy.

The availability or services and efficiency of the referral pathways acted as facilitators to receiving fertility sparing or preserving treatment. However, not all women who wanted to take advantage of these services were easily able to do that. Even though assisted conception services for cancer patients are available under the NHS scheme, some patients could not get an appointment on time or were disqualified from their use based on age or type of diagnosis they received. Some of these patients decided to organise a consultation privately. The lack of experience in navigating through the private healthcare system while trying to set up a private fertility appointment added to their burden at the time of diagnosis. Cost of the procedures was another issue they had to resolve before pursuing FP privately.

So I did feel like in those 3-4 weeks of… from being diagnosed I was going pretty much every day to see an oncologist, or for a blood test or for a different scan or… that every day was taken up with… preparing for my operation and lots of medical appointments… and then on top of that I'm having, I was having to research and try and find somebody to help me [with fertility]. And that was very, very difficult and exhausting I suppose. […] sat trying to get funding, or sat trying to get an appointment for this and that. So, the whole process could have been very much made a lot easier for me and if there was… someone to go to.

P01, breast cancer diagnosed at 32, no children

Timing of the decisions and haste with which they needed to be made constituted further factors which complicated women's decisions. Women's impression was that their cancer treatment was needed urgently. They explained how their physicians stressed the importance of them getting their treatments as soon as possible and without undue delays. Although time pressure did not necessarily affect the decisions for women with gynaecological cancers who could opt for fertility sparing surgery (e. g., trachelectomy), it was a barrier for women who wanted to take advantage of the assisted conception services.

And… when we saw doctor [name], for the… on that first… on that first time she said, 'Look, we can… I can put you forward for egg… for egg collection… and IVF but that's gonna be another month to six-eight weeks that I don't particularly want to wait based

on your diagnosis. So unless you are absolutely dead set on that, my advice is that we start treatment straight away'.

P16, breast cancer diagnosed at 32, 1 child before cancer

Although in a different way, time also played a role in decisions regarding the tamoxifen. Women's biggest issue when considering whether to stop the tamoxifen was the length of time they should have kept taking it for before they could safely interrupt the drug in view of conceiving. Neither the research, nor the opinions of the physicians were clear with respect to that which made women uncertain as to what the best course of action would be.

Unfortunately with… the sort of… amount of research which I haven't been able to find that much 'cause I, I don't know if it just doesn't exist… there hasn't been that much that I can find on the Internet, and articles, medical articles about the risks of re-occurrence with coming off tamoxifen before you are advised to and trying for a baby and the effects of hormones on you etc. So trying to find that information, reading it through and then sort of making that informed decision is important to both of us.

P01, breast cancer diagnosed at 32, no children

4.3.2.5. Evaluation of treatment decisions

The over-riding feeling among women irrespective of the type of decisions they made regarding treatments was that these decisions were right for their particular circumstances.

Most women who preserved fertility were grateful they were able to do this. Those who decided to pursue artificial reproductive technologies admitted that although the process itself was difficult, they were happy that they went through with it. Women found comfort in that their reproductive choices were still theirs as opposed to being entirely out of their hand due to the effects of cancer treatments. They also expressed the relief at managing to avoid the regret that they could have potentially felt, had they not acted in time to preserve fertility. All these women, however, felt well and as far as they were concerned their actions to preserve fertility were not in any way detrimental to their

health. Only one woman (P13) who had recurrence scares subsequently to her treatment questioned her decision about trying to preserve her fertility at all cost.

And it was… almost now made me feel like it was the right decision back then in July and August to have the trachelectomy but with complications that have come up and scares that have come up from them, I now feel a bit like a ticking time bomb in that it was right then but I have elements of doubt as to whether perhaps a hysterectomy may have been… a better option?

P13, cervical cancer diagnosed at 31, no children

Similar to women who preserved fertility, those who did not also felt they made the right decisions regarding their course of treatment. Some found making those decisions easy. Others, despite finding them less straightforward felt that at least they were in control of what was happening to them. Others still did admit that the process was heartbreaking as they had not expected they would need to, at such a young age, decide whether to have one's chances of ever having a biological child taken away. One woman (P05), however, felt that she made a mistake by deciding to undergo the treatment whereby her fertility was permanently lost.

I wish I hadn't done it [had hysterectomy]. It was the biggest mistake in my life.

P05, womb cancer diagnosed at 31, 1 child before cancer

4.3.2.6. The consequences of treatments

Irrespective of whether women decided to preserve their fertility throughout cancer treatments, their treatment decisions inevitably had consequences for their post-cancer lives. Some of them were related to the fertility whereas others were more generally associated with having been diagnosed with cancer.

Fertility-related consequences of cancer treatments are discussed in the subtheme *Persistent fertility issues.* Consequences related to cancer diagnosis and treatment more generally involved the fears that cancer might come back, visible and invisible changes to women's bodies, and early menopause. These issues are discussed under the following respective subthemes: *Fear that cancer might recur; The changed body;* and *Coping with the premature menopause* (see Figure 4.5).

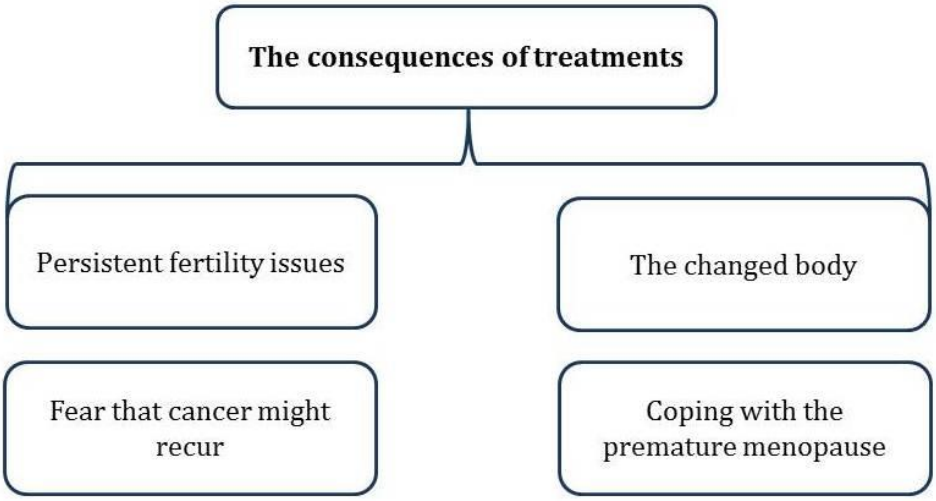


Figure 4.5. Visual representation of the theme *The consequences of treatments*

4.3.2.6.1. Persistent fertility issues

Although FP prevented some women from losing their fertility to cancer, it did not rule out fertility issues completely. Cancer inevitably changed women's lives including the context in which they were making their reproductive choices. It brought about new challenges to the process of fulfilling fertility-related plans. This is described under the subtheme *Cancer-related factors controlling reproductive choices.*

Fertility issues in both women who decided to preserve and those who decided against FP contributed considerably to how they adapted to their post-cancer reality. Although women differed in terms of their emotional responses to fertility issues, there was a common underlying mechanism responsible for women's reactions which seemed to be related to how women conceptualised their fertility through the lens of social norms. Through social interaction, and specifically through the process of comparison with healthy peers women discovered that their fertility issues set them apart from their friends. This in turn made them feel different from healthy women. These issues are presented under the subtheme *Being different – adapting to the new normal?*

Finally, fertility issues also had the potential to affect women's romantic relationships – both the potential/future and the existing ones. The impact of post-cancer fertility concerns on close relationships is discussed under the subtheme *Fertility aspect*

affecting relationships. Figure 4.6 represents the visualisation of all the subthemes within this theme.

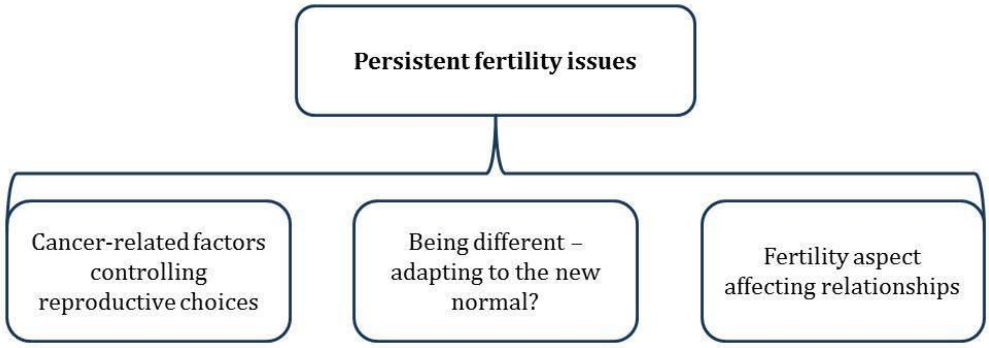


Figure 4.6. Visual representation of the theme *Persistent fertility issues*

4.3.2.6.1.1. Cancer-related factors controlling reproductive choices

Cancer diagnosis and its treatments, irrespective of whether the participant decided to preserve fertility, changed the context of women's reproductive decisions. As discussed previously, under *Pre-cancer attitudes towards fertility*, women considered external factors such as finding a suitable partner, as well as a stable housing and financial situation important preconditions to fulfilling their reproductive plans. However, biologically they felt they were not in any way prevented from conceiving and could therefore be '*spontaneous*' about their reproductive choices. Cancer diagnosis and treatment took away this spontaneity and brought about additional cancer-related external and internal factors that constrained the realisation of women's fertility-related plans. The external factors included dependence on healthcare professionals and other people to help women either conceive, or become a parent through alternative means. Fear of recurrence was an internal factor that acted as a barrier to having children.

Women who pursued artificial reproductive technologies observed that their embryos could only be released to them after a certain amount of time had passed since their treatment.

I don't think you're allowed to have those embryos released prior… prior to two years after treatment.

P07, breast cancer diagnosed at 39, no children

Although they were in a position to make a decision whether to use them, they were not in control of when that would happen. Not only were the healthcare professionals involved in deciding when to release the embryos to the patients but also in carrying out the procedure of the embryo transfer which meant that their assistance was crucial for women to conceive.

I think fertility is the big one because it's just taken away the… the sort of… I suppose being able to spontaneously think about having a family. That has to be now more of a… more steps in place before being able to do that.

P15, breast cancer diagnosed at 33, no children

Since women's decisions regarding the length of time they should be on the tamoxifen were also highly influenced by the advice they were given by their physicians, the time of their eventual pregnancy was again only partially within their control.

Once we'd started the IVF cycle and I went back to see my surgeon, at the time he said that I'd need chemo, he then said 'Well the evidence shows that… tamoxifen is more effective for 10 years…' so in my mind then I was thinking 'Well we're… we're [inaudible] eggs collected we have, you know, we're… we're gonna have embryos but I'm not gonna be able to do anything with them because in 10 years' time I'll be, you know, 44.' Originally when we started thinking about doing IVF cycle… and it would have been 5 years on tamoxifen, that kind of would have been fine cause I'd be sort of 39ish so…

P15, breast cancer diagnosed at 33, no children

Women who underwent trachelectomy for cervical cancer noted multiple possible pregnancy complications that awaited them should they decide to conceive. They were aware that they would require help from the obstetric services to carry the pregnancy and deliver safely.

Although these women preserved the ultimate choice of whether to have children, at the same time cancer diagnosis deprived them of the full control over their reproductive decisions. The help of the healthcare professionals became an inherent part of their reproductive choices.

Additionally, women who received the trachelectomy felt as if by the fact that they were offered this procedure, they were also somehow required to eventually conceive. They were either given a specific timeframe within which they should try for a child or reminded by their physicians that the procedure was done in view of them getting pregnant at some point.

On more than one occasion by more than one person it's been suggested that this was… this operation was given to me almost, and in fact one professional used that expression… it was given to me… because… because of the situation I was in, you know, 31 and childless kind of thing. And… they almost, I kind of… I get the impression I'm meant to be grateful for that. I mean, don't get me wrong, I'm grateful for the fact that and the end of the day it saved my life and it was the best option. But it's almost like by not having a child yet I am… I don't know what the best way to put it is. It's almost like I am insulting them by not seeing it through.

P08, cervical cancer diagnosed at 31, no children

Even women who could not or decided not to preserve fertility noted that their reproductive choices were to a certain extent medicalised. Pursuing surrogacy or adoption depended not only on their wish to do so, but also on their health status and being free of cancer for a specific length of time.

Like I know I've still got options of like adoption and like a hope that I can still go down this route. I know you've got to be cancer-free for 5 years. And I just hope that I can…

P02, womb cancer diagnosed at 32, no children

Women who wished to pursue alternative parenting routes also feared the process of their parenting competencies being assessed by other people – a situation that would not have occurred had they not had cancer in the first place. For them the ability to extend

their families was limited by other people's judgement – potential surrogate mothers in the case of surrogacy, or social services in the case of adoption.

As opposed to these external factors, fear of recurrence was an internal factor which also affected women's plans to have children. Whether they were thinking about biological or alternative parenting, women questioned if it was responsible to have a child knowing that cancer could come back at any time. Some of them thought it would be selfish to pursue pregnancy.

The threat of cancer recurrence was of particular importance to women who were diagnosed with breast cancer. They often linked their disease to hormonal issues and therefore perceived interrupting tamoxifen in order to conceive as potentially increasing their risk of recurrence. They stressed the importance of not '*cutting corners'* with their endocrine treatment to avoid creating a situation whereby driven by a desire to have a child they would provoke a recurrence and eventually leave a child without a mother. Women who already had children before cancer questioned whether they had the right to take the risk extending their families at the potential cost of their existing children's wellbeing.

Yeah… well I do worry about… like… is there a risk of it coming back and… and… and… leaving a child without a mother is an awful thought… and whether that's not a responsible thing to do.

P04, breast cancer diagnosed at 29, no children

Although women who preserved their fertility often spoke about it in terms of preserving their choices, ultimately irrespective of the treatments they received, their choices ended up being controlled by factors brought about by cancer diagnosis and treatment.

4.3.2.6.1.2. Being different – adapting to the new normal?

The end of cancer treatments marked the moment when women no longer wanted to be perceived as cancer patients but simply as who they were before their diagnosis. However, returning to the pre-cancer reality was not straightforward, especially for women who considered their fertility to be a crucial part of who they were. They

expressed a range of negative emotions associated with cancer's impact of their fertility. They also felt that because of their fertility issues caused by cancer, they were different from their peers. They did, however, try to cope with that in many different ways. These issues are discussed under the following respective subthemes: *Emotional response to cancer's impact on fertility and its triggers*, *Being different,* and *Adapting to the new normal* (see Figure 4.7).

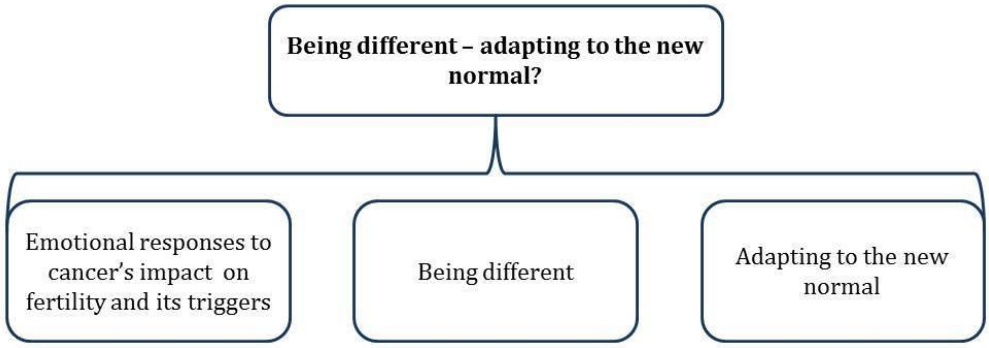


Figure 4.7. Visual representation of the theme *Being different - adapting to the new normal?*

4.3.2.6.1.2.1. Emotional response to cancer's impact on fertility and its triggers

Two groups of women who expressed a range of negative emotions in response to cancer's impact on fertility were identified in this study. The first one consisted of women who had always put their fertility first and had tried or indeed succeeded in preserving it. The second group included women who declared that they had initially made peace with the fact that they might not ever be able to have (more) children. Their priority at the time of diagnosis was to survive the cancer, however, their perspective shifted once they finished their treatments and felt they were in the clear. They were the ones who described how they kept broaching the topic of fertility at every appointment with their clinical team. They felt that not being able to realise fertility-related plans at the time of their choosing was the consequence of cancer they had most problems coming to terms with.

I remember thinking to myself in the… in the two weeks while I was waiting for the bone scan and the MRI scan, while I was waiting for those to come back I remember thinking

to myself 'If… if I'm clear [of metastases] and I just have breast cancer, I will be so… I will be happy enough not to have another child because I'll be so happy that I only have breast cancer.' And I want… I desperately, desperately wanted to believe that. But… I know now that I… that was me just… in a bad, bad place and being very scared of what was… of what could have happened. […] I now… am… that's my biggest… my biggest struggle is the fact that 'cause I now take tamoxifen, my biggest daily struggle is knowing that I can't… that I shouldn't stop it [to conceive] for at least… May, June, July, August next year, 'cause that'll… I'm now on this and need for another two years. And that is the biggest… the biggest challenge of the whole process. Definitely.

P16, breast cancer diagnosed at 32, 1 child before diagnosis

Women who felt strongly about fertility after cancer diagnosis described a range of emotions caused by the fact that cancer had taken something important away from them – either their ability to have children or the ability to choose whether and when to have them.

I mean I think in hindsight the… the not having the third or the fourth baby is quite… quite significant but it's… it's one of those things that you always wonder what if… and I guess it's one of those extra things that gets… gets added on like if the cancer gets blamed for in a way… 'cause once you've had it everything almost goes back to 'Oh well before the cancer' or 'Oh well because of the cancer'. And it… maybe we wouldn't have had another one but it's just that… that ability to choose I think and have the choice is… you feel like it's taken away really.

P17, breast cancer diagnosed at 35, 2 children before diagnosis

The feelings women reported varied from anger at the fact that cancer thwarted their life plans and that they would not be able to give their partner a biological child, through sadness and heartbreak, to embarrassment that they were unable to fulfil a role that seemed most natural to women – to conceive and carry a pregnancy to term. Some women also described how they felt incomplete once their fertility was taken away from them. Others talked about the process of grief they went through as a consequence of losing the possibility to make decisions regarding their fertility.

I think there's maybe something… it's not like a bereavement as in somebody's died but bereaving some of the ideas that you thought you might live. So like I said that thought of a third of a fourth child whilst it was never definite, it… it's definitely not gonna happen now so… it's kind of bereaving the things that you… you thought you might have in… […] you don't know what the different reality would have been had I not had cancer.

P17, breast cancer diagnosed at 35, 2 children before diagnosis

Although these feelings were not constantly there, they resurfaced prompted by everyday life triggers. Both women whose fertility was temporarily affected and those who lost their fertility permanently struggled with being reminded of their situation. The latter group also felt that they would forever be reminded that they were unable to have children.

I suppose… (pause) the biggest consequences psychologically because I can't have children and because I made decisions myself to have the hysterectomy and take away my own chances of having children. Physically I think I am always gonna have problems because of the hysterectomy and the abdominal problems I've got. So I think I'll be reminded of it forever. Even when I am too old to have children. I'll be reminded of it constantly, there will be no escape.

P03, womb cancer diagnosed at 33, no children

It was through interactions with other people that women were most poignantly reminded of their impaired fertility. Being asked whether they had children or listening to other people's conversations about their own children were described as difficult. They found it particularly unfair when people complained about their children in their presence, while they would have given anything to simply be able to have children. Women also struggled to see their friends and family getting pregnant since it reminded them that they could not at that time or possibly ever share that experience. Although it was difficult to witness the pregnancies of others, women were particularly hurt when their friends and family tried to conceal their pregnancies from them. They acknowledged that it was probably done in good faith, to protect them from being hurt, however, they also stressed that they did not want their experience to turn them into

being resentful of other women whose fertility was intact. They did not want their cancer to change who they were.

But then I don't want to be that person… I don't want to be… angry and… resentful. I don't… I don't want people around me to not be able to celebrate their own pregnancies or… you know, having children and extending their families. I… I'd never want that… I… I don't want to be the person that you can't talk about babies in front of… at all.

P20, cervical cancer diagnosed at 31, no children

4.3.2.6.1.2.2. Being different

Yet, unavoidably, women were changed by their experience of cancer. Although most or all of their cancer treatments had finished and they had been discharged from hospital care, women felt their lives were not the same as they used to be before the cancer diagnosis. Hence, they felt they needed to define their new reality and try to adapt to it. For some women it was the ability to have children that was perceived to be a facilitator to moving on from cancer experience and restoring a sense of normality in their changed, post-cancer realities.

Those who succeeded in having a child after diagnosis, either through conceiving and carrying a pregnancy or via surrogacy described how they appreciated it as a normal life experience which allowed them to put their cancer into perspective. Cancer ceased to be their number one focus, and although still in the back of their minds, its effect on their lives decreased gradually.

And that… the process of kind of having that first pregnancy, or my second pregnancy and losing it and then having this pregnancy… and I have managed to breastfeed her exclusively from my… unaffected breast, and that's been incredibly cathartic. […] And I think, coming up to maybe 5 years as well, I mean there's a few things there that, starting to feel maybe… I don't know… I'd… I'd… dare not say the word closure but… […] It's not something that's done and dusted and gone. But I… I don't think of it [cancer] every day and it doesn't affect… everything now. So I don't… I don't think I think of it as a life-long… clearly not because I would have never been able to have her

had it been no… I think that shifted in the last year… kind of unconsciously shifted without me realising.

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Women who could not yet or at all have children felt as if something was missing from their lives. Not being able to have children at all made it difficult for women to plan for the future, especially if motherhood had always been one's cherished life goal. They felt as if their lives lost meaning as one of the most important of their desires became impossible to achieve. Those who had to wait to fulfil their fertility-related plans felt as if they were stuck in a life stage they were unable to move on from to get their normal lives back.

I feel like I'm in kind of limbo-land. We can't complete our family and carry on with the next stage of life, we're kind of waiting for… for something to kind of happen.

P16, breast cancer diagnosed at 32, 1 child before diagnosis

The notion that having children was vital to being able to move on and get back to normal after cancer diagnosis might have stemmed from the fact that compared to their peers, women felt different. On the one hand, witnessing their peers becoming pregnant and able to complete their families triggered negative emotional responses. On the other hand, it made women compare themselves to their friends and realise how different theirs and their friends' lives were. They found it difficult to identify with groups they were part of before their cancer diagnosis. That was especially true if women's peers were at the stage of life where they were extending their families.

Women without children felt robbed of their chance to have a normal parenthood experience, something that came so easily to other women. They felt they could not really relate to other mothers, since they had not experienced that themselves. Those who lost their fertility resented the fact that they would be never able to share the most natural and normal experience of pregnancy and childbirth the way healthy women could. Some of them feared they would be treated as outcasts because of their inability to have children.

I feel a little bit sort of like a freak. When I go out with my friends and they've all got children and I am sort of the odd one out. I got left out on quite a few things because all my friends have got children and they go to… the… the children events and I just feel embarrassed, I feel like I'm… I'm gonna be looked upon like the old spinster, the old childless spinster or the crazy cat lady.

P03, womb cancer diagnosed at 33, no children

Falling behind their peers in terms of childbearing goals made women feel very isolated and unable to connect with their friends even though they were aware that they had no control over their situation.

And I think I felt very isolated from the friends because they were all started to consider maybe another child… or just doing normal family stuff which kind of wasn't an option for us and… I think… just seeing how people… people get on with their lives was very hard.

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Some women also pointed to the differences between them and their peers in terms of another fertility-related issue, notably premature menopause. While their friends were discussing pregnancy and childbirth, these women had to deal with their bodies changing in a completely different way. They felt they had more in common with post-menopausal women and thought it unfair that cancer not only robbed them of their fertility but also of their youth.

Sometimes I feel a lot… older because the only person that has the same experience as me are post-menopausal women. So whereas most of my friends are talking about childbirth and getting ready for babies and… their bodies like changing and lactating milk and stuff… I am going through 'Oh I'm having a hot flush' and… the menopausal mood swings and, and everything so… Sometimes you feel like you're not your age anymore. You feel like you're a lot older.

P02, womb cancer diagnosed at 32, no children

4.3.2.6.1.2.3. Adapting to the new normal

In order to manage their feelings regarding the persistent fertility issues, women engaged in a range of coping strategies. Some of them tried to avoid or distance themselves from the situations that could trigger their negative feelings. Others sought to reappraise the situation and find benefits in the fact that they could not have children. Others still directed their attention to activities other than having children such as building their professional careers, and focusing on close relationships.

And for example I've just started my own business because… part… I mean part of that decision is because I can't have a family now I want something to focus on and build for myself.

P01, breast cancer diagnosed at 32, no children

Although alternative ways to parenting (e.g., adoption, surrogacy, or fostering) were discussed by many women, not all of them found these acceptable. Some women were concerned about the factors that were outwith their control (such as possible behavioural or health problems) had they decided to adopt or foster children. Legal uncertainties surrounding surrogacy posed problems to some while others were worried about the emotional impact of going through the process. Yet, for women who were able to re-define their fertility and were willing to explore these options, their availability provided reassurance and hope of one day becoming a mother.

I want to be a parent more than I want to carry a child so there's hope in the sense of either exploring surrogacy or adoption.

P20, cervical cancer diagnosed at 31, no children

4.3.2.6.1.3. Fertility issue affecting relationships

Both partnered and single women reflected on how the experience of cancer and its impact on fertility affected their existing or could affect their future romantic relationships. Single women found the fact that cancer impacted on their fertility rather problematic. They were aware that they would have to tell their potential partner about their temporary or permanent inability to have children and were unsure when and how to broach the subject. One woman who did meet her partner subsequently to her

diagnosis and treatment said she had told him immediately she could not have children. Others, however, were concerned this could scare the other person before they had a chance to get to know one another. Simultaneously, women were anxious about the possibility of getting close to someone and then being left once they revealed their cancer experience. Some of them wished they would meet a potential partner who would not want to have children even though they themselves might have wanted them, through alternative parenting, for example. Some women found the situation of having to explain what happened to them and why they were unable to have children so distressing that they would rather not date at all to avoid it.

I can't… I can't see myself in a new relationship… You know, when… sometimes I can't even talk to strangers on the phone. […] I don't know 'cause it's the all explaining of the cancer as well… and, and… they say won't care, d'you know, and I can't have kids… I don't know how that's gonna go.

P05, womb cancer diagnosed at 31, 1 child before diagnosis

The majority of partnered women felt that going through the experience of cancer together and dealing with its potential consequences strengthened their relationships. Whether they were in relatively new relationships or already married, they thought that the situation brought them and their partners closer together.

I don't deny that the physical changes that I went through… disrupted physical side of our relationship in a way that, you know, we've never… we've never had to experience anything like that before. But… I would say mentally… yes, we're probably even closer than we were and we've… you know, we've been through a life event together which has… has… not necessarily our relationship but we've learnt a lot about each other I would say.

P14, breast cancer diagnosed at 27, no children

Nonetheless, the physical changes women underwent along with the fertility issues posed challenges especially to the sexual aspect of relationships. Some of them were taken by surprise by how their bodies looked and functioned after treatment and sought advice from their physicians as to how to deal with them. Women considered the sexual

aspect of their relationships important for the wellbeing of their partners and therefore worried about their partners accepting the changes that cancer and its treatments brought about. One woman openly said that her relationship fell apart as a result of her inability to bear children post-cancer.

My ex-partner, yeah my ex-partner… he left because I couldn't… have kids and he hasn't got any kids and he wanted to be a dad.

P05, womb cancer diagnosed at 31, 1 child before diagnosis

4.3.2.6.2. Fear that cancer might recur

The risk of cancer recurrence was previously described as factor that drove women's treatment decisions at the time of diagnosis (see section 4.3.2.4.5) and later on in survivorship (see section 4.3.2.6.1.1). However, after having finished their treatments, the majority of participants were still anxious about the possibility of cancer coming back.

For some women, the fear of cancer recurrence was linked to their perception of treatment. Women found it reassuring when their cancer was confined to a body part that could be removed. This enabled them to visualise how their treatment worked and for them the fact that the organ affected by cancer was removed meant that the disease had nowhere to return. This attenuated the fear of recurrence for some women.

You always worry that something may come back… but I know that having had the ovaries removed then that can't come back…

P21, borderline ovarian tumour diagnosed at 39, 2 children before diagnosis

The majority, however, were not reassured by the removal of the body organ. They struggled with the worry that cancer might come back and a lot of them believed that this feeling would never go away. They described how every little symptom they experienced in their post-cancer life provoked their anxiety about cancer coming back even though most of them were aware that their reactions were probably exaggerated and that the scenarios running through their heads were more sinister than reality.

It was also apparent from women's narratives that their interpretation of bodily symptoms changed from the 'before' to 'after' cancer diagnosis. While before they might have considered similar symptoms benign, after cancer, they became concerned about every single ache or pain and immediately sought medical advice to reassure themselves it was not cancer recurrence.

I think that's the thing, I'm so worried that, you know, if I'd a cough I've got lung cancer, if I find a spot in my head I've got a brain tumour, you know, like things like that, just incredible. I live in fear.

P06, womb cancer diagnosed at 35, no children

Some women tried to cope with their fear of recurrence by concentrating on the potential causes of their cancer. They wanted to learn about what caused it in the first place to be able to eliminate the potential external risk factors and make sure they did everything to prevent the recurrence. Since in most cases it was impossible to pinpoint exactly the causes of cancer, women changed their lifestyle and behaviours by eliminating all the factors that they thought could have potentially contributed to their disease.

I don't have a need to kind of say 'This is what caused it'… I think, things inform my choices about the future, like I won't go on the pill, I wouldn't use a hormonal contraception… I didn't choose to have the tablets after my miscarriage because I was concerned about how that would affect me… it made… informed my choices of things that I'll put in my body…

P10, breast cancer diagnosed at 32, 1 child before and 1 child after diagnosis

Yet, this strategy only worked to a certain extent and eliminating all the potential risk factors did not completely eliminate the fear of recurrence.

And… but I… I think you… I think, you know, I'll always worry that… that it's coming back.

P07, breast cancer diagnosed at 39, no children

4.3.2.6.3. The changed body

Women's bodies also changed subsequently to treatments. They were marked with scars that acted as proof of what they had been through. However, rather than talking about the scars in the literal sense, in their narratives women referred to the symbolic meaning of these scars. Many women associated their female identity with the way they felt about their bodies and how other people perceived them. Having a breast or reproductive organs removed was for many of them a blow to their self-confidence and femininity. Although some of them had come to terms with their new bodies transformed by treatment, others had difficulties accepting the way they looked or felt about themselves.

Now I don't, yeah, I… I don't think about it [body seen in the mirror] I walk past it and it's just part of me. It's just what's happened, it's part of… history in the past of, of what's happened to me so…

P01, breast cancer diagnosed at 32, no children

You know… I hate my body right now, I hate it. […] I don't know whether I'll ever be able to like my body again.

P05, womb cancer diagnosed at 31, 1 child before diagnosis

For some women, female identity was closely related to their potential of becoming a mother. This transpired particularly from the accounts of women who were diagnosed with gynaecological cancers and needed a surgical procedure to treat the disease. Whether their reproductive organs were removed completely or only partially, women felt that the inability to conceive or carry a pregnancy to term without the involvement of healthcare professionals made them '*less of a woman'*. They found changes to their bodies difficult to adapt to as these had shaken to the core their perception of who they were or who they could become.

I think personally… of course I want to have… of course I would like to get married and all that kind of thing… but… just… you don't feel like a complete woman in one way if you can't have kids…

P22, borderline ovarian tumour diagnosed at 39, no children

4.3.2.6.4. Coping with the premature menopause

While some women were worried about their fertility as it is understood in terms of being able to have children, others extended the definition of fertility to the issue of the premature menopause. When considered in this broader sense, even women who might have had completed their families or had not been interested in childbearing, expressed their concern about fertility.

Premature menopause resulted from either surgical bilateral oophorectomy or chemotherapy and pertained specifically to women who were diagnosed with hormone-dependent cancer whereby hormone replacement therapy was contraindicated.

The other thing I did… was… looking for the… the whole fertility side. So… because for me… I wasn't only just concerned about being… you know, having my sort of ability to have children taken away but also you know, going into menopause early.

P19, breast cancer diagnosed at 40, no children

Women reported suffering from a range of symptoms including most commonly hot flushes, night sweats and terrors, general and joint aches and pains, as well as skin and vaginal dryness. They were also concerned about the effect the lack of hormones could have on their musculoskeletal system. The menopausal symptoms led to undesirable consequences varying from sleep pattern disruptions, through difficulties with sexual activity to, in extreme cases, the avoidance of social gatherings due to embarrassment caused by hot flushes. These symptoms affected women's QoL.

Hence, many of them sought advice and help with respect to these symptoms. The majority of women had to bring the fact that they were struggling with menopausal symptoms to the attention of their consultants or GPs themselves. Some of them were automatically offered a referral to the menopause clinic while others had to push for it. Where possible, the suggested treatment to relieve the symptoms and restore life quality was hormone replacement therapy. However, even among the women who were good candidates for it, not all were keen to pursue this route, anxious that taking hormones would be like inviting cancer to develop again. Most women preferred alternative methods such as non-hormonal medications and various supplements, advice regarding behavioural changes that could attenuate the symptoms (e. g., exercising, limiting

caffeine intake, or changing sleep habits) or practical solutions (e. g. using fans in case of hot flushes).

Luckily now, I was recommended sort of a supplement to take for the… to get rid of the hot flushes and it worked a treat so I'm not affected any more by them. Which is brilliant…

P15, breast cancer diagnosed at 33, no children

Yet, not all were advised about ways to deal with the symptoms. Some were simply told to '*put up'* with them as much as possible.

I was advised… due to this cancer that I had and because of the aggressive… not to take any HRT because of the… that can have an impact on the cancer and it could actually help the cancer grow again. So… the advice that I have had is that if I can try and put up with the symptoms (laughter) as much as I can… then that would be beneficial for kind of helping the cancer prognosis.

P02, womb cancer diagnosed at 32, no children

4.4. Discussion

The aim of this qualitative study was to gain an in-depth understanding of young women's cancer treatment decision-making and the extent to which, as well as the reason why, their decisions were influenced by fertility issues and fear of cancer recurrence. The findings of the study are discussed within the context of the Common Sense and the Shared Decision Making models. Where appropriate, the changes to the models are proposed to better reflect the processes of treatment decision-making in the context of maintaining fertility. Where the results do not correspond to any of the models, they are reviewed with reference to the existing literature summarised in Chapter 3.

4.4.1. Summary of evidence

4.4.1.1. The meaning of a cancer diagnosis at a young age

According to Levinson, D.J. (311) who studied adult development, 'early adulthood (17-45) is the season for forming and pursuing youthful aspirations, establishing a niche

in society, raising a family, and as the era ends, reaching a more "senior" position in the adult world' (p. 5). In this period of their lives, individuals make important choices regarding relationships and family, work, and lifestyle (311). Levinson, D.J. (311) purports that whilst early adulthood can be a time of great accomplishment, it can also bring about great stress arising from the fact that people try to simultaneously realise many life goals. Although the need to accommodate for many, often conflicting goals might put a strain on an individual, this is seen as a natural course of affairs. What is not expected in this period of one's life, however, is the occurrence, and the subsequent need to cope with, a life-threatening illness such as cancer.

Women's emotional response to cancer diagnosis described by the majority as shock and surprise was summarised in section 4.3.2.1. Several factors could have contributed to this reaction. According to the CSM, the initial perception of illness (specifically illness identity) is created based on the characteristics of a somatic stimulus (e. g., a symptom or a combination of symptoms one experiences) as well as the heuristics individuals hold which help them decide about the nature of a particular somatic stimulus. These components of the model, which were prevailing throughout women's accounts, are highlighted in the Figure 4.8 and their relevance explained below.

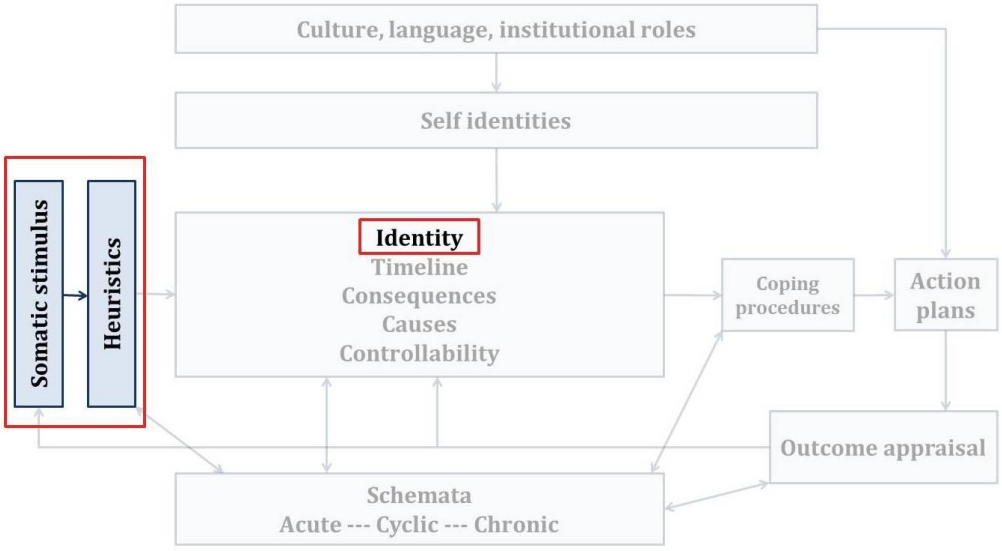


Figure 4.8. Components of the CSM reflected in the theme *Cancer diagnosis as a surprise because of young age and perception of symptoms*

Women in this study reported a relative lack of symptoms at the time of their diagnosis, and if they did experience symptoms, they tended to normalise them. When symptoms were absent, women found it difficult to properly construct the illness perception and particularly form the illness identity. What transpired from their accounts was the difficulty they had accepting that they had cancer without experiencing any symptoms. For the illness identity to be conceptualised, both the symptoms (concrete information about the disease) and the label (abstract information about the disease) need to be present and integrated. This is known as the symmetry rule (64) and situations where it is violated, which was the case for many women in this study, can cause adverse psychological outcomes (72, for details see also section 2.2).

The normalisation process that women engaged in could be due to a recognised heuristic known as prevalence heuristic where individuals downgrade the severity of their symptoms when they are aware that the same symptoms are prevalent in the population (67). Particularly women with breast cancer who presented with a lump looked for alternative explanations of their symptom. The ones that were diagnosed post-pregnancy related it to breastfeeding complications which often occur in this period. Others, who were diagnosed outside the context of breastfeeding, gave examples of other women they knew who had benign breast lumps as a reason for them not initially worrying about their symptoms.

A lot of women also thought that, despite the presence of symptoms, they were too young to be diagnosed with cancer. This perception was additionally reinforced by the attitude of their GPs, who often reassured them that, because of their age, they had nothing to worry about. This can be explained by the age-illness heuristic (67), where age acts as a barrier to cancer diagnosis (64, for details see also section 2.2).

The inability to fully form the perception of illness identity due to lack of symptoms, the normalisation process to explain the existing symptoms stemming from the use of prevalence heuristic, and finally the use of age-illness heuristic introducing bias in the interpretation of one's symptoms could have all contributed to the fact that cancer diagnosis came as a huge shock and was completely unexpected. It was not, however, the only unexpected event that occurred in the lives of these women. The shock of

cancer diagnosis was followed by another, often upsetting realisation – that one's ability to have children could be taken away while undergoing cancer treatments.

4.4.1.2. Fertility issues as a consequence of cancer

The way women perceived their potential post-cancer fertility issues can be conceptualised as a consequence of cancer as understood in terms of the CSM (see Figure 4.9). The conceptualisation of fertility issues as a consequence of cancer required women to (1) become aware that cancer could impair fertility and (2) weigh the importance of fertility against their desire to survive their diagnosis.

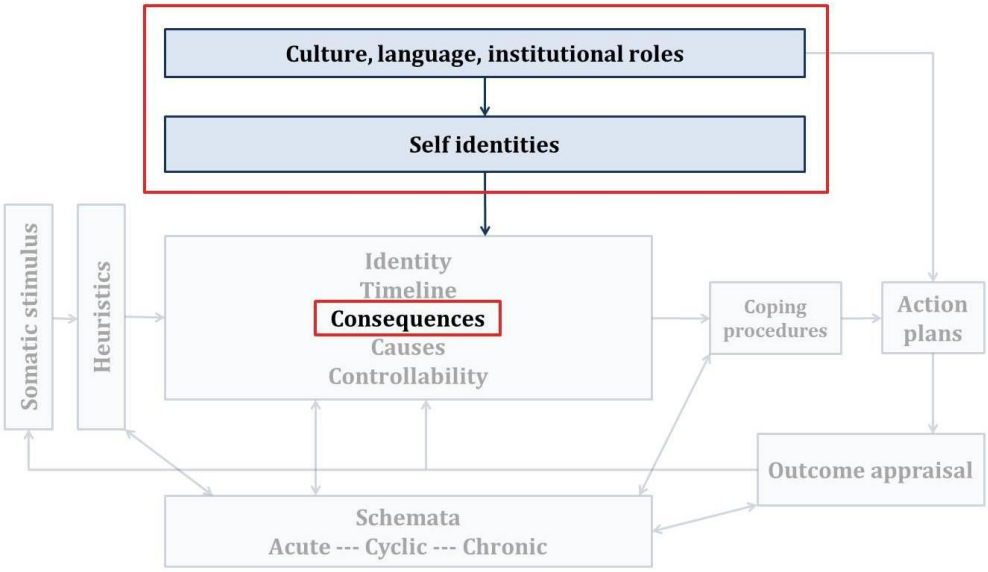


Figure 4.9. Components of the CSM reflected in the themes *Becoming aware of infertility as a potential consequence of cancer treatments* and *Attitudes towards fertility as a factor affecting cancer perceptions*

The former represents the process of forming an illness perception on an abstract level, through acquiring information about it and is summarised in section 4.3.2.2. Whilst this is not represented in Figure 4.9, it is discussed below and placed in the context of the existing evidence about young women's fertility-related information needs.

The process of weighing the importance of fertility against the wish to survive the diagnosis originated from women's general and cancer-specific attitudes towards fertility which are described in section 4.3.2.3. It transpired from women's accounts that these attitudes, giving rise to the representation of the consequences of cancer in terms

of fertility issues, were affected by the women's socio-cultural context with their self-identities acting as a mediating factor. This is illustrated in Figure 4.9 and the details are explained below.

The findings of this study suggest that women needed to know that there was a relationship between cancer treatments and fertility issues (see section 4.3.2.2). Whilst the majority of women in this study described that they had some pre-existing knowledge about cancer's potential impact on fertility, they also found it important for their physicians to provide them with additional information and the options that were available to them should they wish to preserve fertility. For some women, these discussions occurred in the course of their initial consultations and were initiated by a member of their clinical team. For others, that was not the case and these women were often disappointed by their physicians trying to avoid the topic and treating it like an *'add-on'.* This is in line with the findings from the literature review which further suggests that providing women with fertility-related information gives them the sense of agency and control over their lives (see section 3.3.3.2.2), while withholding the information from them engenders the feelings of lack of control and powerlessness (see section 3.3.3.2.2.3). It can be purported that the lack of appropriate information can lead to the failure to fully form one's illness representation (similarly to the case of illness identity described previously) and potentially result in the adverse psychological outcomes. In this study, all of the participants received the relevant information. Nonetheless, some of them reported that they had to take the responsibility for initiating the discussions and felt that had they not done that, the topic might have been ignored which in turn could have led to the problems described above.

The formation of the illness perception in terms of the consequences related to fertility issues was also influenced by women's attitudes towards fertility as described in section 4.3.2.3. As suggested by the CSM, the formation of illness representations can be influenced by culture with self-identities being a mediating factor (see Figure 2.3). Reproductive choices are often influenced by one's socio-cultural background and the meaning of fertility becomes to a certain extent an internalisation of social norms (312). The socio-cultural underpinnings of women's attitudes towards fertility transpired from their accounts through mentioning the external factors that affected the realisation of

their fertility-related plans such as being in a partnered relationship, and a stable housing and financial situation (see section 4.3.2.3.1). They seemed to have incorporated those beliefs into their own personal concepts of fertility and these were crucial in determining the importance of fertility in the context of cancer (see section 4.3.2.3.2). Hence in this study, although not necessarily all of the illness representations, but to an extent the perception of the consequences of cancer in terms of the potential fertility issues, was determined by the socio-cultural and personal value attached to fertility.

Although the CSM explains why attitudes towards fertility could have affected the perception of consequences among young women, it does not provide an answer as to how this process occurs. The literature suggests that upon learning about fertility-related consequences of cancer treatments women engage in the process of finding a balance between survival and fertility (see section 3.3.3.2.1). The findings of this study very closely reflect the current evidence. The balancing-prioritising process transpired from women's accounts and was described in section 4.3.2.3.3. Regardless of whether fertility was of importance to the women, through balancing and prioritising they were able to consolidate their perception of illness and clarify their values with respect to the outcome they wanted to achieve through treatment (preserving fertility or not). This, in accordance with the CSM, allowed them then to devise appropriate coping procedures and action plans to undertake.

While the balancing-prioritising process is described in this particular setting, it is possible that it also takes place when people deal with other health threats. According to the CSM, illness perceptions guide one's coping strategies in line with the 'IF-THEN' rule (see section 2.2.2). For example, if one has a headache, then one takes a painkiller to numb the pain. However, there might be people for whom the side effects of the anaelgesic are unacceptable in a given situation (e. g., the medication renders them incapable of driving while they have errands to run). It can be stipulated that they too would engage in a balancing-prioritising process, albeit on a much smaller scale, to choose the best strategy of coping with the pain for their particular situation. The balancing-prioritising process takes into account not only the characteristics of the health condition, but also other, not necessarily medical factors.

The balancing-prioritising process undertaken by the women in this study defined the outset from which women selected their coping strategies. This study focused particularly on one of these strategies, notably the decisions women made with regard to cancer treatments.

4.4.1.3. Making treatment decisions

As women talked about their experiences with treatment-related decisions it became apparent that many of the processes they described corresponded closely to the ones encompassed by the Shared Decision Making model (see Figure 4.10). Other issues women mentioned were outwith the realms of the Shared Decision Making model and are discussed separately in relation to the existing literature.

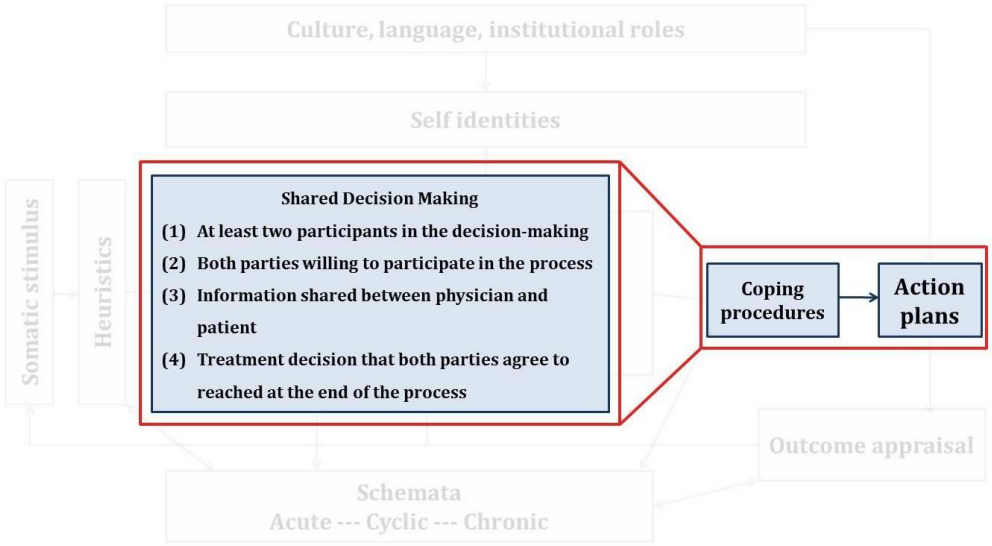


Figure 4.10. Components of the CSM and Shared Decision Making model reflected in the theme *Decisions about treatments*

As presented in Figure 4.10 the Shared Decision Making model (115) assumes that for the shared decision-making to occur four conditions need to be fulfilled. First, there needs to be at least two participants in the decision-making – the patient and the physician. However, Charles, C. et al. (116) specify that this is the minimum number and emphasise that other people such as family members and other physicians can also be involved. Second, both (or all) parties need to be willing to participate in the process in the sense that both (or all) agree to share the decision-making. If one side does not wish to participate, the decision-making cannot be shared. Third, the information needs

to be exchanged between the physician and the patient. The information here encompasses not only the medical knowledge and opinions about different treatments on the part of the physician but also patient's opinions and values that he or she wishes to take into account while making treatment decisions. The information exchange usually happens through the deliberation process where all opinions are weighed and reviewed. Finally, through negotiations, the treatment decision needs to be reached and agreed upon by all parties involved in the process.

The assumptions of the Shared Decision Making model do not preclude the patient from simply agreeing to the treatment suggested by one's physician. However, if one feels coerced to do so, then the process of the decision-making cannot be considered shared.

What is not represented in Figure 4.10, but equally important, is that for shared decision-making to occur, there needs to be a perception on the part of both the physician and the patient, that there are choices to be made (116) (for more information about Shared Decision Making model see section 2.2.2.2). Although mentioned last, as a precondition to shared decision-making, the perception of choice as it was described by the study participants is addressed first, followed by the other components of the Shared Decision Making model.

4.4.1.3.1. Perceptions of choice

As described in section 4.3.2.4.1, women differed in terms of whether they believed they had a choice with respect to treatments. Those, whose cancer stage allowed the physician to suggest several options available to treat the cancer, including ARTs for FP, clearly stated that they were given a choice. For these women a true shared decision-making could occur.

Other women, especially those diagnosed with gynaecological cancers, were in a less fortunate situation in that their cancers were often too advanced for them to be eligible for any kind of fertility preserving treatments. These women recognised that undergoing inappropriate treatments or doing nothing was not an option. This is in line with the evidence that suggests that cancer patients rarely think that they have real treatment choices to make. In a study by Charles, C. et al. (126), women with breast cancer who were deciding whether to undergo chemotherapy or 'wait and see' felt that

doing nothing was not really a choice. More recently, Jansen, S. *et al.* (313) surveyed a group of 448 early-stage breast cancer patients as to whether they perceived they had a choice with regard to treatments. The vast majority (78%) indicated they did not feel they had a treatment decision to make. Interestingly, the reason most frequently cited by the participants was that they followed their doctor's advice (313).

Although the limited availability of options might make patients feel as if they have no choice in their treatments, it has been shown that simply discussing treatments with the physicians and getting involved in the consultations can increase one's perception of treatment choices (314). Hence, accepting the physician's advice neither precludes one from perceiving that one has a choice with respect to treatments, nor does it mean that one cannot participate in the treatment decisions. Indeed, many women in this study felt they had some degree of control over their treatment choices, for example through granting their consent to treatments.

4.4.1.3.2. Participants and willingness to participate in the decision-making process

As described in section 4.3.2.4.2, women in this study sought healthcare professionals' advice and wished to be guided by experts with regard to their treatment choices which is in line with the first two assumptions of the Shared Decision Making model (see Figure 4.10) as well as the literature review (see section 3.3.3.2.3.1.2).

Having a trustworthy relationship with the physician facilitated women's decision-making processes. This type of a relationship was usually achieved through open communication, particularly with respect to fertility issues. According to the women in this study, while physicians were willing to discuss various treatment options, the initiation of fertility-related discussions was often up to the patient (see section 4.4.1.2). On rare occasions, when the physician was reluctant to discuss fertility, women for whom it was an important topic changed their healthcare providers, even if that meant eventually having to pay for the services (see section 4.3.2.4.5).

However, healthcare professionals were not the only people women wanted to include in the decision-making. As suggested in section 4.3.2.4.4, a lot of partnered women wished for their partners to be involved in the decisions which could have impact on

fertility. They often described these decisions as '*joint*'. Some of the single women wished to include their parents in the decision-making processes.

The existing literature on fertility-related decisions in the cancer setting suggests that while some women prefer to be (excluding their physicians) the sole decision-maker, others wish to engage other people in their decisions. This allows them to gain perspective on the matter and, for partnered women, to also take their partner's childbearing desires into account (see section 3.3.3.2.3.1.2). Outside the cancer setting, infertile couples who seek fertility treatments often make relevant decisions mutually (315). Although not specific to fertility, a recent study by Hubbard, G. *et al.* (316) points to other benefits of involving family members in cancer-treatment related decision-making. The findings of this study suggest that family members can act as an additional channel of communication with the physicians as well as aid patients in choosing appropriate treatments (316).

4.4.1.3.3. Information exchange and its role

With respect to the third component of the Shared Decision Making model – the exchange of information between physicians and patients, knowledge was not equally important to all the participants. They differed in terms of how much they wanted and needed to know about their treatments as well as in terms of the role that information played for them.

All women received some information about treatments from their physicians. For some of them, this information was sufficient and if they had questions, they directed them to healthcare professionals, particularly the nurses. These findings corroborate the evidence that healthcare providers tend to be the most important source of information for patients (317), and particularly for people with cancer (105).

Other women, however, assumed the responsibility for getting informed about treatment options and most often took to the Internet. For them searching for information acted as a strategy to cope with their diagnosis and served a variety of purposes. Some of the women used it as a way of reassuring themselves that they were properly cared for by their physicians which is in line with the evidence suggesting that information can generate feelings of safety and security among cancer patients (105, 109). Others

searched for information to be able to actively participate in discussions about treatments. They needed to understand the details of what was going to happen to them and why. This was particularly important in the case of treatments that could impact on fertility.

The existing literature suggests that women's preference is to obtain the relevant information about fertility from their clinical team and then inform themselves in more detail if needed. They also appreciate it if it is the physician who initiates the discussion considering that patients already have a lot to worry about and the fertility aspect might not be on their minds (see section 3.3.3.2.2). However, as shown by both the literature review and this study, this is not always the case and women often need to be assertive and take responsibility for broaching the topic of fertility (see section 4.3.2.2). The lack of sufficient information from the clinical team might have been the reason why women in this study additionally searched for information online. Some of them needed to make sure that they were not making their decisions whilst not being properly informed.

The importance of knowledge transfer cannot be underestimated – whether it is to make sure that patients understand what the treatment entails before giving their informed consent, or to involve them actively – as many young women want (113) – in treatment decision-making processes. For knowledge is a pre-requisite to participating in treatment decisions.

4.4.1.3.4. Discussing preferences as an essential component of information exchange

According to the Shared Decision Making model, information exchanged between the physician and the patient should not only encompass the knowledge and evidence but also the values and preferences of both parties. The way women clarified their values with respect to fertility, which then served as the context in which they made their treatment decisions was previously described (see section 4.4.1.2).

While both the patients' and physicians' preferences played an important role in the treatment-related decision-making processes in this study, it was the concordance between them that proved to be vital. When women's and their physicians' preferences with respect to fertility were congruous, the decision-making took an unproblematic

course. However, when women's preferences with respect to FP differed from their physicians' priorities, accommodating them in the decision-making process seemed to become more problematic. In the latter situation, two scenarios were most common. One involved women following the expert's advice at the cost of their own fertility-related preferences. In the second, women acted in accordance with their priorities, even if that meant searching for second opinions or going against the will of their physicians.

For the majority of women who may have had particular preferences with respect to fertility, the desire to follow the expert's advice overrode their priorities and dictated their treatment decisions. However, these women also exhibited an understanding why physicians were suggesting treatments which, while life-saving, could affect fertility. They accepted that fertility was a price they needed to pay to survive their diagnosis. Their physicians took the time to explain that to them. While there might not have been the concordance between the patients' and the physicians' preferences with respect to fertility in those instances, there was congruence between the patients' expectations regarding treatment-decisions and the physicians' practice styles. In their review Kiesler, D.J. and S.M. Auerbach (127) suggest that it is the latter that matters in terms of satisfaction with the decision-making processes and subsequent psychological outcomes (see also section 2.2.2).

Within this group, however, there were women who considered the fertility-related communication far from ideal. Research has shown that physicians frequently have negative preconceptions about initiating fertility discussions and suggesting FP in the cancer setting [(4), see also section 3.4.1.3]. Additionally, the literature review has demonstrated that women who are unsure of their fertility preferences at the time of diagnosis are more inclined to follow their physician's advice with respect to FP (see section 3.3.3.2.3.1.2). If this advice is not in favour of FP, it could potentially lead to situations where some women opt against FP even if their particular circumstances allow for it. This emphasises the need for the physicians to create an open-minded and non-judgmental environment for the patients to at least be able to discuss their fertility concerns, and clarify their desires with respect to post-cancer childbearing.

The failure to do so in this study may not have resulted in missed opportunities at preserving fertility, however, led some of the women to change their physician or go

against their physician's advice to ensure that their priorities were accounted for. Yet, these cases were women who were adamant from the outset that they did not wish their fertility to be taken away from them. This corroborates the evidence summarised in the literature review indicating that women who have very strong opinions about fertility are less likely to be swayed by their physician's preferences regarding FP (for details see section 3.3.3.2.3.1.2). Nonetheless, it needs to be remembered that in a stressful situation such as cancer diagnosis, not all women (including those who have strong preferences with respect to fertility) are able to be assertive with regard to what they think is right in their circumstances. This in turn might lead to future regrets in relation to the consequences of irreversible treatment decisions.

4.4.1.3.5. Reaching the treatment decision

The last phase of the Shared Decision Making process involves reaching a treatment decision between the physician and the patient. Participants in this study made their treatment decisions mutually with their physicians and significant others, and these decisions were to a variable extent informed, and motivated by women's preferences with regard to fertility.

However, including fertility in the treatment decision-making process brought about its own specific challenges. Women highlighted the problems with availability of FP under the NHS scheme as well as the costs generated if they decided to take advantage of the private services. These issues were also identified in the literature review and seem to act as universal barriers towards FP (see sections 3.3.3.2.3.2.3 and 3.3.3.2.3.2.4).

Another issue specific to FP reported by women in this study was the timing of the decisions. Often the women only had a very short window to make their decision to avoid delaying their cancer treatment. While this evidence corroborates the findings of the literature review that the timing of fertility-related decisions is limited and can act as a barrier (see section 3.3.3.2.3.2.5), it also reveals the preferences that physicians had with respect to their patients' treatments, namely that delaying cancer treatments to preserve fertility was not advisable.

Finally, preserving one's fertility carried a more symbolic meaning to the women. They perceived it not only in terms of preserving the ability to have future children but also in

terms of preserving their choice to do that. This is a novel finding not reported in the existing literature, yet, it is perhaps not surprising that in the era of reproductive freedom (318), women who were diagnosed with cancer wanted the same opportunities that are available to their peers.

4.4.1.4. Evaluating treatment decisions

According to the CSM, outcome appraisal is an integral part of the process of adaptation to a health threat. The information gained throughout this process feeds back into the organisation of a health threat perception. The altered representation acts as new baseline to modulate subsequent coping strategies which promote adjustment to the illness (see Figure 4.11, and for detailed description of the feedback loop see also section 2.2).

Since this study concentrated specifically on treatment-related decision-making as a strategy to cope with cancer diagnosis, the outcome appraisal pertained to the evaluation of the treatment decisions made by the participants and their physicians.

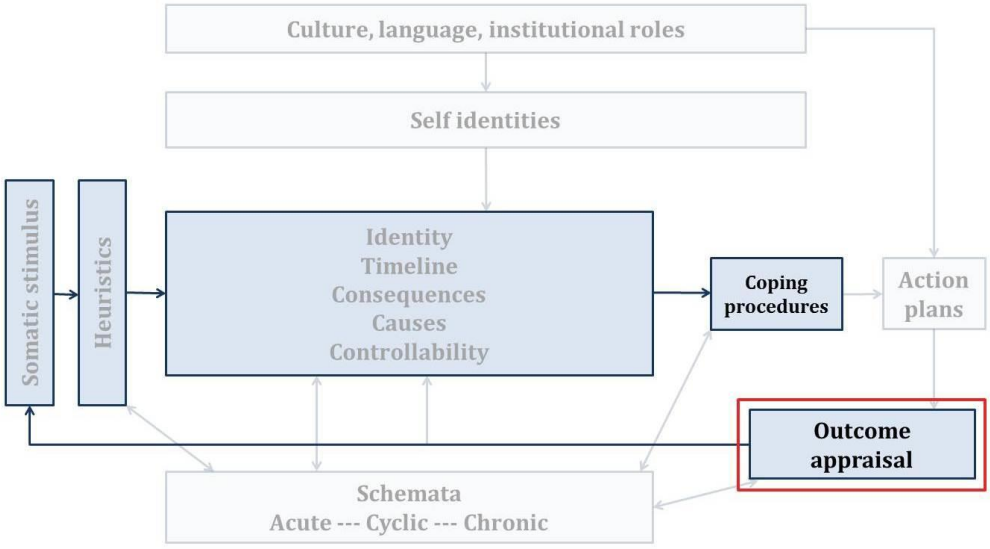


Figure 4.11. Components of the CSM reflected in the themes *Evaluation of treatment decisions* and *The consequences of treatments*

The majority of women in this study felt that the decisions they made with respect to treatments were right for their particular circumstances (see section 4.3.2.5). Two

factors possibly contributed to that – the satisfaction with the outcome of their decisions and the satisfaction with the process of the treatment decision-making.

There were two possible outcomes women could have achieved through making their treatment decisions – FP or lack of thereof. Women who preserved their fertility were generally happy with this outcome although one participant (P13) later on questioned whether that was the right thing to do due to cancer recurrence scares she had. At the time of her interview, she reported she almost regretted choosing conservative, as opposed to radical treatment.

The majority of women whose fertility did get affected by cancer treatments, as difficult as accepting this outcome proved to be, learnt to accept that this was an inevitable consequence of the process that saved their lives. Only one participant (P05) for whom FP was not possible and who, although she disagreed with her physicians' suggested course of action, still underwent cancer treatment in the form of hysterectomy expressed the feelings of regret about doing so.

These findings align with the literature in that deciding either against or for FP can have both positive and negative consequences (see section 3.3.3.2.4). However, women's appraisal of treatment decision-making, depended not only on the outcome of the treatment. The process of decision-making seemed to be equally important.

It is possible that women in this study who were satisfied with their treatment decisions felt that way because they succeeded at assuming their preferred role in the decision-making process – whether it was simply following their consultant's advice or adopting a more active role. This study shows that the latter was not always straightforward and women often needed to stand up for themselves so that their preferences were taken into account during the decision-making process.

Although this should be common practice, the research shows that physicians rarely ask their patients about the role they would wish to assume in the decision-making process (319) and that more often than not, allow their patients a less active than preferred role in the treatment decision-making process (127). This could have been the experience of the participant who regretted having undergone the hysterectomy that took away her fertility (P05, see quote on page 112). However, had she felt her reproductive concerns

had been acknowledged and addressed properly, her experience could have been different.

4.4.1.5. Moving on from diagnosis and treatment

Although most women were satisfied with the decisions they made at the time of diagnosis, going back to life as they knew it before cancer proved to be more difficult than some of them might have expected. As described in section 4.3.2.5, the appraisal of coping procedures serves to refine them and improve the adjustment to illness. In many instances it is possible that when one coping strategy fails or is found unacceptable, one can choose from an array of other strategies. The example of a headache, referred to in section 4.4.1.2, illustrates the point. Should, after all, one decide to take the painkiller even though it has undesirable side effects that can prevent one from driving a car and running errands, the timespan of these side-effects will be relatively short (i.e., they will not prevent one from engaging in those activities for more than a couple of hours) and one might also decide not to use this strategy to deal with the headache in the future. One may take another type of medication or invest in some longer-term behavioural strategies.

This process, however, does not fully apply to the case of cancer treatment decisions that can affect fertility. Women only have one chance at making the 'right' decision because its consequences are irreversible. Any adjustments to treatment decision-making as a coping strategy can only be made before any actions are carried out. Once the treatments have been administered, the feedback loop is interrupted and any adjustments to treatment decision-making as a coping strategy become impossible (see Figure 4.12). In the post-treatment phase women were left to deal with the consequences of their treatments. The three main post-treatment issues mentioned by women in this study – the persistent fertility issues, menopause, and fear of cancer recurrence are discussed below with the reference to the appropriate figures.

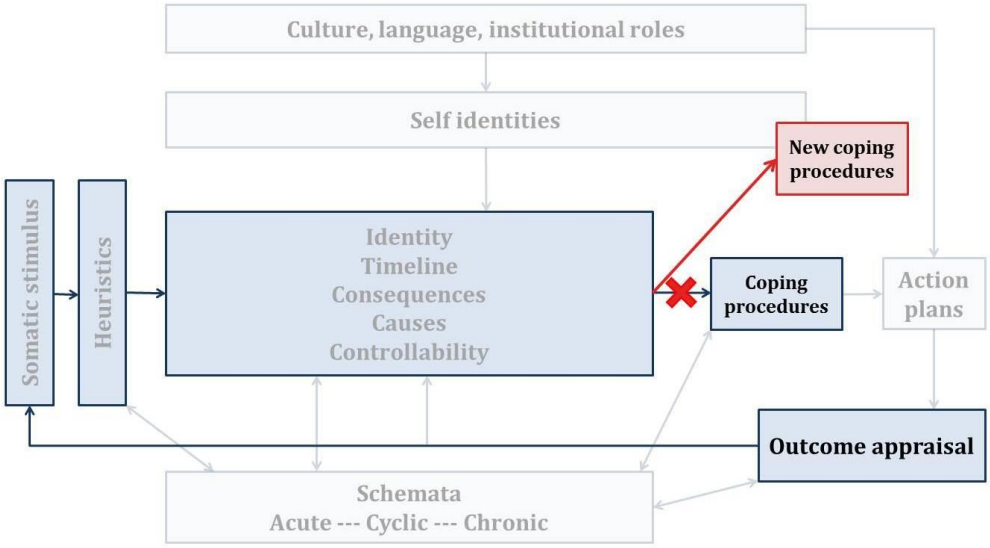


Figure 4.12. An interrupted feedback loop in the CSM as applied to the cancer treatment decisions

4.4.1.5.1. Persistent fertility issues

In this study all women, irrespective of whether they preserved their fertility, needed to come to terms with the persistent fertility issues incurred by cancer. As discussed in section 4.3.2.6.1.1, cancer diagnosis and treatment influenced every woman's reproductive choices.

One of the reasons why women decided to preserve fertility was to preserve their choice, however, this proved to be only partially effective. Whilst after cancer women were still in charge of the ultimate decision of whether to have children at all, they were at the same time constrained in how and when to realise their fertility-related plans. This finding is a novel contribution to the field and may warrant further research to investigate the extent to which these new constraints to one's reproductive freedom affect women's well-being and adaptation to life after cancer.

Other fertility-related consequences identified in this study reflect the evidence summarised in the literature review. The negative emotional repercussions such as the feelings of grief and anger that women described during their interviews are in line with the findings discussed in section 3.3.2.2.1.2. However, as opposed to the existing evidence, women in this study did not report any positive consequences of having their fertility affected by cancer. This might be due to the way the questions were asked

during the interviews, or else the way women were recruited for the study. They were a self-selected sample and were mostly interested in the topic and potentially more likely to find fertility-issues after cancer treatment problematic. However, some of the participants included in the study clearly stated that fertility was not an issue for them, yet, they did not specify any positive outcomes resulting from losing their fertility to cancer.

In addition to describing the emotional repercussions of fertility issues caused by cancer, women specified the triggers of these negative feelings, the most important of which included the comparisons they made between themselves and their peers. Through making these comparisons women discovered that they were different from their friends and that generated the perception of exclusion from the social groups they used to belong to before they were diagnosed with cancer. This corroborates the existing literature in that these perceived differences between oneself and one's peer group can contribute to the challenges of going back to normal life and moving on from the cancer diagnosis (see section 3.3.2.2.2).

The impact of these comparisons can further be explained by the fact that, as suggested by the literature, women generally see motherhood as central to their feminine identity (see section 3.3.2.2.3.1). It was also apparent in this study when women reflected on how the changes to their bodies resulting from treatments (e.g., total or partial removal of reproductive organs) affected the way the perceived themselves as women. They frequently felt as if they were '*less of a woman'* because of their treatment experience (see section 4.3.2.6.3).

Nonetheless, women in this study did also describe ways in which they tried to cope with these negative repercussions of fertility issues after cancer and adapt to their new reality. Some of them used the emotion-focused coping strategies and the majority mentioned alternative ways to parenting as a potential way to adapt to the situation. This reflects the evidence suggesting that one's ability to redefine one's own identity in terms of fertility including the concepts of biological and alternative parenthood seemed to aid in the adjustment to the life following cancer treatment (see section 3.3.2.2.3.3).

The coping strategies used by women to deal with the post-cancer fertility issues from the perspective of the CSM are illustrated in Figure 4.13.

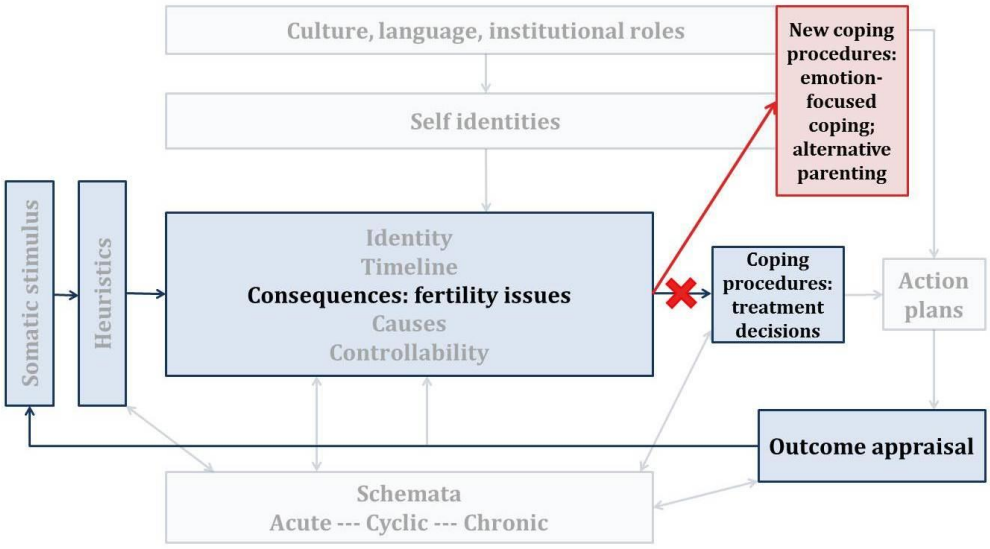


Figure 4.13. Visualisation of the new coping strategies as applied to the fertility issues post-cancer from the perspective of the CSM

The final issue that women raised in relation to post-cancer fertility problems was the impact they may have on close relationships. Whilst the majority of partnered women indicated that the whole experience brought them and their partners closer together, single women felt that their inability to have children could be problematic in terms of entering new relationships. The latter finding in particular aligns with the existing evidence in that single women often find establishing new relationships a challenge after cancer treatment. This is mainly due to the uncertainty about how and when to broach the topic of fertility with the potential partner as well as how that would affect the process of forming a new relationship (see section 3.3.2.2.1.3). Whilst, as presented in this study, fertility aspect of cancer treatments was not necessarily perceived as a barrier to building successful relationships after cancer, in both this study and the literature (see section 3.3.2.2.1.3), women occasionally reported that it could by itself be a 'deal-breaker'.

4.4.1.5.2. Premature menopause

Even though this study was primarily interested in investigating fertility issues in terms of the ability to have children after cancer, a lot of women extended this definition to

include the premature menopause, which many of them were suffering from. Menopause, while being the consequence of cancer, was conceptualised by women similarly to any other illness and in accordance with the CSM (see section 4.4.1.1). However, as opposed to cancer itself, menopausal symptoms women experienced matched the more abstract level of information, namely the label (menopause as a known side effect of cancer treatments), which enabled women to properly form the main illness representation – the illness identity. It also enabled them to promptly choose a strategy to cope with this new health problem and for women in this study it most often meant seeking medical advice as to how to manage their symptoms. Yet, the ultimate decision about the best way to deal with the symptoms was affected by women's initial beliefs regarding the cause of their cancer – another one of illness perceptions. Women who thought that their cancer was hormone-related avoided any type of hormonal treatments for the menopause and leaned towards behavioural changes or natural medications. These processes are illustrated in Figure 4.14.

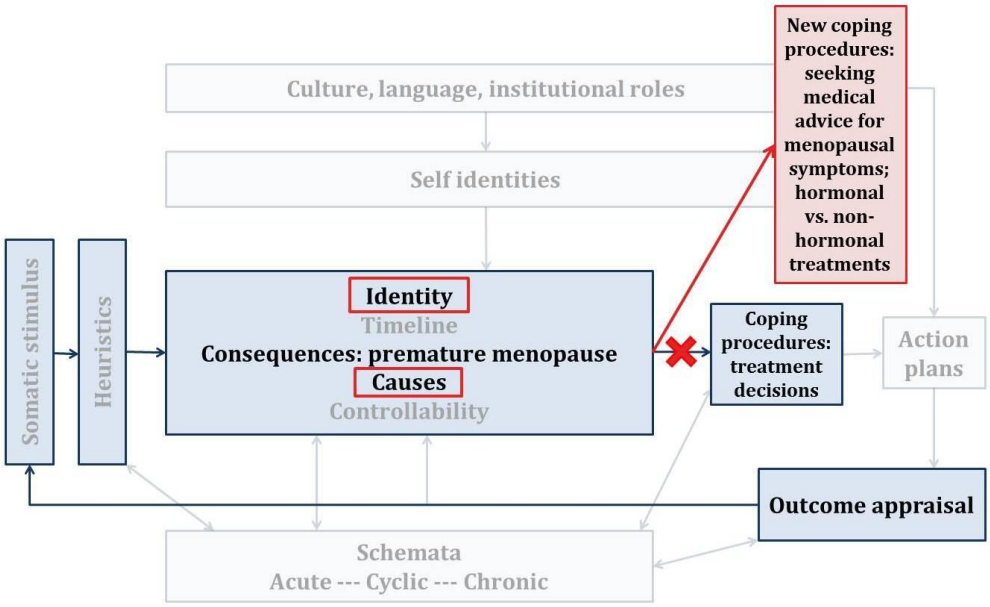


Figure 4.14. Visualisation of the strategies to cope with the premature menopause from the perspective of the CSM

4.4.1.5.3. Fear of cancer recurrence

Another consequence of cancer, perceived through the lens of cancer-related illness representations, was fear of cancer recurrence. Even though many women cited survival

and avoidance of cancer recurrence as main reasons to undergo particular treatments, fear of recurrence was prevalent among them.

Since there was no possibility of altering the treatments women hoped would prevent cancer recurrence, women needed to find ways of coping with their fears. Some of them dealt with it by visualising the treatments they received which helped them understand the process whereby the cancer was eradicated. Others sought help from the healthcare professionals every time they experienced a suspicious symptom. Unlike at the time of cancer diagnosis, in the survivorship stage women were a lot more vigilant towards their bodies and with every new symptom they immediately formulated new illness identity and acted accordingly by consulting their physician. This was potentially driven by a mechanism described by Bradley, E.J. et al. (72) who had investigated a group of gynaecological cancer patients. The authors found that due to the lack of the initial self-diagnosis and subsequent anxiety related to not being able to detect recurrence, women with early stage gynaecological cancer tended to seek reassurance from their physicians (72).

However, it was not only the new illness identity that fuelled women's strategies to cope with fear of cancer recurrence in this study. Another important illness perception to determine women's adaptation included the perceived cause of cancer. Although many women did not find it necessary to pinpoint what exactly provoked their cancer, they did question whether there was anything in their lifestyle they could change to prevent the cancer from recurring. In this way the perceived causes of cancer precipitated a coping strategy based on behaviour change. Figure 4.15 illustrates the described mechanisms to cope with fear of cancer recurrence.

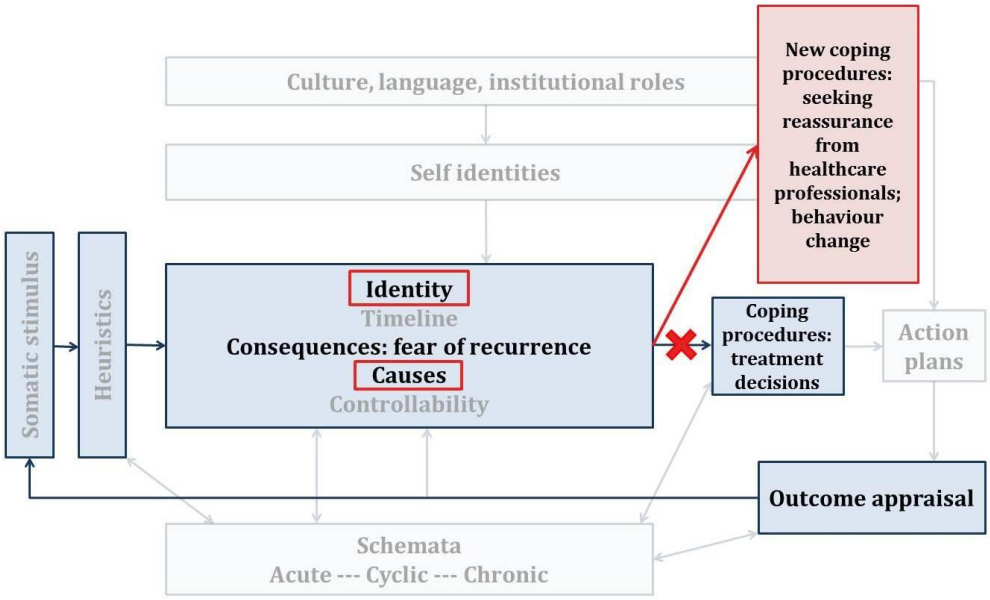


Figure 4.15. Visualisation of the mechanisms to cope with fear of cancer recurrence from the perspective of the CSM

4.4.2. Limitations

The findings of this study should be interpreted bearing in mind its limitations. Because of the methodology of the study, it has the drawbacks inherent to qualitative research in that its results cannot be easily generalisable. The study sample consisted mainly of well-educated, White, British women and this is the population that the findings could potentially be extended to. Any extrapolations, particularly to different cultural setting warrant caution.

It is possible that due to the recruitment strategy, especially the online method, participants who were interviewed for this study were a self-selected sample of women particularly interested in the issue of fertility after cancer. This would mean that the findings may apply to other women similarly preoccupied by fertility in the context of cancer. This is explained in more detail in section 4.4.3.

Finally, the limitations of this study might stem from the bias introduced by the researcher. To account for this a reflexivity statement is provided in section 3.4.3.

4.4.3. The advantages and disadvantages of using multiple recruitment strategies

Recruitment strategy used in this study and its impact on the transferability of its results has been mentioned as one of the study limitations (see section 4.4.2). However, it is perhaps worth expanding on the insights and different perspectives that were gained from using multiple strategies to recruit participants for this study. While only anecdotal, this evidence could potentially assist future research exploring particular issues related to oncofertility among young cancer patients.

In this study I used face to face and online methods to approach and invite women to take part. As described in section 4.3.1, 10 participants were recruited via the NHS and 14 through the online outlets. Tackling the differences between these two groups was not the focus of this study, however, reflecting back on the results the following could be observed:

1. Among participants recruited using the face to face method in the NHS clinics were both women who were and those who were not interested in preserving their fertility at the time of cancer diagnosis. Hence, this group was potentially more representative of the population of young women diagnosed with cancer. Qualitative inquiry does not strive to be generalisable in statistical terms but rather to provide an insight into a particular phenomenon (e.g., in the case of this study it was treatment-related decision-making in the context of fertility), therefore representativeness of the sample can be considered less of an issue in qualitative studies compared to the ones using quantitative approach. However, a sample of participants with diverse points of view can provide a more in-depth account of a particular phenomenon and strengthens the analysis in terms of its credibility through the analysis of negative cases (320).
   It was additionally observed that, in this study, women who were recruited via the NHS had a rather positive experience of how their fertility issues at the time of diagnosis were addressed. Although clinicians were not informed which of their patients eventually participated in the study and all data were anonymised, it is possible that women who had negative experience with treatment provision were less inclined to take part fearing that their accounts could be made known

to their healthcare providers and this in turn could affect the care they were receiving.

2. As opposed to the participants recruited via the NHS, the majority of those who were recruited online reported some issues with how their fertility concerns were addressed at the time of their diagnosis. This could be related to the fact that being informed about the study outside the context of direct healthcare provision (which is in contrast to the women approached for participation via the NHS) potentially made women more confident about and comfortable sharing negative experiences.

   It is also possible that women recruited online were generally more interested in the topic of the study and therefore less representative of the population of young women with cancer. As they were not directly approached for participation, it can be purported that they either actively searched for information about this particular type of project (e.g., by accessing the research sections of cancer charities websites where advertisement of the project was frequently placed) or their attention was drawn by the project topic as the advertisement appeared on Facebook or Twitter accounts of cancer charities.

In conclusion, the differences in participants' experiences of and perspectives on treatment-related decision-making in the context of fertility based on the recruitment method (NHS clinics versus online) could guide recruitment to future oncofertility studies. For projects aiming to obtain a more diverse participant sample and investigate treatment-related decision-making among young women with cancer from a broader perspective it would be advisable to use the clinic-based strategy. For projects that wish to focus on particular issues related to fertility concerns at the time of diagnosis, and the existing issues in addressing them within the clinical setting, an online recruitment strategy would be preferable.

4.4.4. Conclusions

Decisions about cancer treatment that women make at the time of their diagnosis are the first and a crucial step to preserving one's reproductive choices and freedom later in survivorship. Although there is extensive research in the field of cancer treatment-

related decision-making among young women who find fertility important, this study makes several valuable contributions.

It outlines the reasons why cancer diagnosis at a young age comes as a shock and surprise through applying the CSM framework. It also proposes how fertility fits in the conceptualisation of cancer as an illness and provides an explanation as to why and how fertility can affect treatment decisions. It emphasises the importance of the process of balancing and prioritising surviving the prognosis against the desire to preserve fertility that women engage in. This process allows women to establish their preferences and priorities in terms of the outcomes of treatments they wish to achieve and guides their decision-making. However, women's preferences also prove to be the most problematic component to accommodate in the treatment decision-making processes. They play a role to the extent that the physicians find them reasonable and agree with them. Other components of the decision-making process women find crucial are the involvement of physicians and significant others as well as the exchange of information between the patient and the physician, particularly with respect to fertility. These together reflect the main elements of the Shared Decision Making model, which seems to be women's preferred approach to making treatment decisions.

Although women's satisfaction with their decisions depends on the treatment outcome, it seems to also be determined by the quality of the process of the decision-making and the degree to which their expectations with respect to their role in the decision-making process are met by their physicians.

A novel finding of this study is that, although women preserve their fertility in view of preserving their reproductive choices post-cancer, some of these choices are nonetheless taken away from them. It warrants future investigations as to how that may impact on women's well-being in survivorship.

Finally, although treatment decision-making can be conceptualised as a coping mechanism within the CSM, it is a strategy that cannot be further adjusted so women only have one chance at making the 'right' decision. The aftermaths of treatments such as persistent fertility issues, menopause, or fear of cancer recurrence require new coping strategies to be dealt with. These coping strategies are shaped by women's initial

conceptualisation of their own disease as well as the way they perceive these consequences of their disease.

Chapter 5 Fertility issues and fear of cancer recurrence in cancer survivorship – a quantitative study

This chapter focuses on the quantitative study conducted as part of this PhD project. First, the rationale for the study, with reference to the systematic review of literature and the gaps identified within the existing evidence, is provided (section 5.1). The use of the CSM as a theoretical framework guiding the design of the research questions is also discussed in detail in this section. Second, study aims (section 5.1.1) and the research questions it attempts to address (section 5.1.2) are presented. The methodology of the study is then summarised providing details of the study design such as: participant inclusion criteria (section 5.2.1.1), and recruitment strategies (section 5.2.1.2) – with particular focus on differences between particular strategies used (section 5.2.1.2.4). Method of data collection and scales used for the purpose of the study are described in section 5.2.2. Next, data analysis plan including steps to address missing data (section 5.2.3.1), data transformation (section 5.2.3.2), and statistical analysis (section 5.2.3.3) is outlined. The results are described in section 5.3, following the order of the research questions as presented in section 5.1.2. They are then discussed in the context of the CSM as well as compared and contrasted with the existing literature (section 5.4.1). The limitations of the study are also acknowledged and their influence on final study conclusions is explained (section 5.4.2). The chapter concludes with a brief summary of the study findings and highlights the results that are novel in the field (section 5.4.3).

5.1. Introduction

Although cancer treatments are life-saving, they come at a cost of short- and long-term side effects that cancer survivors have to subsequently live with (321). One of the long-term consequences of cancer treatments are reproductive issues since many treatment modalities can impact on patients' fertility (18). It is therefore important to identify who might be at risk of being affected by fertility issues resulting from cancer treatments and how these issues are related to the indicators of psychological well-being. This information would allow the services to deliver appropriate and comprehensive care to patients.

The literature (see section 3.3.1) suggests that among young women diagnosed with cancer those who are unpartnered, do not have children, and have a strong desire to

have (more) children are the ones who experience the highest levels of reproductive concerns. These in turn contribute to women's lower psychological well-being in terms of their QoL and sexual functioning (see section 3.3.2). The evidence addressing the above questions is based on a small number of studies (five and four studies, respectively), of which none were conducted in a UK setting. As mentioned in section 2.2.3, the problem of infertility is not only defined in medical terms. The perception of fertility issues is also determined by one's socio-cultural background and extrapolating results from studies conducted elsewhere might be problematic. Therefore, it is necessary to conduct both culture-specific and cross-cultural studies. This study addresses these two gaps by being the first to investigate the predictors of fertility issues and their consequences in the UK population, and to explore the possible differences between two European populations with particular historical and cultural traditions – British and Polish (see section 2.2.3.2.1).

Another shortcoming of the literature that this study addresses is the lack of theoretical underpinnings to guide the existing studies. Although this does not preclude them from producing valid results, it makes it more problematic for researchers to explain the relationships between the investigated concepts. This project uses the CSM to uncover how the broader socio-cultural context along with illness perceptions can affect emotional responses to cancer in terms of disease recurrence, distress related to fertility issues, and QoL.

Whilst distress related to fertility issues has never been investigated in the context of the CSM, there are some studies that did examine recurrence fears using this theoretical framework (92, 93, also see Chapter 2, section 2.2.1.1.1.1). However, they did not concentrate specifically on young gynaecological or breast cancer survivors who might be particularly susceptible to fear of cancer recurrence as the rates of recurrence for these patients are significant (5-year relative survival rate for ovarian, cervical, uterine and breast cancer being 46.2%, 67.4%, 79%, 86.6% respectively) (322-325). Since fear of recurrence seems to influence QoL (50) particularly in younger cancer survivors, it is important to identify factors that predict recurrence fears in this group of patients in order to design effective interventions to enhance coping with these fears.

5.1.1. Aims

This study has two aims:

1. To investigate the predictors of distress related to reproductive issues and fear of cancer recurrence in young gynaecological and breast cancer survivors. This part of the study is guided by the theoretical framework of the CSM (see section 2.3 and 5.2.1).
2. To examine how distress related to reproductive issues, fear of cancer recurrence, and the way one perceives one's own illness affect QoL and relationship satisfaction or dating experience in this young group of patients.

5.1.2. Research questions

The following research questions were established to achieve the above aims:

5.1.2.1. Question 1

To what extent do contextual factors (cultural: disapproval of childlessness in the society, VOC; individual: one's own desire to have children, partner's desire to have children, and regret over decisions concerning treatment) and illness perceptions predict the distress related to reproductive issues in young gynaecological and breast cancer survivors after controlling for: socio-economic status, demographic characteristics, country of origin, childbearing status, medical factors (disease type and stage, treatment modality, time since diagnosis) and dispositional affect?

5.1.2.2. Question 2

To what extent do contextual factors (disease characteristics, retrospective treatment perceptions, and desire to have children) and illness perceptions predict the distress related to fear of cancer recurrence in young gynaecological and breast cancer survivors after controlling for: socio-economic status, demographic charateristics, country of origin, childbearing status, and dispositional affect?

5.1.2.3. Question 3

To what extent do illness perceptions, fear of cancer recurrence and distress related to reproductive issues predict QoL in young gynaecological and breast cancer survivors?

5.1.2.4. Question 4

To what extent does distress related to reproductive issues predict (1) relationship satisfaction; or (2) dating experience in young gynaecological and breast cancer survivors?

5.2. Materials and methods

5.2.1. Study design

This study was based on the theoretical framework of the CSM and designed as a multi-centre cross-sectional survey addressed to young women diagnosed with gynaecological or breast cancer who underwent treatment that could have effect on their fertility. The model, described in detail in Chapter 2, assumes that one defines one's illness in terms of specific illness perceptions (i.e., identity, timeline, causes, consequences, and control). These representations are affected by one's self-identities and broader socio-cultural background, and can themselves influence one's adaptation to illness in terms of psychological well-being. As outlined in sections 2.2.1.1.1 and 2.2.1.1.2, the way one conceptualised one's own illness (cancer or infertility) determines one's levels of distress and QoL associated with the illness.

In this study, I investigated whether and how illness perceptions and contextual factors affected two specific types of emotional response to illness – the distress related to fertility and fear of cancer recurrence among young women diagnosed with breast or gynaecological cancer. This is reflected by the research questions 1 and 2 (see section 5.2.1). In terms of investigating distress related to fertility issues, it is particularly important to take into account the contextual socio-cultural factors, since fertility, being socially constructed, is inherently related to one's personal background. To explore this, a cross-cultural study was designed to include participants drawn from two distinct European populations – British and Polish. The reasons why these two populations were chosen were previously described in sections 2.2.3.2.1 and 3.4.4.

I also investigated whether and how illness perceptions along with fear of cancer recurrence and distress related to fertility contributed to QoL of young women with breast or gynaecological cancer (research question 3). Based on the literature, all three independently influence QoL in cancer patients in general and young women in

particular (see sections 2.2.1.1.1 and 2.2.1.1.2 for the effect of illness perceptions on QoL in cancer and infertility patients, section 3.3.2 for the effect of fertility issues on QoL among young women, and review by Simard, S. et al. (50) for the effect of fear of cancer recurrence on QoL). Hence, I wanted to establish the cumulative effect of these three important determinants of QoL among young women with cancer and additionally investigate whether there were any cross-cultural differences.

As part of QoL investigations, I also explored the influence of fertility issues on the relationship functioning/dating experiences among young women with breast or gynaecological cancer (research question 4). Although the literature suggests a lack of association between fertility issues and relationship quality, the reviewed studies were all culture-specific. Hence, I investigated this relationship in the cross-cultural setting. Since distress related to fertility might be affected by the socio-cultural context, it might also contribute differently to relationship quality and dating experience among various populations.

5.2.1.1. Participants

Participants for the study were identified and deemed eligible to participate if they:

- were diagnosed with gynaecological or breast cancer;
- were diagnosed between the ages of 18-45 years old;
- were menstruating at the time of diagnosis;
- had chemotherapy (neo-adjuvant or adjuvant) as part of their treatment if they were diagnosed with breast cancer;
- finished active treatment (with the exception of endocrine therapy for breast cancer) prior to participation;
- had no known evidence of cancer recurrence at the time of participation;
- spoke English or Polish.

Women who were diagnosed with types of cancer other than gynaecological or breast; were diagnosed outwith the specified age range; did not undergo chemotherapy as part of breast cancer treatment; were undergoing treatment or having a recurrence at the time of invitation to participate in the study; were menopausal prior to diagnosis, or had psychiatric comorbidities were not eligible for the study.

5.2.1.2. Recruitment strategy

Participants were recruited via several outlets:

- In Scotland: the NHS-based outpatient clinics in Edinburgh (Western General Hospital and Royal Infirmary of Edinburgh), Dundee (Ninewells Hospital) and Kirkcaldy (Victoria Hospital); the Scottish Health Research Register (SHARE); Maggie's Centres (Edinburgh and Dundee);
- In Poland: two hospitals in Warsaw (the Military Medical Institute, Department of Gynaecology and Gynaecological Oncology and Anna Mazowiecka Clinical Hospital, Department of Gynaecological Oncology) and one hospital in Kielce (Swietokrzyskie Cancer Centre, Department of Gynaecological Oncology);
- Both: via online outlets of cancer charities and support organisations.

Depending on the outlet, recruitment strategy varied slightly.

5.2.1.2.1. Scotland

5.2.1.2.1.1. Gynaecology/oncology clinics (Edinburgh, Dundee and Kirkcaldy)

Potential participants were initially informed about the study by one of the collaborating clinicians (consultants or nurses) and if interested in participating, I then approached them after their oncology consultation. They were handed the research pack that contained a cover letter, a participant information sheet, a debriefing form, a questionnaire and a stamped-addressed envelope. I explained the study to the potential participants and they were then able to take the research pack with them and consider in their own time whether they would want to take part in the study. They were advised to complete the questionnaire and send it back to the researcher should they wish to participate. When I was unable to attend the clinic, the clinicians handed the research packs to their patients.

5.2.1.2.1.2. Breast clinic (Dundee)

Potential participants were initially identified through the case notes screening. The Caldicott Approval from the NHS Tayside was obtained to make this process possible. The case notes were screened against a screening chart and where patients met all the

eligibility criteria, a research pack was inserted into the case notes to let the clinician (a consultant or a nurse) treating a patient during consultation know that the patient was eligible for the study. The clinician would then inform the patient about the study during the consultation and if the woman was interested in participating, I approached her after the consultation to explain the study to her. From this point on, the procedure followed the steps outlined in section 5.2.1.2.1.1. When I was unable to attend the clinic during clinic hours, I screened the case notes beforehand and the clinicians would hand the research packs to their patients.

The recruitment through the NHS clinics took place between March 2014 and August 2015 and the overall recruitment rate was 25.49% (for details see Table 5.1).

Table 5.1. Participant recruitment details for NHS clinics

Site	Clinic	Recruitment dates	Research packs given out	Questionnaires returned (participation rate)
Dundee, Ninewells Hospital	gynaecology outpatients	Mar 2014 – Aug 2015	8	3 (38%)
Edinburgh, Western General Hospital	oncology outpatients	Jun 2014 – Aug 2015	92	17 (18.49%)
Edinburgh, Royal Infirmary	gynaecology outpatients	Nov 2014 – Aug 2015	1	0
Kirkcaldy, Victoria Hospital	gynaecology outpatients	Oct 2014 – May2015	3	2 (66.67%)
Dundee, Ninewells Hospital	breast outpatients	Oct 2014 – May 2015	49	17 (34.69%)
Overall			**153**	**39 (25.49%)**

5.2.1.2.1.3. The SHARE register

The SHARE is an initiative conceived by the NHS Research Scotland in partnership with the Scottish government and Scottish universities to create a register of people aged over 16 and residing in Scotland who would be interested in helping out with medical research. The SHARE register was approached and agreed to facilitate the recruitment for the study. The initial inclusion criteria used by SHARE were defined based on the health board the potential participant belonged to (Tayside and Fife were

included), gender (female), age at diagnosis (18 to 45) and the ICD codes for diagnoses of gynaecological cancer. The following codes were provided to the SHARE: C53 (C53.0, C53.1, C53.8, C53.9); C54 (C54.0, C54.1, C54.2, C54.3, C54.8, C54.9); C55; C56; C57.0. The search was conducted by the SHARE staff in June 2014 and returned 91 potential participants who were in the first instance contacted by SHARE and invited to participate in the project using an invitation letter briefly describing the study (see Appendix 13). Twenty-seven women (29.7%) agreed to be contacted by the researcher for participation. Their contact details were sent to the researcher via online software designed by the Health Informatics Centre at the University of Dundee to assure data confidentiality. I subsequently sent out 13 research packs. Three women with correct diagnoses responded as well as four women who were diagnosed with breast cancer. At the time when SHARE was approached for assistance with the project (between March 2014 and June 2014), the diagnosis of breast cancer was not yet an inclusion criterion for this study. A problem with the system identifying potential participants within SHARE was detected and the SHARE assisted recruitment was stopped. This incident was reported to the ethics committees who had given their approval for the project. The data from eligible participants (3) who were all diagnosed with cervical cancer and correctly identified for the study were retained for analysis.

5.2.1.2.1.4. Maggie's Centres

Maggie's Centres provide emotional, practical, social as well as informational support for cancer patients and their relatives by organising workshops, support groups and individual counselling. Maggie's centres in Dundee and Edinburgh along with the online centre were approached to facilitate the recruitment for the study.

5.2.1.2.1.4.1. Dundee

A poster was placed on the advertisement board in Maggie's Dundee centre. The poster provided information about the study as well as a link to the online survey. It also advised potential participants that if they wished to participate in the study but did not want to complete the online version of the questionnaire, they could obtain a research pack from one of the centre staff. On one occasion I also attended a meeting of a cervical cancer support group for young women where I presented the study and distributed the research packs among the participants. Two questionnaires were

subsequently returned. One of the participants who returned the questionnaire did not meet all the study inclusion criteria, therefore, her questionnaire was excluded from the analysis.

5.2.1.2.1.4.2. Edinburgh

The centre head agreed to inform potentially suitable women who came to the centre about the study and give out the research packs. Six research packs were left in the centre, yet no questionnaires were returned.

5.2.1.2.2. Poland

5.2.1.2.2.1. Anna Mazowiecka Clinical Hospital

Potential participants were identified by the collaborating consultants and those interested in taking part in the study were given a research pack. They were advised by the consultants to fill the questionnaire out and send it back to the researcher should they wish to participate. A special post box with a unique address located at a local post office was rented for this purpose. Two participants were recruited through this centre (see Table 5.2).

5.2.1.2.2.2. Swietokrzyskie Cancer Centre

Potential participants were identified by the collaborating consultant and those interested in taking part in the study were given a questionnaire. They were advised by the consultant to complete the questionnaire in their own time and bring it back to the clinic at the time of their next follow-up consultation and leave it with the consultant. Eighteen participants were recruited through this centre (see Table 5.2).

5.2.1.2.2.3. Military Medical Institute

Potential participants were first identified by the collaborating consultant from the hospital electronic database. Their contact details were passed on to the researcher who contacted the patients via phone and invited them to participate in the project. Initially 83 participants were identified from the hospital electronic database based on the age criterion. They were all diagnosed in the years 2010-2014. The telephone number was missing for 21.7% of women (18/83). Another 9.6% of the telephone numbers (8/83) were identified as wrong or non-existent upon calling. The remaining 57 women were first called in August 2014. Two women were deceased by this time (one diagnosed

with cervical cancer and one with uterine cancer). One was still receiving treatment at the time of the invitation and thus was not eligible to take part. Four women declined participation in the project. Twenty-seven women did not answer the phone. The remaining 24 women who verbally consented to participate in the study agreed to receive the research pack via post (9/24) or a link to the survey via email (15/24). Of the women who were sent the questionnaire, 61% returned it. The response rates were 44% and 67% for postal and online survey, respectively. The 27 women who did not answer the first phone call were re-contacted in March 2015. Eighteen of them were still unreachable and the remaining nine consented to participate. They were all sent a link to the online survey via email. Four of them (44.44%) did participate, however, one needed to be excluded from the final analysis due to the disease recurrence.

In total, 36 participants were recruited from Polish hospitals (see Table 5.2).

Table 5.2. Participant recruitment in Polish hospitals

Site	Clinic	Recruitment dates	Research packs given out	Questionnaires returned (participation rate)
Anna Mazowiecka Clinical Hospital	gynaecology outpatients	May 2014 – Aug 2015	unrecorded	2
Swietokrzyskie Cancer Centre	oncology outpatients	Aug 2015 – Aug 2015	unrecorded	18
Military Medical Institute	oncology outpatients	Aug 2014 – Apr 2015	33	16 (48.48%)
Overall				**36**

5.2.1.2.3. Online outlets

Information about the study was also distributed online by British and Polish cancer charities and cancer support organisations. They were first approached via email or private message on Facebook to inquire whether they would be willing to disseminate information about the study. Organisations which agreed to facilitate the recruitment did so in their own capacity using different online outlets (for details see Table in Appendix 10). The most frequently used Twitter-based strategy involved the researcher tweeting about the study and the organisations retweeting the information. In the process, tweets were not only retweeted by the charities but also by anybody on Twitter who wished to

do so. Overall, I tweeted the information about the study 148 times and it was retweeted 244 times over a period of 18 months.

The tweet included the age (18-45) and diagnosis (gynaecological or breast cancer diagnosis) criteria to give an indication of who would be eligible to participate in the study and a link to an advertisement that contained more information about the study. The advertisement (see Appendix 14) was designed in a way that potential participant could anonymously access the online survey hosted by the Smart Survey (www.smartsurvey.co.uk) without contacting the research team. However, it also displayed contact details to the research team if a potential participant wished to contact the researchers with any questions or concerns. The online survey consisted of the participant information sheet, the questionnaire and the debriefing form. Since the survey was anonymous and participants did not need to contact the researcher to participate, the researcher could not personally check whether the participants met all the inclusion criteria. However, to assure that participants recruited online met the inclusion criteria, three filtering questions checking participant's eligibility preceded the questionnaire (see Appendix 16). Where the potential participant missed any of the inclusion criteria, she was directed to a *Thank you* page without being able to complete the questionnaire. Eligible participants were able to proceed to the survey.

The participation rates were 41.18% and 89.53% for Polish and British online recruitment, respectively (see Table 5.3).

Table 5.3. Participant recruitment through online outlets

	UK	**Poland**
Clicked on the survey	136	54
Met all the inclusion criteria	86	17
Provided analysable data	77	7
Participation rate (provided analysable data / met all the inclusion criteria)	89.53%	41.18%

5.2.1.2.4. Differences in recruitment depending on the outlet

While the practicalities of the recruitment strategies were described in detail in sections 5.2.1.2.1, 5.2.1.2.2, and 5.2.1.2.3, it is perhaps worth outlining how these strategies differed due to the project's organisational and practical issues and how those

differences could have potentially impacted on the type of participants that were recruited using them.

The recruitment through the clinics and Maggie's centres in Scotland was most of the time conducted face to face. This means that I was present in the clinic or in the centre to introduce the project to the patients and personally invite them to participate. This could have potentially influenced recruitment in that women felt that by participating they were helping somebody they had met and were therefore doing it for altruistic reasons. Both women who were and those who were not interested in fertility were approached through the clinics and this recruitment strategy allowed for obtaining a balanced sample of the studied population (as it would be expected that women's interest in fertility would vary).

For practical reasons, recruitment in two of the Polish clinics was conducted by the treating consultants. As approach to the patient-physician relationship in Poland still tends to be rather paternalistic, using this recruitment strategy could mean that patients were more inclined to participate as they were asked to do it by the person who was in charge of their medical care. In one clinic, the recruitment occurred over the phone – I made the first contact with the patients who were treated in the clinic within the previous 5 years (which was made possible due to a contract signed directly with the hospital) and invited them to participate. As in the case of recruitment in Scotland, this might have yielded a sample of patients who participated in the study for altruistic reasons.

Finally, as the recruitment online occurred mostly using the outlets of cancer charities, it is possible that women who get involved with charities are generally more altruistic and again that could have been the reason why they participated in the study. Also, it is possible that women who found the study advertisement and accessed the online survey constituted a self-selected sample of participants who were more interested in the topic of fertility. Indeed the results of this study suggest that women recruited online significantly differed from women recruited through the clinics in terms of the reported fertility-related distress.

In conclusion, these differences in recruitment strategies and various reasons for which women participated in the study need to be borne in mind when interpreting the results of the study.

5.2.2. Data collection

Participants filled out a one-off anonymous questionnaire. All the data were collected via self-report.

5.2.2.1. Variables and measures

The final version of the questionnaire was prepared in two languages – English and Polish. It consisted of four types of measures. Socio-demographic and disease characteristics were measured using multiple choice or open-ended questions. Where available, the standardised instruments were used to measure the predictor and outcome variables. If no standard instruments were available, single items were developed based on evidence from the literature. Where Polish adaptations of instruments were available, these were used. Scales that did not have Polish translations (VOC Scale, FCR, CSI(4), and CARES dating subscale) as well as single item measures were adapted for use in Polish using the standard procedure of translation to Polish and back-translation to English. The English versions were then compared and the Polish translations adapted accordingly.

All the questions and scales included in the survey are outlined below. Their psychometric properties are available in Appendix 15 and the internal consistency scores obtained in this study are presented in Table 5.4.

5.2.2.1.1. Predictor variables

1. *Socio-demographic variables* (age, country of origin, relationship status, childbearing status, monthly income level before tax, and the highest education level).
2. *Disease characteristics* (type of cancer diagnosis, stage of cancer at diagnosis, type of treatment received, and date of diagnosis).
3. *Illness perceptions.* Illness perceptions were measured using the 9-item Brief Illness Perception Questionnaire (Brief-IPQ) (326). The Polish version of the Brief-IPQ (Kwestionariusz Percepcji Choroby – wersja skrócona) was obtained

from the author. The Brief-IPQ uses an 11-point Likert scale to assess eight dimensions of illness perception. Two items reflect the emotional representation of illness (coherence and emotions), five items reflect the cognitive representation (consequences, treatment control, personal control, identity, and timeline), and one item reflects the comprehensibility (coherence). The overall score of the scale represents the degree to which an illness is perceived as threatening. The scale also contains an open-ended question asking about the likely causes of the illness.

4. *Decision regret.* Regret related to the outcome of the treatment process, specifically the fertility impairment due to treatment, was measured using a single item designed for the purpose of the study (see Appendix 16). Participants rated the item on a 5-point Likert scale with responses ranging from 'not at all' to 'extremely'.
5. *Treatment perceptions at the time of diagnosis*. Patient's perceptions of the appropriateness of treatment were measured retrospectively using a single item designed specifically for the purpose of this study. Participants were asked to assess on a 5-point Likert scale (with responses ranging from 'not at all' to 'extremely') the extent to which they believed the treatment they were about to receive was the best option for them (see Appendix 16).
6. *Dispositional affect*. The negative affect (NA) was measured using the NA subscale of the Positive and Negative Affect Scale (PANAS) (327) or the Polish equivalent SUPIN (Skala Uczuć Pozytywnych i Negatywnych) (328). PANAS/SUPIN measure both the positive and negative affect using 20 adjectives (10 pertaining to PA and 10 to NA) that participants evaluate on a 5-point Likert scale. The total subscale score is produced by summing responses to 10 items, with a range 10-50. A higher score indicates a higher level of affect. Depending on the instructions the scale can measure affect as a state ('to what extent do you feel this way right now') or as a trait ('to what extent you generally feel this way'). For the purpose of this study, the NA subscale of PANAS/SUPIN was used to measure negative affect as trait.
7. *Cultural factors*. Two types of culturally relevant factors that might affect the psychological well-being of women with fertility problems: the social

disapproval of not having children and the value that women attach to having children were measured in this study.

a. Social disapproval of not having children was assessed using a single item designed based on the literature for the purpose of this study (see Appendix 16). Participants rated the item on a 5-point Likert scale with responses ranging from ‘not at all’ to ‘extremely’.
b. The value that women attach to having children was assessed using a scale adapted from a cross-cultural study on VOC. This scale was constructed based on the concept by Hoffman, L.W. (139) pertaining to the role children serve to their parents. The scale consists of 27 items that form three general dimensions of VOC: the psychological-emotional value (12 items), the economic-utilitarian value (five items) and the social-normative VOC (seven items). The remaining three items are independent items not included in any subscale. Each item is scored on a 5-point Likert scale with responses ranging from “not important at all” to “very important”.

8. *Desire to have children.* Since no validated scale to assess this construct was available, participant’s and partner’s desire to have children at the time of cancer diagnosis was measured using two items designed for the purpose of this study. Participants were asked to evaluate one’s own and partner’s desire to have children on a 5-point Likert scale with responses ranging from ‘not at all’ to ‘extremely’ (see Appendix 16). Participants who were single at diagnosis were asked to rate their own desire to have children only.

5.2.2.1.2. Outcome variables

1. *Distress related to reproductive issues.* The Impact of Event Scale Revised (IES-R) (329) was used to measure distress related to reproductive issues. The Polish version of the scale (Zrewidowana Skala Wpływu Zdarzeń) (330) was obtained from the authors. The IES-R consists of 22 items scored on a 5-point Likert scale (with responses ranging from ‘not at all’ to ‘extremely’). The items form three subscales paralleling the diagnostic criteria of post-traumatic stress disorder: intrusion, avoidance, and hyperarousal. The subscale scores are produced by obtaining the mean score of the items belonging to a subscale and

are within the range of 0-4. The overall scale score can be obtained by summing responses to all 22 items, with a range 0-88.

2. *Fear of cancer recurrence*. Fear of cancer recurrence scale (FCR) (331, 332) was used to measure fears and worries about cancer coming back. The questionnaire consists of six items scored on a 5-point Likert scale (with responses ranging from ‘not at all’ to ‘all the time’) and one statement scored on a 10-point Likert scale (with responses ranging from ‘not at all’ to ‘a great deal’).
3. *Quality of life*. The Quality of Life Adult Cancer Survivors (QLACS) (333) was used to measure QoL. It is an instrument recommended for use among cancer survivors “due to its multidimensional approach to QoL and its domain-specific sensitivity to a number of potential self-management outcomes” (334, p. 22). The Polish version of the questionnaire (Ankieta Oceniająca Subiektywne Poczucie Jakości Życia) (335) was obtained from the authors. QLACS is a 47-item questionnaire scored on a 7-point Likert scale (with responses ranging from ‘never’ to ‘always’) that measures the general and cancer-specific QoL. The part of scale assessing the general QoL consists of 28 items that form seven following subscales: negative feelings, positive feelings, cognitive problems, pain, sexual problems, energy/fatigue, and social avoidance. The cancer-specific part of the scale consists of 19 items which form five following subscales: financial problems, benefits, distress-family, appearance, and distress-recurrence. For the purpose of the study, two subscales from the cancer-specific domain – the financial burden and distress-recurrence subscales were removed from the questionnaire. The financial burden subscale was not deemed suitable for the population under study (due to the differences in health care systems in the UK and Poland where the study took place and the US where the scale was developed). Distress-recurrence subscale was removed since fear of recurrence was already being measured using another instrument.
4. *Relationship satisfaction/dating behaviour*.
    a. Relationship satisfaction was measured among partnered participants using the CSI(4) (336). Of the four items, one is scored on a 6-point Likert scale (with responses ranging from “extremely unhappy” to

"perfect"), whereas the remaining three on the 5-point Likert scale (with responses ranging from "not at all (true)" to "completely (true)"). Authors provide the distress cut-off score of 13.5 points (336).

b. Dating behaviour among single participants was measured using the dating subscale from CARES (337). This subscale contains five items rated on a 5-point Likert scale (with scores ranging from 'not at all' to 'very much').

Table 5.4. Scales reliability indicators for the English and Polish versions of the questionnaire

	Scale reliability (Cronbach's α)	
	English version	**Polish version**
VOC_U	0.66	0.82
VOC_S	0.75	0.74
VOC_P	0.86	0.89
PANAS	0.91	0.93
IESR_I	0.93	0.94
IESR_A	0.88	0.90
IESR_H	0.91	0.93
IESR_T	0.96	0.97
FCR	0.91	0.90
QLACS_NF	0.77	0.87
QLACS_PF	0.91	0.87
QLACS_CP	0.90	0.92
QLACS_P	0.93	0.89
QLACS_SP	0.88	0.78
QLACS_F	0.90	0.88
QLACS_SA	0.89	0.91
QLACS_B	0.86	0.86
QLACS_DF	0.91	0.85
QLACS_A	0.85	0.88
QLACS_GT	0.90	0.92
CSI_T	0.95	0.93
CARES	0.95	0.92

5.2.3. Data analysis

Prior to the start of data collection process, I created an Excel spreadsheet containing all the variables. Questionnaire data were entered into this spreadsheet as they arrived throughout the recruitment period. At the end of the data collection period, I inspected the database for errors using visual and statistical methods to assure quality control. The

database was first cross-checked against the original questionnaires and any mistakes were corrected. In addition, descriptive statistics of all the variables were analysed and where outliers or abnormal values were detected, these were corrected as appropriate. The data were also examined for missing values and where appropriate, missing data were substituted (see section 5.2.3.1). The prepared database was exported to the Statistical Package for Social Sciences for Windows, version 22 (338) which was used to transform the data where necessary (see section 5.2.3.2) and conduct statistical analyses (see section 5.2.3.3).

5.2.3.1. Dealing with missing data

Of the 164 questionnaires returned, some contained unclear or missing data.

5.2.3.1.1. Unclear data

Unclear data were addressed in the following manner:

1. Where two responses were indicated for one item and there were no missing responses for adjacent items (above or below):
    a. the item was coded based on the more conservative response if the responses were adjacent (e. g., the participant chose two answers, one signifying 4 and the other one 5 on a Likert scale)
    b. the item was coded as missing if the responses were non-adjacent (e. g., the participant chose two answers, one signifying 3 and the other one 5 on a Likert scale)
2. Where two responses were indicated for one item and none for the item beneath, the less conservative one was used as answer to the item with missing response.
3. Where participant indicated her relationship status and subsequently ignored the skip logic and filled out scales for both single (CARES dating subscale) and partnered [CSI(4)] women, only the responses to the scale corresponding to the relationship status were used for analyses.
4. Where participant did not indicate her relationship status but subsequently filled out only one scale for either single or partnered women, her relationship status was inferred based on the responses she provided.

5. Where the participant did not indicate her relationship status and subsequently filled out scales for both single and partnered women, her relationship status was coded as missing and data from both scales were used for analyses.
6. In two cases where current age was not provided, this information was obtained from patient lists available in the clinic or from the interview with the participant for the other part of the project.

5.2.3.1.2. Missing data

By design, the questionnaire used for the purpose of this study yielded missing data. This is because skip logic based on participant's relationship status (*single* or *in a relationship*) was applied to administer a scale appropriate to the participant's current situation (CSI(4) for partnered and CARES dating subscale for single women). Excluding these systematically missing data, 30.49% of participants returned questionnaires without any missing values. The remaining 69.51% of participants returned questionnaires with at least one missing data point due to inadvertently missing or choosing not to answer one or more questions.

The proportion of missing values across all questionnaire items applicable to groups of participants based on relationship status was 2.70%. Although Schafer, J.L. (339) concluded that missing rate of 5% or less is negligible in terms of providing accurate parameter estimates, excluding cases with incomplete data can greatly reduce statistical power of the study (340). Hence, whenever possible, missing data were imputed to preserve the sample size.

5.2.3.1.2.1. Missing data imputation

Where the participant failed to provide information on socio-demographic, disease-related, or Likert-type single items (e.g., not forming scales), these were coded as missing and cases were excluded from subsequent analyses. In the case of item non-response within scales, imputation methods were used.

5.2.3.1.2.1.1. Patterns of missing data

First, the patterns of missing data were explored for scalar data. This was initially done by comparing the distributions of missing data on scales or subscales between groups based on socio-demographic (country of origin, relationship status, childbearing status,

income, and education level) and disease related (type of diagnosis, stage at diagnosis, type of treatment received) characteristics using the Chi-square or Fisher's exact test where Chi-square test's assumptions were violated. The Bonferroni correction was applied and tests were considered significant at $p<0.0045$. Since only 1.82% of the results (4 out of 220 tests) proved significant (see Table 5.5), it was concluded that missing data patterns were independent of socio-demographic or disease-related characteristics and that data were therefore missing at random. Hence, standard imputation methods were used to substitute missing data.

Table 5.5. Significance levels of Chi-square or Fisher's exact test investigating whether missing data patterns in scalar data were dependent on socio-demographic or disease characteristics. Tests significant at *p<0.0045*.

	VOC_U	VOC_S	VOC_P	PANAS	IESR_I	IESR_A	IESR_H	IESR_T	FCR	QLACS_NF	QLACS_PF	QLACS_CP	QLACS_P	QLACS_SP	QLACS_F	QLACS_SA	QLACS_B	QLACS_DF	QLACS_A	QLACS_GT
*country of origin	0.25	0.24	0.49	0.07	0.1	0.24	0.04	0.16	0.001*	0.79	1	1	0.55	1	1	0.76	0.09	0.73	0.44	0.91
*relationship status	1	0.07	1	1	1	1	0.64	0.58	0.02	0.52	0.75	0.69	1	0.55	1	0.73	1	0.45	0.31	0.88
*childbearing status	0.89	0.50	0.38	0.23	0.51	0.06	0.02	0.12	0.91	0.40	0.26	0.54	0.33	0.80	0.39	0.59	0.20	0.33	0.29	0.47
*education level	0.1	0.53	0.18	0.27	0.07	0.02	0.001*	0.002*	0.03	0.07	0.67	0.06	0.09	0.11	0.49	0.12	0.07	0.27	0.23	0.001*
*income	0.66	0.89	1	0.45	0.90	0.45	0.85	0.97	0.33	0.82	0.91	0.22	0.58	1	0.62	1	1	0.44	0.69	0.55
*type of diagnosis	0.86	0.85	0.95	0.08	0.42	0.65	0.88	0.70	0.1	0.86	0.94	0.89	0.38	0.86	0.91	0.38	0.47	0.89	0.07	0.73
*stage of diagnosis	0.06	0.02	0.35	0.83	0.94	0.76	1	0.69	1	0.40	0.65	0.20	0.92	0.95	0.64	0.86	1	0.92	0.72	0.69
*surgery	1	0.46	0.37	0.10	0.75	0.31	0.74	0.57	0.92	0.37	0.85	0.14	0.81	0.93	0.79	1	0.53	1	0.84	0.47
*radio-therapy	0.47	0.74	0.44	0.15	0.36	0.76	0.7	0.95	0.47	0.19	0.44	0.74	0.76	0.81	0.74	0.76	0.89	0.74	0.89	0.80
*chemo-therapy	0.45	0.34	0.99	1	0.87	0.54	0.7	0.54	0.01	0.18	0.93	0.51	0.54	0.99	0.75	0.66	0.01	1	0.06	0.97
*endocrine therapy	0.7	1	1	0.36	0.22	0.21	1	0.13	0.7	1	0.70	1	0.69	1	0.67	0.69	0.7	1	0.7	0.61

5.2.3.1.2.1.2. Imputation method

Roth, P.L. *et al.* (341) suggested that for multiple item scales, item imputation based on the individual's average of other responses to that scale is an appropriate method for dealing with missing data. The use of person-mean imputation method has been further supported by studies investigating the performance of various imputation techniques. Shrive, F.M. *et al.* (342) compared multiple imputation to five single imputation methods on a Zung Self-reported Depression scale and reported that when up to 10% of the values were missing, person-mean imputation was not inferior to multiple imputation. Although the results yielded by person-mean imputation became less favourable as the frequency of missing values increased, with 30% of missing values the agreement between data imputed by person-mean and multiple imputation strategies was still substantial ($\kappa = 0.76$) (342). Bono, C. *et al.* (343) used four single imputation strategies to address missing data on Center for Epidemiologic Studies – Depression scale. They found that the item-mean, person-mean, regression, and hot-deck imputation methods all performed similarly well when participants missed 20% or fewer items on the scale (343). Downey, R.G. and C. King (344) also suggested that the use of person-mean imputation resulted in a good representation of data when the number of participants with missing data on a particular scale and the number of items missing per participant on that scale were both 20% or less. Finally, Fairclough, D.L. and D.F. Cella (345) investigated non-response to individual items on a QoL scale and concluded that if the scale reliability was acceptable and the proportion of missing values was low (up to 8% across the scale), participant-specific estimates of missing data points generated the most accurate imputation of the participant's total score. They also suggested that item-level imputation based on the individual subscale mean was more accurate then imputation based on the scale average and advised to use subscale means when more than 50% of subscale items were observed (345).

In light of this evidence, the missing data were investigated for:

1. the proportions of missing items across subscales and scales;
2. the proportions of participants with missing data on scales and subscales.

As shown in Table 5.6 the proportions of missing items across scales and subscales as well as the proportions of participants with missing data on scales and subscales were

low and within limits outlined by Fairclough, D.L. and D.F. Cella (345) and Downey, R.G. and C. King (344) for all the scales and subscales.

Table 5.6. Proportions of missing data across all items of a scale/subscale (column 1) and proportion of participants with at least one missing data point for a scale/subscale (column 2)

	Across items of the scale/subscale	Participants with at least one missing data point for the particular scale/subscale
VOC_U	1.22-3.66%	7.93%
VOC_S	1.22-2.44%	6.10%
VOC_P	0.61-3.05%	9.76%
PANAS	0.61-2.44%	4.88%
IESR_I	0.61-3.05%	7.32%
IESR_A	0.61-3.66%	6.71%
IESR_H	1.22-2.44%	4.27%
FCR	0-3.05%	7.93%
QLACS_NF	3.05-4.88%	7.93%
QLANC_PF	3.05-4.88%	8.54%
QLACS_CP	3.05-3.66%	5.49%
QLACS_P	3.66-4.27%	6.71%
QLACS_SP	4.88-6.10%	9.76%
QLACS_F	3.05-3.66%	6.10%
QLACS_SA	3.05-5.49%	7.32%
QLACS_B	3.66-6.10%	7.93%
QLACS_DF	3.05-4.88%	5.49%
QLACS_A	3.05-6.10%	7.93%
CSI	3.23-5.65%	6.45%
CARES	7.14%	7.14%

Missing data were also investigated within participant per scale or subscale and the threshold of 20% was adopted as a cut off for imputation as suggested by Downey, R.G. and C. King (344). Based on this criterion excluded from imputation were CSI and CARES scales. CSI items were not imputed since this scale only has four items and therefore missing data within participant were always above the 20% threshold. CARES data were not imputed since the few cases where CARES data were missing involved the whole instrument having been left uncompleted.

For the remaining scales, missing data were imputed according to the following rules:

1. For scales with defined subscales (VOC and IES-R) – the participant's subscale mean score was imputed in place of a missing value if all the missing values constituted less than 20% per case within that subscale.
2. For scales without defined subscales (PANAS and FCR) – the participant's scale mean score was imputed in place of a missing value if all the missing values constituted less than 20% per case within that scale. However, when imputing FCR missing items, only items 1 to 6 were imputed based on the average or the observed ones. Item 7 has a different scoring system and therefore was excluded from imputation.
3. For QLACS scale – missing values were imputed as suggested by Ashley, L. *et al.* (346) following the scale developers' recommendations: where one item was missing per domain, the score was imputed as individual's average of the present responses. However, where two or more items were missing, the domain score was coded as missing.

5.2.3.1.2.1.3. Evaluation of imputation methods

The goodness-of-fit of the imputation methods used was assessed by comparing the measures of central tendency and distributions between the imputed and non-imputed datasets for all the scales and subscales. Potential differences in the measures of central tendency were evaluated using t-test for normally distributed and Mann-Whitney U test for non-normally distributed variables (the normality was checked using one-sample Kolmogorov-Smirnov test, for details see Table in Appendix 17). Potential differences in the distributions were investigated using two-sample Kolmogorov-Smirnov Z test.

There were no significant differences in terms of either the measures of central tendency or distributions between the variables in the non-imputed and imputed datasets (see Table 5.7). It was therefore concluded that the imputation methods provided reliable substitutes for the missing data and the imputed dataset was used for all the subsequent analyses.

Table 5.7. Test parameters and significance levels for t-test, Mann-Whitney-U and Kolmogorov-Smirnov tests assessing the goodness-of-fit of imputation methods

	T-test		Mann-Whitney-U test		Two-sample KS test	
	t	***p***	**Z**	***p***	**KS**	***p***
VOC_U	-	-	-0.06	*0.95*	0.17	*1*
VOC_S	-0.33	*0.74*	-	-	0.18	*1*
VOC_P	0.22	*0.83*	-	-	0.16	*1*
PANAS	-0.30	*0.77*	-	-	0.18	*1*
IESR_I	-	-	-0.12	*0.91*	0.11	*1*
IESR_A	-0.10	*0.92*	-	-	0.11	*1*
IESR_H	-	-	-0.02	*0.99*	0.08	*1*
FCR	0.16	*0.87*	-	-	0.15	*1*
QLACS_NF	0.01	*0.99*	-	-	0.08	*1*
QLACS_PF	0.6	*0.55*	-	-	0.36	*1*
QLACS_CP	-0.10	*0.92*	-	-	0.12	*1*
QLACS_P	-	-	-0.05	*0.96*	0.09	*1*
QLACS_SP	-0.15	*0.88*	-	-	0.16	*1*
QLACS_F	-0.02	*0.98*	-	-	0.07	*1*
QLACS_SA	-	-	-0.11	*0.91*	0.10	*1*
QLACS_B	-0.12	*0.90*	-	-	0.12	*1*
QLACS_DF	-	-	-0.21	*0.83*	0.12	*1*
QLACS_A	-	-	-0.09	*0.93*	0.14	*1*
QLACS_GT	-0.46	*0.65*	-	-	0.29	*1*

5.2.3.2. Data transformation

Some of the variables were transformed or recoded prior to being included in the analysis (see Table 5.8).

Table 5.8. Data recoding and transformations

Variable	**Original measurement**	**Transformation/recoding**
Time since diagnosis	Date of diagnosis (year)	The indicated year of diagnosis was deducted from the year of participation. Unit – years (0 indicates that the participant was recruited in the same year she had her cancer diagnosis)
Age at diagnosis	Age at enrolment (years) and time since diagnosis	The time since diagnosis was deducted from the age at enrolment.
Education level	see Appendix 16, Questionnaire, p. 1	Data were transformed into below university level (English version answers: a, b, and f; Polish version answers: a, b, c, and d) and at least some university education (English

		version answers: c, d, and e; Polish version answer e).
Income level	see Appendix 16, Questionnaire, p. 1	Data were transformed into two categories – below monthly average (English version answers: a, b, and c; Polish version answers a and b) and above monthly average (English version answers: d, e, f, and g; Polish version answers c, d, and e) using the cut-off points as provided by the Office for National Statistics (347) and Główny Urząd Statystyczny (348) for the UK and Poland, respectively. Category 'prefer not to say' was retained.
Childbearing status	see Appendix 16, Questionnaire, p. 1	Data were recoded into two categories: women who did not have children (questionnaire answer a in both language versions) and women who had children (questionnaire answers b, c, and d in both language versions).
Type of cancer	see Appendix 16, Questionnaire, p. 1	Data were recoded into two categories: women who had gynaecological cancer (questionnaire answers a, b, c, and e in both language versions) and women who had breast cancer (questionnaire answer d).
Cancer stage	see Appendix 16, Questionnaire, p. 1	Data were recoded into two categories: women who had stage 1 disease (questionnaire answer a in both language versions) and women who had stage 2, 3, or 4 disease (questionnaire answers b, c, and d in both language versions).
Type of treatment	see Appendix 16, Questionnaire, p. 1	For the purpose of answering research questions 1 and 3a the type of treatment was recoded in the following manner: women diagnosed with gynaecological cancer who received radical surgery or radio-chamotherapy were assigned to a category 'sterilising treatment'; women diagnosed with gynaecological cancer who received conservative surgery and all women diagnosed with breast cancer were assigned to a category 'uncertain fertility post-treatment'. For the purpose of answering research questions 2 and 3 the type of treatment was recoded in the following manner: four separate variables including surgery (no or yes), chemotherapy (no or yes), radiotherapy (no or yes), and endocrine

		therapy (no or yes) were created.
Treatment related regret	see Appendix 16, Questionnaire, p. 1	For the purpose of answering research question 1 data were recoded into two categories: women who responded 'not at all' were assigned to one category (no regret) and women with all other types of response were assigned to another category (some degree of regret). In mediation and moderation analyses, the variable was used as continuous.
Cultural disapproval of childlessness	see Appendix 16, Questionnaire, p. 1	For the purpose of answering research question 1 data were recoded into two categories: women who responded 'not at all' were assigned to one category (no perceived disapproval) and women with all other types of response were assigned to another category (some degree of perceived disapproval). In mediation and moderation analyses, the variable was used as continuous.
Treatment perceptions	see Appendix 16, Questionnaire, p. 1	Data were recoded into two categories: women who responded 'extremely' were assigned to one category (no doubt that treatment was the best option) and women with all other types of response were assigned to another category (some degree of doubt whether treatment was the best option).
Recruitment site	Data were collected on where exactly the participant was recruited: British online, Polish online, British hospitals, Polish hospitals, SHARE register, Maggie's centre	Data were recoded into two categories: women who were recruited online (online) and women who were recruited elsewhere (other).

5.2.3.3. Statistical analysis

Statistical analyses were conducted using Statistical Package for Social Sciences for Windows, version 22 (338). Additional PROCESS macro was used to conduct mediation and moderation analyses (349).

First, the distributions of all the variables were inspected visually and assessed for normality using one sample Kolmogorov-Smirnov test (see Table in Appendix 17). Descriptive statistics for socio-demographic and cancer-related characteristics,

predictors, and outcome variables were then calculated and these are reported as frequencies and percentages for categorical variables, medians and ranges for continuous, non-normally distributed variables, and means and standard deviations for continuous, normally distributed variables.

Differences in socio-demographic and cancer-related characteristics between groups based on country of recruitment (UK and Poland), site of recruitment (online and other outlets including clinics, SHARE register and Maggie's Centres, referred to as 'other') and type of diagnosis (gynaecological and breast) were evaluated using Chi-square or Fisher's exact tests for categorical variables, Mann-Whitney U test for continuous, non-normally distributed variables, and t-test for continuous, normally distributed variables. Since all the breast cancer patients were recruited in the UK, this cancer type was omitted from the comparisons between samples recruited in the UK and in Poland. For the same reason, country of recruitment was omitted from socio-demographic comparisons between the two groups based on cancer type. These groups were also not compared with respect to treatments received since treatment modalities differ for the two types of cancer.

Differences in culture-related variables (cultural disapproval of childlessness and VOC scores) were also investigated between groups based on the country of origin using the Chi-square, Mann-Whitney U or t-test.

Linear regression was used to answer the research questions. First, the univariate associations between hypothesised predictors and outcomes were investigated using:

1. parametric tests (*t*-tests or one-way ANOVA) for normally distributed continuous outcomes and categorical predictors,
2. non-parametric tests (Mann-Whitney U test or Kruskal-Wallis H test) for non-normally distributed continuous outcomes and categorical predictors
3. Spearman correlations where both outcomes and predictors were continuous.

Additionally, scatterplots were visually inspected to ascertain the linear relationship between predictors and outcomes.

Due to a relatively small sample size (n = 164), a limited number of predictors [k = 14, calculated based on a formula from Green, S.B. (350)] could be entered simultaneously into the multivariate regression models. Therefore, only predictors associated with the outcomes at $p \leq 0.05$ were entered into the final multivariate models.

Hierarchical regression was used to produce multivariate models with control variables entered in the first step, followed by literature-based predictors entered in the subsequent steps, and new predictors specific to this study entered in the final step (351). To avoid multicollinearity [which can lead to error inflation and weaken the analysis (352)] bivariate correlations between predictors were investigated. Where these were higher than 0.8 (351, p. 224, 353, p. 453), a decision regarding the exclusion of one of the variables from the model was made on a case by case basis. The final models were tested as to whether they met the regression assumptions as outlined by Field, A.P. (351, p. 220). These are reported under appropriate tables summarising the models.

Subsequent to the regression analysis addressing research question 1, mediation and moderation analyses were conducted to further examine the relationships between the predictor variables and distress related to fertility. These investigations were of exploratory character, due to the lack of empirical research in this particular field.

Mediation analyses aimed particularly to examine whether the impact of the predictor 'desire to have children' – most widely described in the literature, on total distress related to fertility was mediated by other variables included in the original model. To do this, Spearman correlations were first performed between the predictors from the original model and 'desire to have children'. For the purpose of this analysis both treatment-related regret and cultural disapproval of childlessness were used as continuous variables (as opposed to their dichotomised versions used in the regression model) due to the restriction of PROCESS macro in using dichotomous variables as mediators.

Since this project focused particularly on cross-cultural differences, the variable country of origin was tested as a potential moderator in the mediation models. Correlations between the variables which proved to be significant mediators, desire to have children, and distress related to fertility were analysed in the study sample split by the country of

origin. Where differences between the direction, or significance level of the associations were detected, moderation analysis was applied to investigate which of the paths of the mediation model were subject to moderation.

5.3. Results

5.3.1. Participant characteristics

A total of 164 women were recruited for the study between March 2014 and August 2015. Eighty-four participants were recruited online (51.2%), 75 were recruited via clinics (45.7%), three via the SHARE register (1.9%), and two through Maggie's Centres (1.2%). One hundred eighteen participants in the study were British (72%), 43 were Polish (26.2%), and two were of other nationalities (1.2%).

Women were on average 37.6 years old at the time of the study and diagnosed on average 3.4 years prior to study participation. The majority (74.4%) were in a partnered relationship and almost half did not have any children (48.8%) at the time of the study. More than half of the participants had at least some university education. One hundred twenty-nine women were diagnosed with gynaecological cancer, cervical cancer being the most prevalent diagnosis (44.96%). Thirty-five women were diagnosed with breast cancer and they were all recruited in the United Kingdom. Almost half of the participants were diagnosed with stage 1 disease (42.1%). The majority of women among both gynaecological and breast cancer patients underwent radical surgery as part of their treatment regimen. More than half or all the participants had chemotherapy and almost 40% had radiotherapy. Among women with breast cancer, more than 70% received or were still receiving tamoxifen. Participant characteristics are detailed in Table 5.9.

Table 5.9. Demographic and medical characteristic of participants

Variable	Range	Mean ±SD
Age at diagnosis (years) (n = 148)	19-46	34.55 ± 6.66
Age at enrolment (years) (n = 157)	21-54	37.55 ± 6.87
Time since diagnosis (years) (n = 155)	0-18	3.36 ± 2.93

Variable	Value	N	%
Country of origin	Britain	118	72.0
	Poland	43	26.2
	Other	2	1.2
	Missing	1	0.6
Partnership status at enrolment	Partnered	122	74.4
	Unpartnered	40	24.4
	Missing	2	1.2
Childbearing status	No children	80	48.8
	1 child	33	20.1
	2 children	35	21.3
	3 or more children	14	8.5
	Missing	2	1.2
Education	Less than university education	66	40.2
	At least some university education	97	59.1
	Missing	1	0.6
Income	Less than average for the country	102	62.2
	More than average for the country	43	26.2
	Prefer not to say	17	10.4
	Missing	2	1.2
Cancer diagnosis	Cervical	58	35.4
	Ovarian	41	25.0
	Uterine	27	16.5
	Other gynaecological	3	1.8
	Breast	35	21.3
Stage of cancer	1	69	42.1
	2	49	29.9
	3	30	18.3
	4	2	1.2
	Missing	14	8.5
Surgery – gynaecological	Conservative	29	22.5
	Radical	82	63.6
	None	18	14
Surgery – breast	Conservative	13	37.1
	Radical	19	54.3
	None	3	8.6
Chemotherapy	Yes	92	56.1
	No	72	43.9
Radiotherapy	Yes	66	40.2
	No	98	59.8
Endocrine therapy	Yes	25	15.2
	No	10	6.1
	N/A	129	78.7

There were no significant differences with regard to any of the socio-demographic or cancer characteristics between the participants recruited in the UK and in Poland.

Women recruited via online outlets were significantly younger both at the time of enrolment and the time of the diagnosis than women recruited via other outlets (t = -2.87, $p < 0.01$ and t = -2.66, $p < 0.01$, respectively). They were also more likely to be in a partnered relationship at the time of enrolment (83.33% vs 66.67%, $p \leq 0.05$), to not have any children (59.52% vs 38.46%, $p < 0.01$) and to have at least some university education (67.47% vs 51.25%, $p \leq 0.05$) compared to women recruited via other outlets. There were no significant differences between the two groups in terms of any of the disease characteristics (e.g., time since diagnosis, type of cancer, stage at diagnosis, type of surgery, receipt of chemotherapy or radiotherapy, receipt of tamoxifen for breast cancer). These differences may suggest that women recruited online constituted a self-selected group who might have been more interested in the study and therefore decided to participate. To account for these differences, the method of recruitment (online or via other outlets) was controlled for in the subsequent analyses.

Mean age at enrolment and at diagnosis, and the pattern of recoding the average monthly income were the only sociodemographic characteristics that differed significantly between the two groups of women based on cancer diagnosis. Women with breast cancer were significantly older than women with gynaecological cancer both at the time of enrolment and diagnosis (t = -3.26, $p < 0.01$ and t = -2.96, $p < 0.01$, respectively). They were also less likely to choose the answer 'prefer not to say' when asked about their average monthly income (0 vs. 13.39%, $p \leq 0.05$). To account for these differences, the type of cancer diagnosis (gynaecological or breast) was also controlled for in the subsequent analyses.

5.3.2. Descriptive statistics

5.3.2.1. Predictor variables

All women were asked to assess their own desire and partnered women were also asked to evaluate their partner's desire to have children as perceived at the time of their diagnosis. For 59.7% of women their desire to have children ranged from 'not at all' to 'moderately', while 40.3% indicated that they wanted children 'quite a bit' or

'extremely'. Similar results were obtained for partner's desire for children (see Table 5.12). Among 127 women who assessed both their own and their partner's desire to have children, 69.3% provided answers that were in complete agreement (no difference between one's own and partner's desire for children) and 30.7% provided answers which were not concordant (either one of the partners wanted children more than the other one). Where participants perceived a difference between their and their partner's desire for children at the time of diagnosis, women's wish to have children was higher than her partners in 56.4% of cases. An opposite trend was reported by 43.6% of participants.

Women were also asked a single question to evaluate their regret with regard to the fact that cancer might have or did impair their fertility and the majority of participants (65.2%) reported feeling no regret at all (see Table 5.12).

Sixty-four out of 160 women who answered the question inquiring about the extent to which the culture they came from disapproved of people who did not have children, indicated that they did not at all feel that people without children were socially disapproved of (see Table 5.12). Contrary to what was expected, there were no differences in terms of the perceived cultural disapproval of people without children between women from the UK and those from Poland.

Women evaluated three aspects of the value that children might have for their parents – the utilitarian, social, and psychological value. For the whole study sample, the median score on the utilitarian value subscale was 1.6 (range 1-5), and the mean scores were 2.02 (*SD* = 0.72, range 1-4.29), and 3.41 (*SD* = 0.78, range 1-4.92) for the social and psychological subscales, respectively. Median or mean scores for groups based on the country of origin are presented in table 5.10.

Polish women scored significantly higher than British women on both utilitarian and social value subscales, with no differences detected between groups on the psychological value subscale (see Table 5.10). To account for these differences, the country of origin was controlled for in the subsequent regression analyses.

Table 5.10. Summary statistics for utilitarian, social and psychological based on country of origin

Variable	Britain		Poland		Mann-Whitney U test	
	Median	**Range**	**Median**	**Range**	**U**	***p***
VOC_U	1.4	1-5	2.0	1-4.29	1279	*<0.01*
					T-test	
	M	**SD**	**M**	**SD**	***t***	***p***
VOC_S	1.88	0.65	2.37	0.77	-3.93	*<0.01*
VOC_P	3.37	0.75	3.50	0.86	-0.91	*n.s.*

The mean score on the scale measuring negative affect as trait for the whole study sample was 24.48 (n = 162, *SD* = 9.47, range 10-50).

Eight items that form the Brief-IPQ scale assessed women's illness perceptions and a single item evaluated their treatment perceptions at the time of diagnosis. Table 5.11 shows the summary statistics for the illness perception items. The mean overall score on the Brief-IPQ suggesting the extent to which the disease was perceived as threatening was 39.03 (n = 160, *SD* = 14.02, range 0-75).

Table 5.11. Summary statistics for illness perception items

Variable	Mean	SD
Consequences (IPQ1) (n = 164)	5.45	2.73
	Median	**Range**
Timeline (IPQ2) (n = 163)	5	0-10
Personal control (IPQ3) (n = 164)	3	0-10
Treatment control (IPQ4) (n = 163)	8	0-10
Identity (IPQ5) (n = 163)	4	0-10
Concern (IPQ6) (n = 163)	6	0-10
Coherence (IPQ7) (n = 164)	8	0-10
Emotional representation (IPQ8) (n = 163)	7	0-10

Of 160 women who answered the question about how much they believed at the time of their diagnosis that the treatment they were receiving was optimal for them, the majority (58.8%) chose the option 'extremely' (see Table 5.12).

Table 5.12. Summary statistics for single item variables: desire to have children, partner's desire to have children, treatment regret, cultural disapproval of childlessness, and treatment perceptions

Variable	Median (range)	N	%
Desire to have children (n = 161)	3 (1-5)		
not at all		53	32.9
a little bit		20	12.4
moderately		23	14.3
quite a bit		30	18.6
extremely		35	21.7
Partner's desire to have children (n = 127)	3 (1-5)		
not at all		46	36.2
a little bit		13	10.2
moderately		23	18.1
quite a bit		23	18.1
extremely		22	17.3
Treatment regret (n = 161)	1 (1-5)		
not at all		107	65.2
a little bit		24	14.6
moderately		12	7.3
quite a bit		14	8.5
extremely		4	2.4
Cultural disapproval of childlessness (n = 160)	2 (1-5)		
not at all		64	40.0
a little bit		35	21.9
moderately		32	20.0
quite a bit		20	12.5
extremely		9	5.6
Treatment perceptions (n = 160)	5 (1-5)		
not at all		2	1.3
a little bit		6	3.8
moderately		16	10.0
quite a bit		42	26.3
extremely		94	58.8

5.3.2.2. Outcome variables

Women's distress related to fertility issues was measured using the IES-R that forms three subscales – the intrusion, avoidance, and hyperarousal subscales. The overall score is obtained by summing the individual scores of all the items, and the higher the score, the higher the distress level. The median scores for all women participating in the study on the intrusion and hyperarousal subscales were 1.38 (n = 160, range 0-4) and 0.83 (n = 161, range 0-4), respectively. Women's mean score on the avoidance subscale was

1.39 (n = 159, *SD* = 0.98, range 0-4) and the average overall score was 29.36 (n = 157, *SD* = 21.71, range 0-86).

The mean fear of cancer recurrence score was 26.38 (n = 163, *SD* = 8.85, range 7-40).

Participants' QoL was measured by QLACS. The questionnaire generates a general QoL score which can be sub-divided into seven domains: *negative feelings, positive feelings, cognitive problems, pain, sexual problems, fatigue,* and *social avoidance.* Three cancer-specific subscales: *benefits, family distress*, and *appearance* were also measured in this study. A higher general score as well as a higher score obtained for a particular domain indicates worse QoL, with the exception of the *positive feelings* and *benefits*, where higher score indicates better QoL. Table 5.13 presents the summary statistics for all QoL-related variables.

Table 5.13. Summary statistics for QoL-related variables

Variable	**Mean**	**SD**
Negative feelings (n = 158)	14.60	5.33
Positive feelings (n = 160)	17.61	5.18
Cognitive problems (n = 159)	13.70	5.95
Sexual problems (n = 155)	16.46	7.06
Fatigue (n = 159)	15.74	6.23
Benefits (n = 158)	17.25	6.09
Total generic subscale (n = 154)	99.52	32.55
	Median	**Range**
Pain (n = 159)	11	4-28
Social avoidance (n = 159)	10	4-28
Family distress (n = 158)	9.5	3-21
Appearance (n = 159)	13	4-28

Partnered women's relationship satisfaction was measured by the CSI(4). Their median score was 16 (n = 116, range 1-21) and 29.3% of the participants achieved a score of less than 13.5 which is reported by the authors of the scale to be the cut-off for distress (336).

Single women were asked to evaluate their dating experience using the dating subscale of the CARES which consists of five items. The scale produces three indicators – the number of endorsed problems (the count of all items where participant's answer ranged from 'a little' to 'very much'), the average severity of experienced problems (the sum of

all the item scores divided by the number of endorsed problems) and the global severity of experienced problems (the sum of all the item scores divided by the number (n = 5) of all presented problems). Of 39 women who completed the scale, 94.9% endorsed at least one of the listed problems and 69.2% endorsed all of the presented problems. The mean average severity and the global severity scores were 2.62 (*SD* = 1.18, range 0-4) and 2.45 (*SD* = 1.34, range 0-4), respectively. The global severity index was used in the final analyses.

5.3.3. Predicting fertility-related distress

To address research question 1[4], univariate analyses including the hypothesised predictors and total distress related to fertility as outcome were performed. The results of these analyses are presented in Tables 5.14 and 5.15. Overall, 21 predictors were significantly associated with total distress related to fertility, including six illness perception items (i. e., consequences, timeline, identity, illness concern, coherence, and emotional representation) as well as the illness perception total score. Correlations between these predictors were also investigated and two variables – desire to have children and partner's desire to have children – were found to be highly correlated ($\rho = 0.811$, $p < 0.01$). To avoid multicollinearity and to preserve the sample size (only 127 participants had a partner at the time of diagnosis and hence were able to report their partner's desire to have children), partner's desire to have children was excluded from the final analysis.

Because of the restriction in the number of predictors that could be simultaneously entered into the multivariate model, the first model was calculated using variables associated with the outcome at $p \leq 0.05$ and the total illness perceptions scale score. Subsequent models were then tested individually, entering illness perception items significantly associated with the outcome to gain insight into which ones particularly contribute to total fertility-related distress.

[4] To what extent do contextual factors (cultural: disapproval of childlessness in the society, value of children; individual: one's own desire to have children, partner's desire to have children, and regret over decision concerning treatments) and illness perceptions predict the distress related to reproductive issues in young gynaecological and breast cancer survivors after controlling for: socio-economic status, demographic characteristics, country of origin, childbearing status, medical factors (disease type and stage, treatment modality, time since diagnosis) and dispositional affect?

Table 5.14. Univariate associations between categorical predictors and total fertility-related distress as outcome (t-test, ANOVA)

Variable		Mean (SD)	Mean difference	95% CI		*p*
				Lower bound	Upper bound	
Education level						
	less than university (n = 61)	27.64 (22.64)	2.70	-4.36	9.76	*n.s.*
	at least some university (n = 95)	30.34 (21.23)				
Income						
	below average (n = 98)	31.77 (23.33)				*n.s.*
	above average (n = 41)	23.55 (17.16)				
	prefer not to say (n = 16)	27.86 (20.52)				
Country of origin						
	Britain (n = 115)	26.51 (20.52)	-10.02	-17.76	-2.29	*≤0.05*
	Poland (n = 40)	36.53 (23.55)				
Relationship status						
	partnered (n = 116)	29.59 (22.68)	0.46	-6.85	7.77	*n.s.*
	single (n = 40)	29.13 (19.05)				
Type of cancer						
	gynaecological (n = 123)	32.23 (21.62)	13.22	5.15	21.29	*<0.01*
	breast (n = 34)	19.01 (18.97)				
Stage of cancer						
	stage 1 (n = 67)	28.97 (19.84)	-2.47	-9.42	4.48	*n.s.*
	other stages (n = 76)	31.44 (21.95)				
Type of treatment						
	sterile (n = 95)	34.26 (22.30)	12.40	5.66	19.15	*<0.01*
	uncertain (n = 62)	21.86 (18.58)				
Recruitment site						

	others (n = 81)	34.38 (19.92)	10.36	3.69	17.03	*≤0.05*
	online (n = 76)	24.02 (22.39)				
Childbearing status						
	no (n = 77)	22.58 (19.31)	8.09	1.32	14.85	*≤0.05*
	yes (n = 79)	25.49 (23.29)				
Treatment related regret						
	no (n = 103)	24.18 (20.31)	-16.57	-23.35	-9.78	*<0.01*
	all others (n = 52)	40.75 (19.96)				
Cultural disapproval of childlessness						
	no (n = 62)	24.94 (21.70)	-8.29	-15.20	-1.39	*≤0.05*
	all others (n = 92)	33.23 (20.98)				

Table 5.15. Univariate associations between continuous predictors and total fertility-related distress as outcome

Variable		**Fertility-related distress**
Fertility-related distress	ρ	1
	p	.
Age at diagnosis	ρ	-0.26
	p	*<0.01*
Time since diagnosis	ρ	-0.09
	p	*n.s.*
Negative affect	ρ	0.54
	p	*<0.01*
Desire to have children	ρ	0.40
	p	*<0.01*
Partner's desire to have children	ρ	0.35
	p	*<0.01*
VOC_U	ρ	0.26
	p	*<0.01*
VOC_S	ρ	0.25
	p	*<0.01*
VOC_P	ρ	0.27
	p	*<0.01*
Consequences (IPQ1)	ρ	0.48
	p	*<0.01*
Timeline (IPQ2)	ρ	0.22

	p	*<0.01*
Personal control (IPQ3)	ρ	-0.14
	p	*n.s.*
Treatment control (IPQ4)	ρ	-0.12
	p	*n.s.*
Identity (IPQ5)	ρ	0.28
	p	*<0.01*
Illness concern (IPQ6)	ρ	0.41
	p	*<0.01*
Coherence (IPQ7)	ρ	-0.16
	p	*≤0.05*
Emotional representation (IPQ8)	ρ	0.52
	p	*<0.01*
Brief-IPQ total	ρ	0.50
	p	*<0.01*

Note. ρ – Spearman's rho; *p* – significance level

A five step hierarchical regression was performed. Based on previous research (see section 3.3.1) the predictors were entered into the model in the following order:

- Block 1 (control variables): age at diagnosis, country of origin, type of cancer, type of treatment, recruitment site, childbearing status, negative affect
- Block 2: desire to have children
- Block 3: treatment-related regret
- Block 4 (culture-related variables): cultural disapproval of childlessness, utilitarian, social, and psychological VOC
- Block 5: total illness perception score

The model is presented in Table 5.16.

Table 5.16. Multivariate model predicting total fertility-related distress

	B	**SE B**	**β**	***p***
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.059	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.075	*n.s.*

Negative affect	1.06	0.153	0.461	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.053	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.271	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.044	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.184	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.214	*≤0.05*
Childbearing status (no vs yes)	-0.48	2.89	-0.011	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*≤0.05*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*≤0.05*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*≤0.05*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
VOC_U	1.50	2.66	0.05	*n.s.*
VOC_S	-0.99	3.01	-0.03	*n.s.*
VOC_P	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions				
Constant	-11.68	11.54		*n.s.*
Age at diagnosis	-0.27	0.24	-0.08	*n.s.*
Country of origin (Britain vs Poland)	11.58	3.55	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	-0.17	4.61	-0.01	*n.s.*
Type of treatment (sterile vs uncertain	-5.49	3.98	-0.12	*n.s.*

fertility)				
Recruitment site (other vs online)	-6.41	3.01	-0.15	*≤0.05*
Childbearing status (no vs yes)	-2.31	3.01	-0.05	*n.s.*
Negative affect	0.70	0.16	0.31	*<0.01*
Desire to have children	2.03	0.99	0.15	*≤0.05*
Treatment related regret (no vs all others)	7.27	2.97	0.16	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	2.94	2.66	0.07	*n.s.*
VOC_U	1.28	2.57	0.05	*n.s.*
VOC_S	-1.70	2.92	-0.06	*n.s.*
VOC_P	4.10	2.20	0.15	*n.s.*
Brief-IPQ total	0.35	0.11	0.23	*<0.01*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, p = n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.593$, adjusted $R^2 = 0.548$, $F(1, 127) = 9.99$, $p < 0.01$, $\Delta R^2 = 0.032$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (350). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.26 (acceptable range 1-3), suggesting that residuals were independent. Potentially influential cases were investigated using Cook's distance, leverage and the covariance ratio (351). These parameters suggested there were no cases unduly affecting the model. Finally, the standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met by the model.

The regression model suggests that the control variables contributed significantly to the model ($F(7, 134) = 16.69$, $p < 0.01$) explaining 43.8% of the variance in fertility-related distress. Introduction of 'desire to have children' in step 2 explained an additional 4.6% of the variance and the change in R^2 was significant ($F(1, 133) = 12.55$, $p < 0.01$). Similarly, the addition of 'treatment-related regret' further increased the explained variance by 2.9% with the change being statistically significant ($F(1, 132) = 8.31$, $p < 0.01$). Although the next step including culture-related variables produced a statistically significant overall model ($F(13, 128) = 12.58$, $p < 0.01$), it did not contribute significantly to the explained variability in total fertility-related distress ($F(4, 128) = 1.48$, p = n.s.). Finally, the introduction the illness perception score explained an additional 3.2% of the variance with the change again being statistically significant ($F(1, 127) = 9.99$, $p < 0.01$). The ultimate model explained 54.8% of the variability in total fertility-related distress and six predictors including the country of origin, recruitment site, negative affect, desire to have children, treatment regret, and total illness perception score remained individually significant. Excluding control variables, treatment-related regret, and illness perception were the two strongest

predictors of total fertility-related distress ($\beta = 0.16$, $p \leq 0.05$ and $\beta = 0.23$, $p < 0.01$, respectively).

Additional models to investigate which illness perceptions in particular contributed to total fertility-related distress revealed that when all the other predictors were held constant, the consequences, identity, illness concern, and emotional representation significantly explained the variability in the fertility-related distress in four separate models (see Tables 1-6 in Appendix 18). Moreover, models including illness concern and emotional representation as final predictors achieved a better fit to the data (adjusted R^2 of 55.2% and 55.6%, respectively) than the model including the total illness perception score. This suggests that the emotional dimensions of illness perceptions, rather than the cognitive ones, contributed to the overall distress related to fertility in survivorship.

The same univariate and multivariate analyses were performed separately for IES-R subscales (intrusion, avoidance, and hyperarousal). These analyses yielded results similar to the primary model and are available in the Appendix 19.

5.3.3.1. Testing for mediated relationships

To further examine the relationships between the predictor variables and fertility-related distress, exploratory mediation analyses were conducted. These aimed to investigate whether the impact of the predictor 'desire to have children' on total fertility-related distress was mediated by other variables included in the original model.

The correlation coefficients for 'desire to have children' and total fertility-related distress, and the predictors from the original model are presented in Table 5.17. Variables significantly correlated with both 'desire to have children' and total fertility-related distress included 'treatment-related regret', psychological VOC, and three dimensions of illness perceptions – the consequences, coherence, and emotional representation. These variables were subsequently subject to mediation analysis. The effects and confidence intervals for the models were calculated for 1000 bias-corrected bootstrapped samples and the significance of the effects was assessed by investigating the bootstrapped 95% confidence intervals.

Table 5.17. Spearman correlation coefficients between original model predictors and 'desire to have children' and between the original model predictors and total fertility-related distress

Variable		Fertility-related distress	Desire to have children
Treatment-related regret (continuous)	ρ	0.37	0.33
	p	*<0.01*	*<0.01*
Cultural disapproval of childlessness	ρ	0.25	0.11
	p	*<0.01*	*n.s.*
VOC_U	ρ	0.26	0.05
	p	*<0.01*	*n.s.*
VOC_S	ρ	0.25	0.10
	p	*<0.01*	*n.s.*
VOC_P	ρ	0.27	0.16
	p	*<0.01*	*≤0.05*
Illness perceptions dimensions			
Consequences (IPQ1)	ρ	0.48	0.17
	p	*<0.01*	*≤0.05*
Timeline (IPQ2)	ρ	0.22	-0.03
	p	*<0.01*	*n.s.*
Personal control (IPQ3)	ρ	-0.14	-0.20
	p	*n.s.*	*≤0.05*
Treatment control (IPQ4)	ρ	-0.12	-0.03
	p	*n.s.*	*n.s.*
Identity (IPQ5)	ρ	0.28	0.05
	p	*<0.01*	*n.s.*
Concern (IPQ6)	ρ	0.41	0.08
	p	*<0.01*	*n.s.*
Coherence (IPQ7)	ρ	-0.16	0.16
	p	*≤0.05*	*≤0.05*
Emotional representation (IPQ8)	ρ	0.52	0.17
	p	*<0.01*	*≤0.05*
Brief-IPQ total	ρ	0.50	0.08
	p	*<0.01*	*n.s.*

Note. ρ – Spearman's rho; *p* – significance level

From these five simple mediation models the desire to have children indirectly influenced fertility-related distress separately through treatment-related regret (see Figure 5.1), psychological VOC (see Figure 5.2), consequences (see Figure 5.3), and emotional representation (see Figure 5.4). Illness coherence did not produce a statistically significant mediation model.

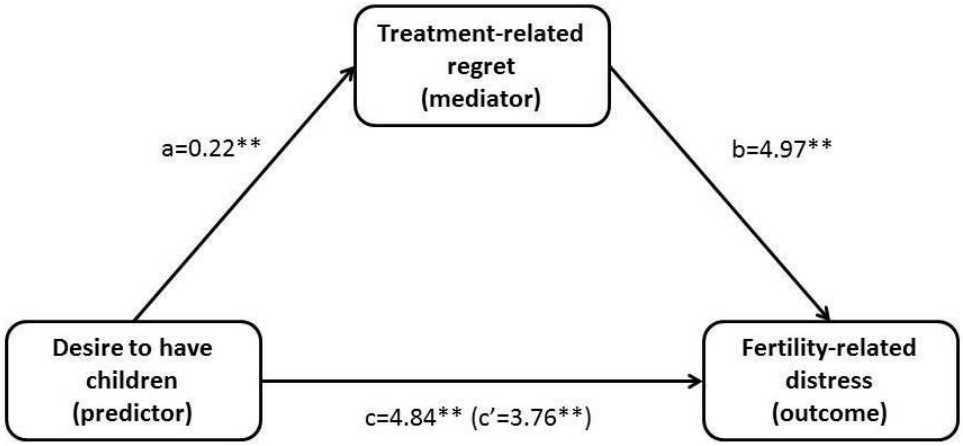


Figure 5.1. Mediation model 1 including desire to have children as predictor, treatment-related regret as mediator and fertility-related distress as outcome (*$p \leq 0.05$, **$p < 0.01$)

Table 5.18. Mediation model 1 including desire to have children as predictor, treatment-related regret as mediator and fertility-related distress as outcome

		Consequent						
		Treatment-related regret				**Fertility-related distress**		
Antecedent		B	SE	*p*		B	SE	*p*
Constant	i	1.03	0.15	*<0.01*	i	11.09	3.71	*<0.01*
Desire to have children	a	0.22	0.06	*<0.01*	c'	3.76	1.10	*<0.01*
Treatment related regret		-	-	-	b	4.97	1.58	*<0.01*
		$R^2 = 0.10$ $F(1, 151) = 14.69$, $p < 0.01$				$R^2 = 0.18$ $F(2, 150) = 16.94$, $p < 0.01$		

As illustrated by Figure 5.1 and Table 5.18, women who had higher desire to have children at the time of diagnosis also expressed more treatment-related regret (a = 0.22), and those who experienced more treatment-related regret reported more fertility-related distress (b = 4.97). The unstandardised indirect effect was 1.08 with the bias-corrected bootstrapped 95% confidence interval above 0 (0.42, 2.07). The standardised indirect effect was 0.08 (95% CI 0.03, 0.15) and treatment-related regret accounted for 22.35% of the total effect of desire to have children on fertility-related distress.

As shown in Figure 5.2 and Table 5.19, women who had higher desire to have children at the time of diagnosis also attached more importance to the psychological VOC (a = 0.12), and those for whom psychological VOC was more important experienced more fertility-related distress (b = 4.97). The unstandardised indirect effect was 0.62 with the bias-corrected bootstrapped 95% confidence interval above 0 (0.09, 1.53). The standardised indirect effect was 0.04 (95% CI 0.007, 0.11) and psychological VOC accounted for 12.76% of the total effect of desire to have children on fertility-related distress.

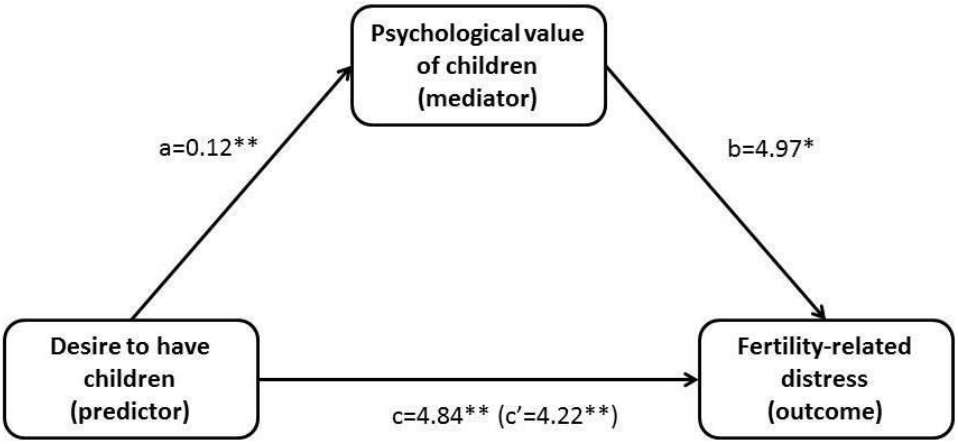


Figure 5.2. Mediation model 2 including desire to have children as predictor, psychological VOC as mediator and fertility-related distress as outcome (*$p \leq 0.05$, **$p < 0.01$)

Table 5.19. Mediation model 2 including desire to have children as predictor, psychological VOC as mediator and fertility-related distress as outcome

		Consequent						
		VOC_P				Fertility-related distress		
Antecedent		B	SE	*p*		B	SE	*p*
Constant	i	3.04	0.15	*<0.01*	i	1.14	8.82	*n.s.*
Desire to have children	a	0.12	0.04	*<0.01*	c'	4.22	1.02	*<0.01*
VOC_P		-	-	-	b	4.97	2.45	*≤0.05*
		R^2 = 0.06 $F(1, 151) = 9.06$, $p<0.01$				R^2 = 0.15 $F(2, 150)12.12$, $p<0.01$		

As presented in Figure 5.3 and Table 5.20, women with a greater desire to have children at the time of diagnosis perceived their illness to have more consequences (a = 0.29), and those who experienced more consequences of cancer also reported more distress related to fertility (b = 3.29). The unstandardised indirect effect was 0.96 with bias-corrected bootstrapped 95% confidence interval above 0 (0.09, 2.12). The standardised indirect effect was 0.07 (95% CI 0.005, 0.15) and the consequences accounted for 19.49% of the total effect of desire to have children on fertility-related distress.

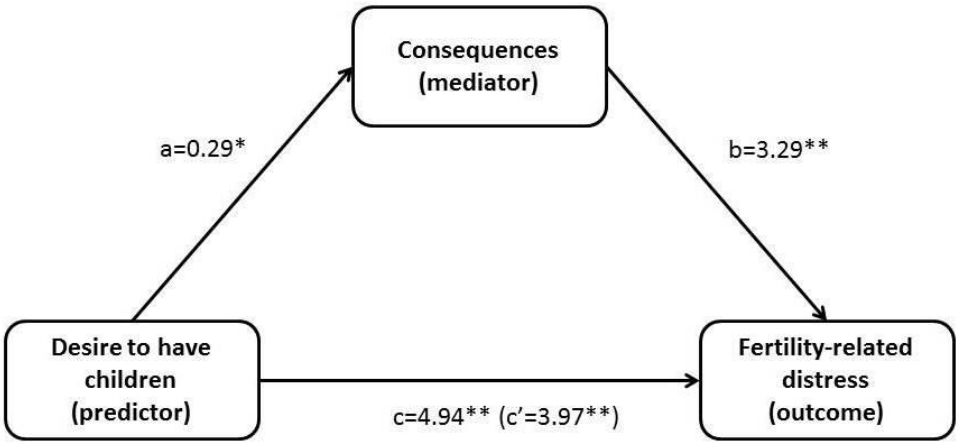


Figure 5.3. Mediation model 3 with desire to have children as predictor, illness consequences as mediator and fertility-related distress as outcome (*$p \leq 0.05$, **$p < 0.01$)

Table 5.20. Mediation model 3 with desire to have children as predictor, illness consequences as mediator and fertility-related distress as outcome

		Consequent						
		Consequences (IPQ1)				Fertility-related distress		
Antecedent		B	SE	*p*		B	SE	*p*
Constant	i	4.73	0.61	*<0.01*	i	0.28	3.47	*n.s.*
Desire to have children	a	0.29	0.14	*≤0.05*	c'	3.98	1.00	*<0.01*
Consequences (IPQ1)		-	-	-	b	3.29	0.58	*<0.01*
		$R^2 = 0.03$ $F(1, 152) = 4.15$, *p≤0.05*				$R^2 = 0.29$ $F(2, 151) = 44.34$, *p<0.01*		

Finally, as illustrated in Figure 5.4 and Table 5.21, women with higher desire to have children at the time of diagnosis experienced their cancer as more emotionally burdensome (a = 0.29), and those with more negative emotions in response to their diagnosis reported more distress related to fertility (b = 3.71). The unstandardised indirect effect was 1.09 with bias-corrected bootstrapped 95% confidence interval above 0 (0.11, 2.18). The standardised indirect effect was 0.08 (95% CI 0.008, 0.15) and emotional representation accounted for 21.96% of the total effect of desire to have children on fertility-related distress.

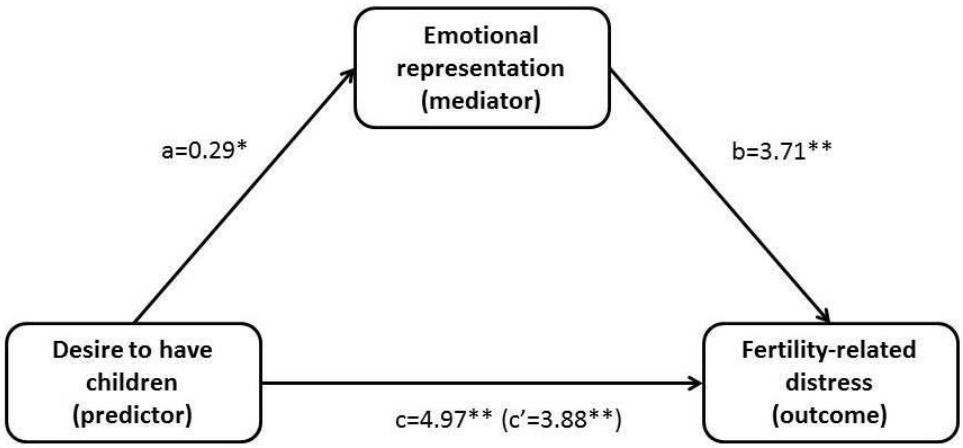


Figure 5.4. Mediation model 4 with desire to have children as predictor, emotional representation as mediator and fertility-related distress as outcome (*$p \leq 0.05$, **$p < 0.01$)

Table 5.21. Mediation model 4 with desire to have children as predictor, emotional representation as mediator and fertility-related distress as outcome

		Consequent						
		Emotional representation (IPQ8)				Fertility-related distress		
Antecedent		B	SE	*p*		B	SE	*p*
Constant	i	5.72	0.48	*<0.01*	i	-5.46	3.66	*n.s.*
Desire to have children	a	0.29	0.14	*≤0.05*	c'	3.88	0.93	*<0.01*
Emotional representation (IPQ8)		-	-	-	b	3.71	0.53	*<0.01*
		R^2 = 0.03 $F(1, 151) = 4.43$, $p \leq 0.05$				R^2 = 0.34 $F(2, 150) = 49.62$, $p < 0.01$		

Subsequent to the single mediation analyses, a multiple mediation analysis including all four independently significant mediators was performed to investigate whether the mediators remained statistically significant in the presence of others and, if so, whether indirect effects were significantly different from each other.

As illustrated in Figure 5.5 and Table 5.22, components a and b of all four indirect pathways remained significant in the multiple mediation model. Also, the investigation of the bootstrapped confidence intervals confirmed that all four indirect effects: a_1b_1, a_2b_2, a_3b_3, and a_4b_4 were significant. This means that when other mediators were held constant, the unstandardised indirect effect of 'desire to have children' on fertility-related distress through 'treatment-related regret' was 0.74 with bias-corrected bootstrapped 95% confidence interval entirely above 0 (0.21, 1.54). The standardised indirect effect for this path was 0.05 (95% CI 0.02, 0.11) and the mediator accounted for 15.43% of the total effect of desire to have children on fertility-related distress.

The unstandardised indirect effect of 'desire to have children' on fertility-related distress produced through the importance of the psychological value that children carry for their parents was 0.53 with bias-corrected bootstrapped 95% confidence interval entirely above 0 (0.07, 1.25). The standardised indirect effect for this path was 0.04 (95% CI 0.004, 0.09) and the mediator accounted for 11.14% of the total effect of 'desire to have children' on fertility-related distress.

'Desire to have children' also influenced fertility-related distress through its impact on the two illness perceptions – the perceived consequences and the emotional representation of illness. The unstandardised indirect effect for the former path (through IPQ1) was 0.38 with bias-corrected bootstrapped 95% confidence intervals entirely above 0 (0.009, 1.31) and for the latter path (through IPQ8) it was 0.77 with bias-corrected bootstrapped 95% confidence intervals similarly entirely above 0 (0.12, 1.68). The respective standardised indirect effects for the two paths were 0.03 (95% CI 0.0002, 0.09) and 0.06 (95% CI 0.01, 0.12). The indirect effect produced through the perceived consequences of illness accounted for 8.03% of the total effect, while the indirect effect generated through the emotional representation of illness accounted for 16.07% of the total effect of desire to have children on fertility-related distress.

Pairwise comparisons between the four indirect effects (through the investigation of the bootstrapped 95% confidence intervals of contrasts between them) suggested that these effects were not significantly different from each other.

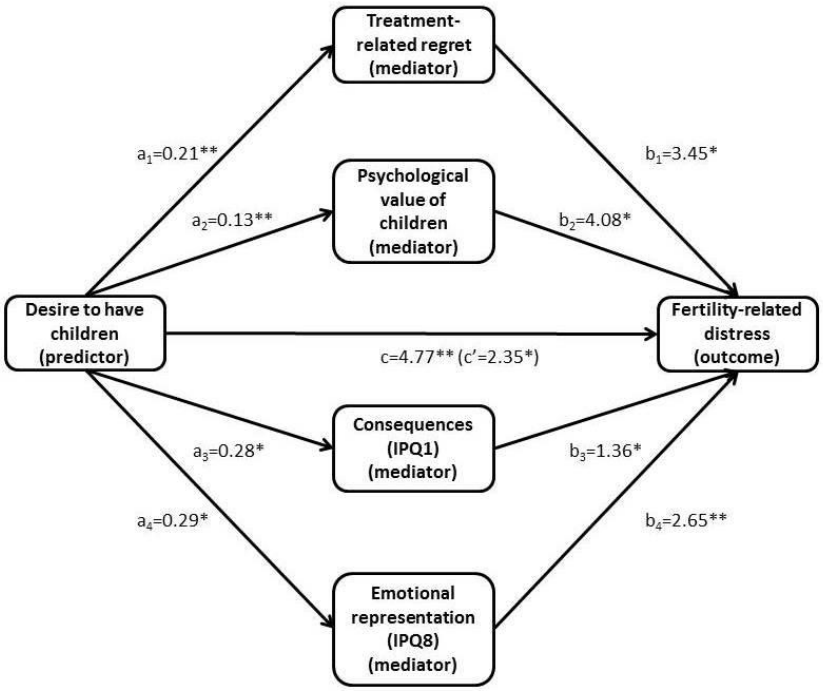


Figure 5.5. Multiple mediation model with desire to have children as predictor, treatment-related regret, psychological VOC, consequences and emotional representation as mediators and fertility-related distress as outcome (*$p \leq 0.05$, **$p < 0.01$)

Table 5.22. Multiple mediation model with desire to have children as predictor, treatment-related regret, VOC_P, consequences and emotional representation as mediators and fertility-related distress as outcome

	Consequent																		
		Treatment-related regret				VOC_P				Consequences (IPQ1)				Emotional representation (IPQ8)				Fertility-related distress		
Antecedent		B	SE	*p*		B	SE	*p*		B	SE	*p*		B	SE	*p*		B	SE	*p*
Constant	i_{M_1}	1.04	0.18	*<0.01*	i_{M_2}	3.02	0.13	*<0.01*	i_{M_3}	4.76	0.46	*<0.01*	i_{M_4}	5.74	0.46	*<0.01*	i_Y	-20.98	6.83	*<0.01*
Desire to have children	a_1	0.21	0.06	*<0.01*	a_2	0.13	0.04	*<0.01*	a_3	0.28	0.14	*≤0.05*	a_4	0.29	0.14	*≤0.05*	c’	2.35	0.97	*≤0.05*
Treatment-related regret		-	-	-		-	-	-		-	-	-		-	-	-	b_1	3.45	1.37	*≤0.05*
VOC_P		-	-	-		-	-	-		-	-	-		-	-	-	b_2	4.08	1.83	*≤0.05*
Consequences (IPQ1)		-	-	-		-	-	-		-	-	-		-	-	-	b_3	1.36	0.65	*≤0.05*
Emotional representation (IPQ8)		-	-	-		-	-	-		-	-	-		-	-	-	b_4	2.65	0.64	*<0.01*
Model fit		R^2 = 0.09 F(1, 149) = 15.49, *p<0.01*				R^2 = 0.07 F(1, 149) = 10.70, *p<0.01*				R^2 = 0.03 F(1, 149) = 4.21, *p≤0.05*				R^2 = 0.03 F(1, 149) = 4.21, *p≤0.05*				R^2 = 0.40 F(5, 145) = 19.71, *p<0.01*		

6.3.3.2. Testing for moderated mediation

Moderation analyses aimed to investigate the country of origin as a moderator of the mediated relationships described in section 5.3.3.1. These were exploratory and based on statistical criteria. As shown in Tables 5.23 and 5.24, the associations between treatment-related regret and distress related to fertility, and treatment-related regret and desire to have children differed between the British and Polish participants. Country of origin was therefore investigated as a moderator of those associations.

Table 5.23. Spearman correlation coefficients for the 'desire to have children', fertility-related distress and the significant mediators for the British subsample of study participants

Variable		**Fertility-related distress**	**Desire to have children**
Fertility-related distress	ρ	1	0.42
	p	.	*<0.01*
Desire to have children	ρ	0.42	1
	p	*<0.01*	.
Treatment-related regret	ρ	0.48	0.40
	p	*<0.01*	*<0.01*
VOC_P	ρ	0.20	0.12
	p	*≤0.05*	*n.s.*
Consequences (IPQ1)	ρ	0.47	0.16
	p	*<0.01*	*n.s.*
Emotional representation (IPQ8)	ρ	0.52	0.12
	p	*<0.01*	*n.s.*

Note. ρ – Spearman's rho; *p* – significance level

Table 5.24. Spearman correlation coefficients for the 'desire to have children', fertility-related distress and the significant mediators for the Polish subsample of study participants

Variable		**Fertility-related distress**	**Desire to have children**
Fertility-related distress	ρ	1	0.38
	p	.	*≤0.05*
Desire to have children	ρ	0.38	1
	p	*≤0.05*	.
Treatment-related regret	ρ	0.12	0.03
	p	*n.s.*	*n.s.*
VOC_P	ρ	0.37	0.22
	p	*≤0.05*	*n.s.*

Consequences (IPQ1)	ρ	0.47	0.15
	p	*≤0.05*	*n.s.*
Emotional representation (IPQ8)	ρ	0.67	0.22
	p	*<0.01*	*n.s.*

Note. ρ – Spearman's rho; *p* – significance level

The first moderation analysis investigating the country of origin as a moderator of the relationship between 'treatment-related regret' and fertility-related distress, showed that while the model was statistically significant (R^2 = 0.16, F(3,149) = 9.11, p < 0.01), the interaction term between treatment-related regret and country of origin was not.

In the second analysis, examining the country of origin as a moderator of the association between treatment-related regret and desire to have children, the obtained model was statistically significant (R^2 = 0.13, F(3,152) = 7.10, p < 0.01), as was the interaction term between desire to have children and country of origin (B = -0.27, $p \leq 0.05$). The effect of country of origin on the relationship between desire to have children and treatment-related regret is illustrated in Figure 5.6.

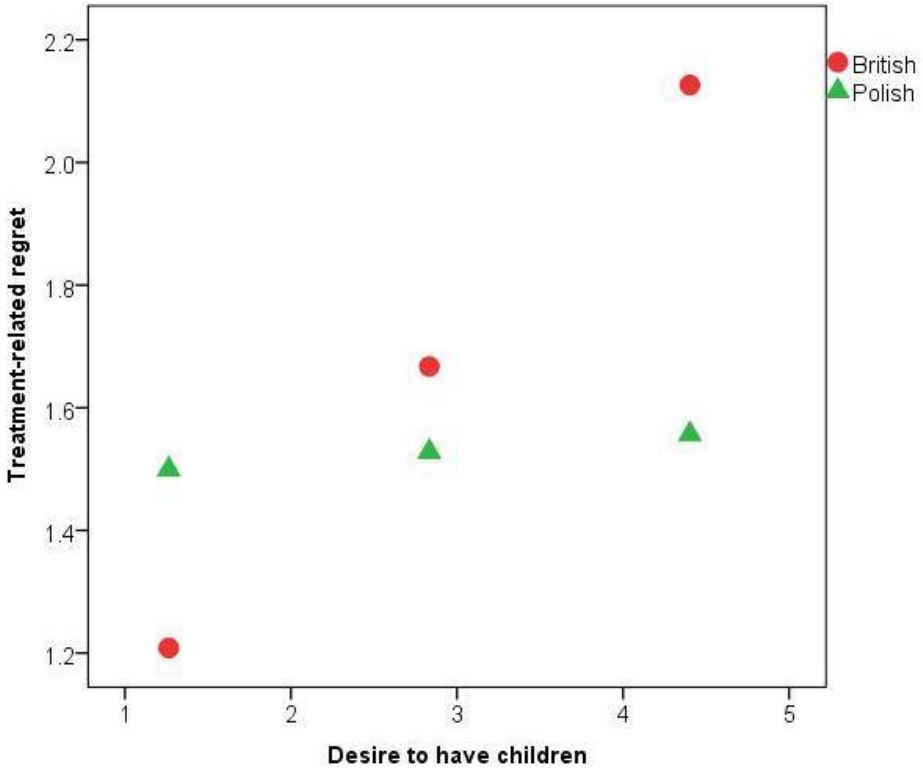


Figure 5.6. The conditional effect of desire to have children on treatment-related regret

Since country of origin acted as a moderator affecting the relationship between desire to have children and treatment-related regret, it was introduced into the mediation model as depicted in Figure 5.7.

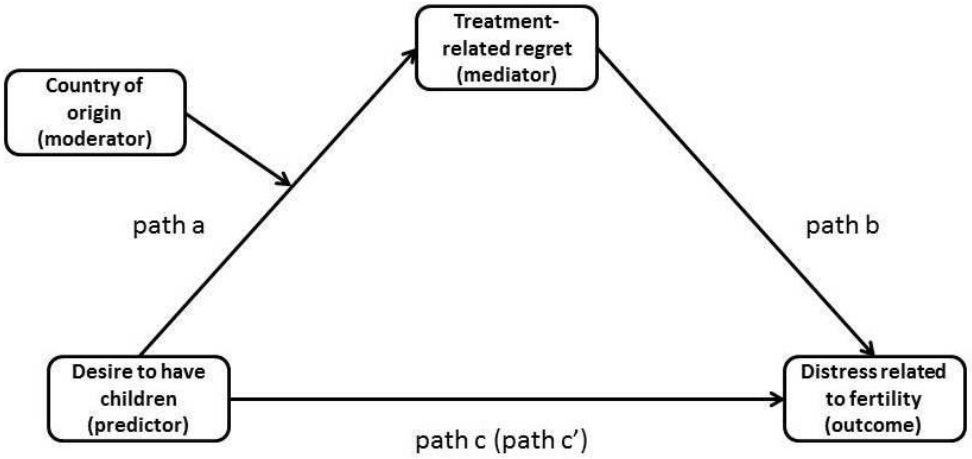


Figure 5.7. Moderated mediation with the moderator influencing path a

As presented in Table 5.25 country of origin moderated path 'a' and hence the indirect path between desire to have children and fertility-related distress through 'treatment-related regret'. The unstandardised indirect effect of 'desire to have children' on fertility-related distress conditional on country of origin was 1.37 for the British population with the bias-corrected bootstrapped 95% confidence interval entirely above o (0.60, 2.52), indicating that the effect was significant. For the Polish population the indirect effect was 0.008 with the bias-corrected bootstrapped 95% confidence interval including 0 (-1.13, 1.03), indicating that the effect was not significant. These effects are visualised in Figure 5.8.

Table 5.25. Moderated mediation with desire to have children as predictor, treatment-related regret as mediator, fertility-related distress as outcome and country of origin as mediator influencing path a

		Consequent						
		Treatment-related regret				**Fertility-related distress**		
Antecedent		B	SE	*p*		B	SE	*p*
Constant	i	0.87	0.15	*<0.01*	i	11.15	3.78	*<0.01*
Desire to have children	a_1	0.28	0.06	*<0.01*	c'	3.72	1.10	*<0.01*
Treatment-related regret		-	-	-	b	4.96	1.62	*<0.01*

Country of origin	a_2	0.68	0.38	*n.s.*		-	-	-
Desire to have children x country of origin	a_3	-0.27	0.13	*≤0.05*		-	-	-
		$R^2 = 0.12$ *F*(3, 147) = 6.19, *p<0.01*				$R^2 = 0.17$ *F*(2, 148) = 15.29, *p<0.01*		

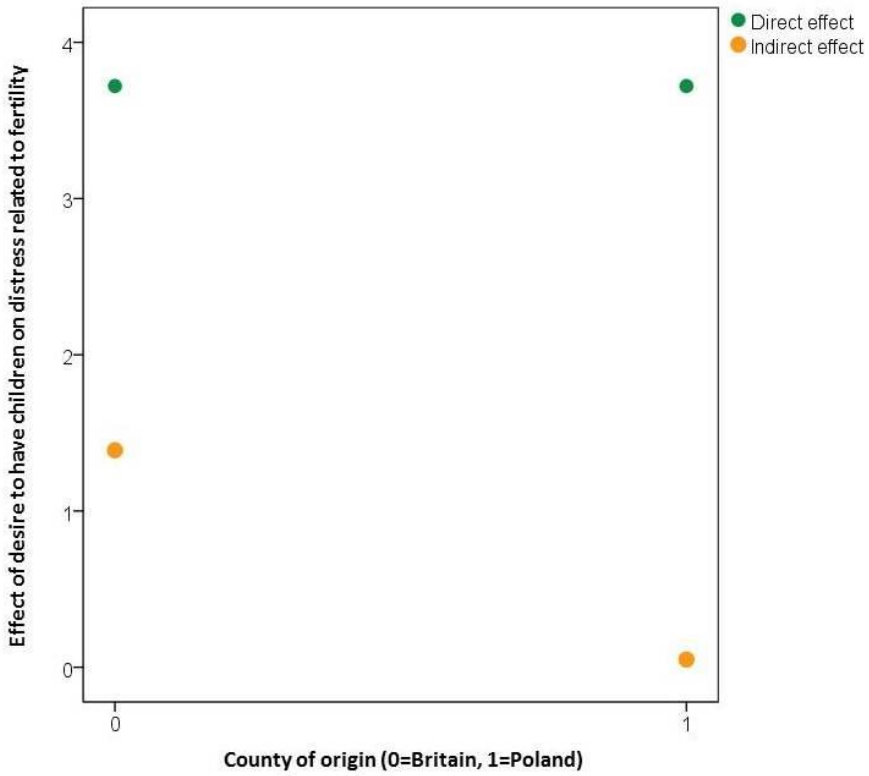


Figure 5.8. A visual representation of the conditional indirect effect of the desire to have children on fertility-related distress as a function of the country of origin

The difference between the conditional indirect effects between the British and Polish participants was statistically significant as suggested by the index of moderated mediation which equalled -1.36 with its bias-corrected bootstrapped 95% confidence interval entirely below 0 (-3.13, -0.26). These results indicate that while the mediation model held for the British subsample of the participants, it became non-significant for the Polish subsample.

5.3.4. Predicting fear of cancer recurrence

To address research question 2[5], univariate analyses including the hypothesised predictors and fear of cancer recurrence as outcome were first performed. The results of these analyses are presented in Tables 5.26 and 5.27.

Table 5.26. Univariate associations between categorical predictors and fear of cancer recurrence as outcome (t-Test, ANOVA)

Variables		Mean (SD)	Mean difference	95% CI		*p*
				Lower bound	Upper bound	
Education level						
	less than university (n = 66)	26.67 (9.06)	0.63	-2.16	3.42	*n.s.*
	at least some university (n = 96)	26.04 (8.68)				
Income						
	below average (n = 101)	27.12 (8.84)				*n.s.*
	above average (n = 43)	24.00 (8.69)				
	prefer not to say (n = 17)	27.88 (9.16)				
Country of origin						
	Britain (n = 117)	27.10 (8.59)	2.68	-0.41	5.77	*n.s.*
	Poland (n = 43)	24.53 (9.28)				
Relationship status						
	partnered (n = 122)	26.83 (8.90)	1.89	-1.30	5.08	*n.s.*
	single (n = 39)	24.93 (8.42)				
Type of cancer						
	gynaecological (n = 128)	25.65 (8.96)	1.25	-2.89	4.59	*n.s.*
	breast	25.40				

[5] To what extent do contextual factors (disease characteristics, retrospective treatment perceptions, and desire to have children) and illness perceptions predict the distress related to fear of cancer recurrence in young gynaecological and breast cancer survivors after controlling for: socio-economic status, demographic characteristics, country of origin, childbearing status, and dispositional affect?

	(n = 35)	(8.49)				
Stage of cancer						
	stage 1 (n = 68)	25.21 (8.16)	-2.58	-5.46	0.31	*n.s.*
	other stages (n = 81)	27.79 (9.43)				
Type of treatment						
	no surgery (n = 21)	29.33 (10.40)	3.39	-0.68	7.45	*n.s.*
	surgery (n = 142)	25.95 (8.55)				
Type of treatment						
	no chemotherapy (n = 71)	25.69 (8.55)	-1.24	-4.00	1.52	*n.s.*
	chemotherapy (n = 92)	26.92 (9.09)				
Type of treatment						
	no radiotherapy (n = 97)	26.17 (8.62)	-0.52	-3.31	2.27	*n.s.*
	radiotherapy (n = 66)	26.69 (9.24)				
Type of treatment						
	no endocrine therapy (n = 136)	26.20 (9.07)	-1.09	-4.48	2.30	*n.s.*
	endocrine therapy (n = 27)	27.29 (7.73)				
Recruitment site						
	others (n = 84)	29.44 (8.24)	6.30	3.73	8.87	*<0.01*
	online (n = 79)	23.13 (8.34)				
Childbearing status						
	no (n = 79)	26.06 (8.87)	-0.63	-3.41	2.14	*n.s.*
	yes (n = 82)	26.70 (8.96)				
Treatment perceptions						
	very much (n = 94)	26.60 (8.98)	0.11	-2.72	2.95	*n.s.*
	all others (n = 65)	26.49 (8.79)				

Table 5.27. Univariate associations between potential predictors and fear of cancer recurrence as outcome (Spearman correlation)

		Fear of cancer recurrence
Age at diagnosis	ρ	-0.05
	p	*n.s.*
Time since diagnosis	ρ	-0.06
	p	*n.s.*
Negative affect	ρ	0.48
	p	*<0.01*
Desire to have children	ρ	0.02
	p	*n.s.*
Brief-IPQ total	ρ	0.73
	p	*<0.01*
Consequences (IPQ1)	ρ	0.56
	p	*<0.01*
Timeline (IPQ2)	ρ	0.42
	p	*<0.01*
Personal control (IPQ3)	ρ	-0.30
	p	*<0.01*
Treatment control (IPQ4)	ρ	-0.16
	p	*≤0.05*
Identity (IPQ5)	ρ	0.33
	p	*<0.01*
Illness concern (IPQ6)	ρ	0.73
	p	*<0.01*
Coherence (IPQ7)	ρ	-0.10
	p	*n.s.*
Emotional representation (IPQ8)	ρ	0.68
	p	*<0.01*

Note. ρ – Spearman's rho; *p* – significance level

Overall, ten variables were significantly associated with fear of cancer recurrence including the total illness perception score as well as the following illness perceptions: the consequences, timeline, personal control, treatment control, identity, illness concern, and emotional representation. Total illness perception score was, however, excluded from the analysis for two reasons. First, as a composite of the single illness perception items, it was a redundant variable in the analysis. Also, this study aimed to explore the contribution of particular illness perceptions to the fear of recurrence, therefore, including the total score would not contribute to answering the research question.

A three-step hierarchical regression was performed. Based on previous research (see section 2.2.1.1.1.1) and theoretical considerations reflected in the construction of the

scale which conceptualises illness perceptions as contributing to either emotional (i.e., concern and emotional representation) or cognitive (i.e., identity, timeline, consequences, personal control, and treatment control) representation of illness (326), the significant predictors were entered into the regression model in the following order:

- Block 1 (control variables): recruitment site, negative affect;
- Block 2 (items contributing to emotional representation): concern and emotional representation;
- Block 3 (items contributing to cognitive representation): consequences, timeline, treatment control, identity, personal control.

The model is presented in Table 5.28.

Table 5.28. Multivariate model predicting fear of cancer recurrence

	B	SE B	β	*p*
Step 1 – control variables				
Constant	20.03	1.88		*<0.01*
Recruitment site (other vs online)	-5.11	1.22	-0.29	*<0.01*
Negative affect	0.36	0.06	0.39	*<0.01*
Step 2 – emotional representation				
Constant	12.08	1.60		*<0.01*
Recruitment site (other vs online)	-1.92	0.97	-0.11	*≤0.05*
Negative affect	0.04	0.06	0.04	*n.s.*
Illness concern (IPQ6)	1.36	0.22	0.48	*<0.01*
Emotional representation (IPQ8)	0.91	0.26	0.28	*<0.01*
Step 3 – cognitive representation				
Constant	13.05	2.22		*<0.01*
Recruitment site (other vs online)	-2.14	0.98	-0.12	*≤0.05*
Negative affect	0.01	0.06	0.01	*n.s.*
Illness concern (IPQ6)	1.24	0.23	0.42	*<0.01*
Emotional representation (IPQ8)	0.81	0.27	0.25	*<0.01*
Consequences (IPQ1)	0.42	0.23	0.13	*n.s.*
Timeline (IPQ2)	0.25	0.14	0.11	*n.s.*
Personal control (IPQ3)	0.02	0.16	0.01	*n.s.*
Treatment control (IPQ4)	-0.16	0.20	-0.05	*n.s.*
Identity (IPQ5)	-0.28	0.19	-0.09	*n.s.*

Note. Step 1: $R^2 = 0.272$, adjusted $R^2 = 0.262$, $F(2, 158) = 29.45$, $p < 0.01$
Step 2: $R^2 = 0.588$, adjusted $R^2 = 0.578$, $F(2, 156) = 59.97$, $p < 0.01$, $\Delta R^2 = 0.317$
Step 3: $R^2 = 0.618$, adjusted $R^2 = 0.595$, $F(5, 151) = 2.35$, $p \leq 0.05$, $\Delta R^2 = 0.030$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include nine predictors in the analysis (350). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 1.92 (acceptable range 1-3), suggesting that residuals were independent. Potentially influential cases were investigated using Cook's distance, leverage and the covariance ratio (351). These parameters

suggested there were no cases unduly affecting the model. Finally, the standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met by the model.

The regression model suggests that the control variables significantly ($F(2, 158) = 29.45$, $p < 0.01$) accounted for 26.2% of the variance in the fear of cancer recurrence. Introduction of the indicators of emotional representation (illness concern and emotions) contributed an additional 31.7% to the explained variability in the outcome and the R^2 was significant ($F(2, 156) = 59.97$, $p < 0.01$). The last step which included the indictors of cognitive illness representation (consequences, timeline, personal control, treatment control, and identity) significantly increased the explained variance by another 3% ($F(5, 151) = 2.35$, $p \leq 0.05$), however, none of the individual predictors were individually significant. The final model accounted for 59.5% of the explained variability in the fear of cancer recurrence scores among the participants and three variables including the recruitment site, emotional representation and illness concern remained individually significant. Illness concern also proved to be the strongest predictor of the fear of recurrence among the participants ($\beta = 0.42$, $p < 0.01$).

5.3.5. Predicting QoL

To address research question 3[6], univariate analyses including the hypothesised predictors and the overall QoL as outcome were first performed. The results are presented in Tables 5.29 and 5.30.

Table 5.29. Univariate associations between categorical predictors and the overall QoL as outcome (t-Test, ANOVA)

Variables		Mean (SD)	Mean difference	95% CI		*p*
				Lower bound	Upper bound	
Education level						
	less than university (n = 60)	104.09 (34.19)	7.50	-3.10	18.09	*n.s.*
	at least some university (n = 94)	96.60 (31.29)				

[6] To what extent do illness perceptions, fear of cancer recurrence and distress related to reproductive issues predict the quality of life in young gynaecological and breast cancer survivors?

Income						
	below average (n = 101)	104.21				*≤0.05*
	above average (n = 43)	87.95				
	prefer not to say (n = 17)	100.75				
Country of origin						
	Britain (n = 112)	100.84 (32.44)	4.84	-7.23	16.92	*n.s.*
	Poland (n = 39)	95.99 (34.13)				
Relationship status						
	partnered (n = 115)	100.59 (33.09)	4.21	-7.87	16.29	*n.s.*
	single (n = 37)	96.38 (29.86)				
Type of cancer						
	gynaecological (n = 120)	99.79 (33.73)	1.22	-11.31	13.75	*n.s.*
	breast (n = 34)	98.57 (28.45)				
Stage of cancer						
	stage 1 (n = 64)	93.95 (36.37)	-13.14	-24.18	-2.11	*≤0.05*
	other stages (n = 77)	107.10 (28.28)				
Type of treatment						
	no surgery (n = 19)	111.63 (27.26)	7.92	-1.84	29.47	*n.s.*
	surgery (n = 135)	97.81 (32.96)				
Type of treatment						
	no chemotherapy (n = 68)	94.24 (33.59)	-9.45	-19.81	0.91	*n.s.*
	chemotherapy (n = 86)	103.69 (31.27)				
Type of treatment						
	no radiotherapy (n = 92)	97.53 (33.43)	-4.94	-15.51	5.64	*n.s.*
	radiotherapy (n = 62)	102.47 (31.23)				
Type of treatment						
	no endocrine therapy (n = 128)	99.39 (33.52)	-0.78	-14.66	13.10	*n.s.*
	endocrine	100.17				

	therapy (n = 26)	(27.83)				
Recruitment site						
	others (n = 79)	109.00 (31.58)	19.48	9.55	29.40	*<0.01*
	online (n = 75)	89.53 (30.69)				
Childbearing status						
	no (n = 77)	99.00 (31.90)	-0.87	-11.32	9.58	*n.s.*
	yes (n = 75)	99.87 (33.31)				

Table 5.30. Spearman correlations between potential predictors and QoL as outcome

		QoL
Age at diagnosis	ρ	-0.009
	p	*n.s.*
Time since diagnosis	ρ	-0.029
	p	*n.s.*
Negative affect	ρ	0.661
	p	*<0.01*
IPQ total	ρ	0.713
	p	*<0.01*
Consequences (IPQ1)	ρ	0.627
	p	*<0.01*
Timeline (IPQ2)	ρ	0.327
	p	*<0.01*
Personal control (IPQ3)	ρ	-0.367
	p	*<0.01*
Treatment control (IPQ4)	ρ	-0.227
	p	*<0.01*
Identity (IPQ5)	ρ	0.427
	p	*<0.01*
Illness concern (IPQ6)	ρ	0.561
	p	*<0.01*
Coherence (IPQ7)	ρ	-0.117
	p	*n.s.*
Emotional representation (IPQ8)	ρ	0.622
	p	*<0.01*
Fertility-related distress	ρ	0.513
	p	*<0.01*
Fear of cancer recurrence	ρ	0.685
	p	*<0.01*

Note. ρ – Spearman's rho; *p* – significance level

Overall 13 variables including four controls (income, cancer stage, recruitment site, and negative affect) along with the cognitive and emotional illness representations, fear of recurrence and fertility-related distress proved to be significantly associated with total QoL scores. These were entered into the regression model in the following blocks:

- Block 1 (control variables): income, cancer stage, recruitment site, negative affect;
- Block 2 (illness perceptions): cognitive (consequences, timeline, personal control, treatment control, identity), emotional (concern, emotions);
- Block 3: fear of cancer recurrence;
- Block 4: fertility-related distress.

Distress related to fertility was entered in the last block to investigate whether it individually and significantly contributed to the explained variance in QoL. Table 5.31 presents the final regression model predicting the overall QoL.

Table 5.31. Multivariate model predicting QoL

	B	**SE B**	**β**	**p**
Step 1 – control variables				
Constant	54.32	7.44		*<0.01*
Recruitment site (other vs online)	-13.94	4.24	-0.22	*<0.01*
Cancer stage (stage 1 versus others)	8.89	4.29	0.14	*≤0.05*
Income (below average versus above average)	-2.73	4.99	-0.04	*n.s.*
Income (below average versus prefer not to say)	2.46	7.02	0.02	*n.s.*
Negative affect	1.94	0.24	0.57	*<0.01*
Step 2 – illness perceptions				
Constant	56.42	9.74		*<0.01*
Recruitment site (other vs online)	-7.22	4.00	-0.11	*n.s.*
Cancer stage (stage 1 versus others)	2.74	3.93	0.04	*n.s.*
Income (below average versus above average)	-1.26	4.47	-0.02	*n.s.*
Income (below average versus prefer not to say)	1.10	6.16	0.01	*n.s.*
Negative affect	1.19	0.24	0.35	*<0.01*
Consequences (IPQ1)	3.32	0.93	0.28	*<0.01*
Timeline (IPQ2)	-0.02	0.60	-0.002	*n.s.*
Personal control (IPQ3)	-1.26	0.63	-0.12	*≤0.05*
Treatment control (IPQ4)	-1.39	0.79	-0.11	*n.s.*
Identity (IPQ5)	1.19	0.74	0.11	*n.s.*
Illness coherence (IPQ6)	0.46	0.93	0.04	*n.s.*

Emotional representation (IPQ8)	0.87	1.10	0.07	*n.s.*
Step 3 – fear of cancer recurrence				
Constant	38.94	9.74		*<0.01*
Recruitment site (other vs online)	-4.30	3.75	-0.07	*n.s.*
Cancer stage (stage 1 versus others)	2.20	3.64	0.03	*n.s.*
Income (below average versus above average)	-2.00	4.14	-0.03	*n.s.*
Income (below average versus prefer not to say)	-1.39	5.73	-0.01	*n.s.*
Negative affect	1.17	0.22	0.34	*<0.01*
Consequences (IPQ1)	2.77	0.86	0.23	*<0.01*
Timeline (IPQ2)	-0.37	0.55	-0.04	*n.s.*
Personal control (IPQ3)	-1.27	0.59	-0.12	*≤0.05*
Treatment control (IPQ4)	-1.20	0.73	-0.09	*n.s.*
Identity (IPQ5)	1.59	0.69	0.14	*≤0.05*
Illness coherence (IPQ6)	-1.30	0.94	-0.12	*n.s.*
Emotional representation (IPQ8)	-0.35	1.05	-0.03	*n.s.*
Fear of recurrence	1.43	0.30	0.39	*<0.01*
Step 4 – fertility-related distress				
Constant	40.01	9.79		*<0.01*
Recruitment site (other vs online)	-3.97	3.76	-0.06	*n.s.*
Cancer stage (stage 1 versus others)	2.55	3.65	0.04	*n.s.*
Income (below average versus above average)	-2.02	4.14	-0.03	*n.s.*
Income (below average versus prefer not to say)	-1.07	5.73	-0.01	*n.s.*
Negative affect	1.08	0.24	0.32	*<0.01*
Consequences (IPQ1)	2.63	0.87	0.22	*<0.01*
Timeline (IPQ2)	-0.37	0.55	-0.04	*n.s.*
Personal control (IPQ3)	-1.31	0.59	-0.13	*≤0.05*
Treatment control (IPQ4)	-1.17	0.73	-0.09	*n.s.*
Identity (IPQ5)	1.53	0.69	0.13	*≤0.05*
Illness coherence (IPQ6)	-1.26	0.94	-0.12	*n.s.*
Emotional representation (IPQ8)	-0.45	1.06	-0.04	*n.s.*
Fear of recurrence	1.39	0.30	0.38	*<0.01*
Fertility-related distress	0.11	0.10	0.07	*n.s.*

Note. Step 1: $R^2 = 0.459$, adjusted $R^2 = 0.439$, $F(5, 135) = 22.94$, $p < 0.01$
Step 2: $R^2 = 0.620$, adjusted $R^2 = 0.584$, $F(7, 128) = 7.70$, $p < 0.01$, $\Delta R^2 = 0.16$
Step 3: $R^2 = 0.677$, adjusted $R^2 = 0.644$, $F(1, 127) = 22.47$, $p < 0.01$, $\Delta R^2 = 0.057$
Step 4: $R^2 = 0.680$, adjusted $R^2 = 0.644$, $F(1, 126) = 1.10$, p = n.s., $\Delta R^2 = 0.003$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (350). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.12 (acceptable range 1-3), suggesting that residuals were independent. Potentially influential cases were investigated using Cook's distance, leverage and the covariance ratio (351). These parameters suggested there were no cases unduly affecting the model. Finally, the standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met by the model.

According to the regression model with QoL as outcome, control variables significantly explained 43.9% of its variance ($F(5, 135) = 22.94$, $p < 0.01$). Introduction of illness perceptions including the cognitive representations (consequences, timeline, personal control, treatment control, and identity) and the emotional representations (concern and emotions) in the second step contributed an additional 16% to the explained variability in QoL and the R^2 was significant ($F(7, 128) = 7.70$, $p < 0.01$). Similarly, addition of fear of cancer recurrence in the third step significantly increased the explained variance in the outcome by another 5.7% ($F(1, 127) = 22.47$, $p < 0.01$). The final step including distress related to fertility, although produced an overall significant model ($F(14,126) = 19.09$, $p < 0.01$) did not significantly add to the explained variability in the outcome. The ultimate model accounted for 64.4% of the variance in QoL and five predictors including negative affect, consequences, personal control, identity, and fear of recurrence remained individually significant. Fear of recurrence proved to be the strongest individual predictor of QoL ($\beta = 0.38$, $p < 0.01$).

5.3.6. Predicting relationship satisfaction and dating experience

To address the research question 4[7], univariate analyses including control variables and fertility-related distress were first conducted separately for participants who declared they had a partner at the time of the survey (n = 122) and those who declared they were single (n = 40). The two participants for whom data on relationship status were missing but who provided answers to both CSI(4) and CARES dating subscale were included in the respective analyses.

The univariate associations between relationship satisfaction and control variables as well as fertility-related distress are presented in Tables 5.32 and 5.33. As can be seen, neither of the control variables, nor fertility-related distress were associated with relationship satisfaction among partnered women.

[7] To what extent does distress related to reproductive issues predict (1) relationship satisfaction; or (2) dating experience in young gynaecological and breast cancer survivors?

Table 5.32. Univariate associations between categorical predictors and relationship satisfaction as outcome (Mann-Whitney U test, Kruskal-Wallis H test)

Variables		Mean rank	Mann-Whitney U	Z	*p*
Education level					
	less than university (n = 45)	55.34	1455.5	-0.81	*n.s.*
	at least some university (n = 71)	60.50			
Income					
	below average (n = 72)	57.11	$\chi^2 = 0.41$		*n.s.*
	above average (n = 28)	60.39			
	prefer not to say (n = 14)	53.71			
Country of origin					
	Britain (n = 85)	59.23	1000.5	-1.27	*n.s.*
	Poland (n = 28)	50.23			
Type of cancer					
	gynaecological (n = 88)	58.65	1218.5	-0.09	*n.s.*
	breast (n = 28)	58.02			
Stage of cancer					
	stage 1 (n = 53)	56.10	1319.5	-0.70	*n.s.*
	other stages (n = 54)	51.94			
Type of treatment					
	sterile (n = 69)	58.94	1591.0	-0.17	*n.s.*
	uncertain (n = 47)	57.85			
Recruitment site					
	others (n = 64)	58.75	1648.0	-0.09	*n.s.*
	online (n = 52)	58.19			
Childbearing status					
	no (n = 48)	62.80	1425.5	-1.16	*n.s.*
	yes (n = 68)	55.46			
Agreement with respect to having children					
	no (n = 77)	56.74	867	-1.78	*n.s.*
	all others (n = 29)	44.90			

Table 5.33. Spearman correlations between potential predictors and relationship satisfaction

Variables		CSI_T
Total fertility-related distress	ρ	-0.092
	p	*n.s.*
Age at diagnosis	ρ	-0.039
	p	*n.s.*
Time since diagnosis	ρ	-0.161
	p	*n.s.*
Negative affect	ρ	-0.153
	p	*n.s.*
Desire to have children	ρ	-0.02
	p	*n.s.*
Partner's desire to have children	ρ	0.07
	p	*n.s.*

Note. ρ – Spearman's rho; *p* – significance level

The univariate associations between dating experience (conceptualised as CARES global severity index), control variables, and fertility-related distress are presented in Tables 5.34 and 5.35. The results show that the difficulties experienced while dating differed significantly only between the Polish and British single participants, with the former reporting significantly less difficulties on average (1.88 vs. 2.8, $p \leq 0.05$). Contrary to expectations, fertility-related distress was not significantly associated with dating experience among single women and neither was the desire to have children at the time of diagnosis.

Table 5.34. Univariate associations between categorical predictors and dating experience as outcome (t-Test and one-way ANOVA)

Variables		Mean (SD)	Mean difference	95% CI		*p*
				Lower bound	Upper bound	
Education level						
	less than university (n = 19)	2.69 (1.30)	0.48	-0.38	1.35	*n.s.*
	at least some university (n = 20)	2.21 (1.37)				

Income						
	below average (n = 26)	2.72 (1.30)				*n.s.*
	above average (n = 12)	1.92 (1.34)				
	prefer not to say (n = 1)	1.6				
Country of origin						
	Britain (n = 24)	2.8 (1.33)	0.92	0.07	1.77	*≤0.05*
	Poland (n = 15)	1.88 (1.18)				
Type of cancer						
	gynaecological (n = 33)	2.36 (1.39)	-0.53	-1.74	0.67	*n.s.*
	breast (n = 6)	2.90 (1.01)				
Stage of cancer						
	stage 1 (n = 13)	2.22 (1.46)	-0.43	-1.44	0.57	*n.s.*
	other stages (n = 21)	2.65 (1.36)				
Type of treatment						
	sterile (n = 25)	2.64 (1.22)	0.54	-0.36	1.44	*n.s.*
	uncertain (n = 14)	2.10 (1.50)				
Recruitment site						
	others (n = 14)	2.87 (1.39)	0.66	-0.23	1.55	*n.s.*
	online (n = 25)	2.21 (1.28)				
Childbearing status						
	no (n = 26)	2.45 (1.31)	-0.20	-1.13	0.72	*n.s.*
	yes (n = 12)	2.65 (1.28)				

Table 5.35. Spearman correlations between potential predictors and dating experience

Variables		**CARES global severity**
Total fertility-related distress	ρ	0.23
	p	*n.s.*
Age at diagnosis	ρ	0.16
	p	*n.s.*

Time since diagnosis	ρ	-0.06
	p	*n.s.*
Negative affect	ρ	0.29
	p	*n.s.*
Desire to have children	ρ	0.05
	p	*n.s.*

Note. ρ – Spearman's rho; *p* – significance level

5.4. Discussion

5.4.1. Summary of evidence

5.4.1.1. Research question 1 – predicting fertility-related distress

Research question 1 sought to determine potential predictors of fertility-related distress among young gynaecological and breast cancer patients. The univariate analyses suggested that multiple factors including the country of origin, age at diagnosis, recruitment site, childbearing status, type of cancer, type of treatment received, negative affect, treatment-related regret, cultural factors (i.e., cultural disapproval of not having children and the value attached to children – utilitarian, social, and psychological), one's and one's partner's desire to have children, and illness perceptions – both cognitive and emotional, were all associated with the distress related to fertility issues after cancer.

In multivariate analysis, however, only some of these predictors remained significant. Polish participants; those recruited through clinics as opposed to online; those with higher desire to have children; higher negative affect; those who reported regret with respect to the treatment outcome; and finally those who perceived their illness as more threatening were more likely to experience higher levels of fertility-related distress. An in-depth analysis of illness perceptions also indicated that it was the emotional representation (reflected through more concern with regard to illness and more emotional consequences of the disease), as opposed to the cognitive representation that mainly contributed to higher levels of fertility-related distress.

These results correspond with the findings from the literature review (see section 3.4.1.1). This study corroborates the evidence that the wish to have a child or more children is a likely predictor of post-treatment distress related to fertility among young women with cancer. However, it does not support the evidence suggesting that not

having children or being single may contribute to higher distress. This is potentially important for clinical practice in that a patient's preferences regarding family life, rather than objective indicators such as relationship or childbearing status, seem to determine the patient's emotional responses post-treatment. These findings emphasise the role of patient-physician communication if preventative measures such as FP are desired prior to cancer treatments.

The fact that distress was not predicted by objective characteristics of the disease (such as type of diagnosis, stage, or type of treatment) is consistent with evidence from the literature (63) and further supports the core idea of the CSM (62, 64, 65) that subjective conceptualisation of disease determines one's response to illness.

The subjective conceptualisation of illness in this study was measured through participants' illness perceptions. While the research focusing on infertility in otherwise healthy women indicates that distress related to the condition was predicted by the perception of more severe consequences and less control over the condition (see section 2.2.1.1.2), the findings of this study indicate that although the indicators of cognitive representation (i.e., consequences and identity) contributed to the distress, it was in fact the emotional representation of the illness that best predicted the levels of distress. In other words, the more concerned women were about their illness and the more emotionally burdened they were by cancer diagnosis, the more fertility related-distress they experienced.

Not only the emotional representation of the illness itself, but also what women brought to the situation from the outset, namely their affective predisposition determined the level of post-treatment fertility-related distress. Women who described themselves as generally experiencing more negative emotions also reported higher levels of fertility-related distress. Some research indicates that people who express higher levels of negative affect generally score higher on self-report measures of distress (354). For this reason, in this study the negative affectivity was used as a control variable. Although it remained significant in the final model predicting distress, so did the emotional representation of illness suggesting that the disease-specific response predicted fertility-related distress above the general negative affectivity understood as one's predisposition.

Another factor which predicted fertility-related distress was the regret related to the outcome of treatments – the so called 'outcome regret' (see section 2.2.2.3). Women who regretted the fact that cancer treatments impacted on their fertility were more likely to experience fertility-related distress than those who did not experience regret. Studies which investigated the concept of fertility-related regret among young women diagnosed with cancer mainly concentrated on the other side of the issue, namely the extent to which women experience regret with respect to the decisions about FP (63). The existing evidence suggests that counselling about fertility (185) and provision of decisional aids (242) can minimise regret with respect to decisions about FP. It does not, however, answer the question about the extent to which regret can impact on fertility-related distress. Although a common sense finding, this study is the first to demonstrate the relationship between treatment-related regret and the increased risk of fertility-related distress post-cancer.

The particular focus of this study was to investigate the role of culture in determining distress related to fertility after cancer. Although the variables reflecting potential cultural differences in the importance attached to fertility (e.g., cultural disapproval of not having children, psychological, social, and utilitarian VOC) did not predict fertility-related distress, the country of origin did: being Polish predisposed participants to experience more fertility-related distress. This finding can potentially be explained by the differences between Polish and British women which were not covered by the culture specific questions asked but which nonetheless exist. As suggested in section 2.2.3.2.1, Polish culture is very family-orientated and attached to traditional values often dictated by the Catholic Church which stresses the importance of having children and condemns contraception and abortion. The prevalence of such beliefs in society might make the situation in which a woman is unable to have children more stressful. Limited cross-cultural research into cancer-related fertility issues also suggests that women from Eastern Europe are generally less likely to accept the risk of infertility related to chemotherapy compared to their counterparts from Western Europe (233). This might be because they value their fertility more, however, the reasons for that require further research.

While the desire to have children has been widely reported to be a predictor of fertility-related distress, the mechanisms behind this relationship remain unknown. Although additional investigations conducted for the purpose of this study should be treated with caution due to their exploratory nature, they shed some light on this association.

Separate mediation analyses suggest that desire to have children could affect fertility-related distress through its impact on four other variables – the treatment-related regret, psychological VOC, perceived consequences, and emotional burden of the disease. In other words experiencing a strong desire to have children before cancer diagnosis was not only directly related to higher levels of fertility-related distress post-cancer but also resulted in higher regret with respect to the treatment outcome, more perceived consequences, and more emotional burden, and through these relationships indirectly affected distress levels. A stronger wish to have children also seemed to determine the degree of importance attached to the psychological rewards related to having children and via this mechanism influenced distress levels.

In a subsequent multiple mediation analysis, all four mediators remained statistically significant. The paths leading through the consequences as well as emotional representation of illness appear to be in line with the CSM, which suggests that factors inherent to self (e.g., desire to have children) can affect illness perceptions (see section 2.2 and Figure 2.3), and these in turn influence the response to illness (see section 2.2.1.1). This draws attention to the fact that illness perceptions can be influenced not only by the characteristics of the particular disease one suffers from, but also by factors seemingly unrelated to one's health. The particular contribution of this preliminary finding lies in the fact that while desire to have children is a non-modifiable factor affecting distress, both perceived consequences and emotional representation of illness could potentially be susceptible to interventions to tackle fertility-related distress.

The path involving the psychological VOC could potentially be linked to the socio-cultural dimensions of having children with women who desired children more also perceiving their psychological value as more prominent and through this mechanism being affected by higher levels of fertility-related distress.

The socio-cultural influences were explored further through the analysis of the effect that country of origin had on the last significant mediator, namely treatment-related regret and this was done through the means of moderated mediation. The results of this investigation suggest that while for the British participants a higher desire to have children contributed to higher treatment outcome regret and indirectly to more fertility-related distress, this indirect relationship did not exist in the Polish subsample. Among Polish women, the wish to have children, although related to distress, did not have effect on regret. With the lack of cross-cultural research in the field it is difficult to explain this result, nonetheless, it may be due to the organisational differences between the Polish and British medical systems. While the NICE guidelines suggest discussing FP with all cancer patients (17) and the NHS has services in place to facilitate FP for cancer patients, the same is not true for Poland. Therefore, British women who desired children may have regretted not acting upon the possibility of preserving fertility, while at the same time Polish women, not having had that opportunity, did not experience the regret.

More importantly, however, what this finding indicates is that different factors might be playing a role in determining levels of distress across different cultural settings. This stresses the need for cross-cultural research in the field and the importance of physicians' awareness of cross-cultural differences between their patients.

5.4.1.2. Research question 2 – predicting fear of recurrence

Research question 2 aimed to identify the predictors of fear of cancer recurrence among young women with breast or gynaecological cancer. In univariate analyses the negative affect, recruitment site and both cognitive (consequences, timeline, personal control, treatment control, identity) and emotional (concern and emotions) illness representations as well as the total illness representation score were associated with fear of cancer recurrence. However, in the multivariate model only the recruitment site and the components constituting the emotional representation of illness remained significant predictors of fear of cancer recurrence.

These results corroborate to a certain extent the evidence summarised in section 2.2.1.1.1.1 and a recent review of factors influencing fear of recurrence among cancer patients (355). These two suggest the association between recurrence fears and both

cognitive and emotional components of illness representation. This study indicates that it is the emotional component that predicts young women's fear of recurrence when other factors are controlled for.

In line with the results of the systematic review by Simard, S. et al. (50), the objective cancer characteristics such as cancer type, stage, or treatment modalities did not determine the levels of fear of recurrence among young women in this study. Other studies concentrating specifically on young female populations also support these findings (52, 53). The predictors that remained significant, and particularly the two components that represent the emotional aspect of illness perception, again indicate that subjective interpretation of the disease is key to understanding one's reaction to a health threat (62, 64, 65) including the fear of cancer recurrence.

Contrary to the existing evidence (50, 52), age at diagnosis was not related to the level of fear of cancer recurrence among women in this study. This might be due to the fact that the study population consisted only of young women and was relatively homogenous in terms of age. Simard, S. et al. (50) suggest that young cancer survivors report higher levels of recurrence fears than their older counterparts, yet, it is possible that the age range in this study was not wide enough to capture a significant effect of age on fear of recurrence.

Finally, since this study was primarily interested in fertility issues, childbearing status and desire to have children were investigated as potential predictors of recurrence fears. However, supporting the results of two studies by Thewes, B. et al. (52, 53), these factors were not associated with fear of recurrence suggesting that it is prevalent among young women regardless of whether they have children or the extent of their desire to have them.

5.4.1.3. Research question 3 – predicting QoL

Research question 3 sought to establish the extent to which illness perceptions, fear of cancer recurrence, and distress related to fertility influenced young cancer survivors' QoL. While in univariate analyses the income, cancer stage, recruitment site, negative affect, illness perceptions including consequences, timeline, personal control, treatment control, identity, concern and emotions, as well as fear of recurrence, and fertility-

related distress were all associated with QoL, only the cognitive illness representations (consequences, personal control, and identity), negative affect, and fear of recurrence remained significant in the multivariate model. Women who perceived more consequences of their illness, who felt they had less control over the cancer, those who experienced more symptoms, as well as those with higher negative affect and higher fear of recurrence were more likely to report lower overall QoL in survivorship.

Contrary to the two previous outcomes of this study, namely the distress related to fertility and fear of cancer recurrence, QoL was predicted by the cognitive components of illness perception including the consequences, personal control, and identity rather than the emotional components. This corresponds with previous research summarised in section 2.2.1.1.1.2 which suggests that QoL among cancer patients is generally associated with illness consequences and identity.

The finding that the lower the perceived personal control over the disease the worse the QoL is perhaps not surprising. Research has shown that maintaining positive control in the situation of cancer diagnosis can have beneficial effects on QoL (356, 357), however, the loss of control in such a situation is frequent (358). These results, along with the fact that none of the objective disease characteristics were related to QoL also support the argument that it is in fact the personal perception of one's illness that affects one's adaptation to the health threat situation as suggested by the CSM (62, 64, 65).

Fear of cancer recurrence also emerged as a significant predictor of QoL among young women diagnosed with breast or gynaecological cancer. It proved to be the strongest predictor of QoL when other factors were controlled for. While Simard, S. et al. (50) found strong evidence for the association between QoL and recurrence fears, they did not specifically review literature on a young cancer patient population. This finding might be important in that fear of recurrence tends to be higher in younger patients (50) and hence this group might equally be more at risk of a decreased QoL even though the research in this field remains inconclusive (359).

Finally, although fertility-related distress proved to be significantly associated with QoL, it did not retain its significance in the final model when other factors were accounted for. The three quantitative studies included in the literature review all

indicated that fertility issues were correlated with QoL, however, only one further explored this association and found that reproductive concerns significantly predicted QoL when controlled for cancer distress, spiritual well-being, and maladaptive coping (213) (see section 3.3.2.1.1).

This study investigated whether fertility-related distress predicted QoL when other known predictors such as illness perceptions and fear of recurrence were accounted for. Although both fear of recurrence (50, 52, 53) and fertility concerns and related distress (23) are important issues experienced by young cancer survivors this model has not previously been tested.

The findings of this study suggest that even though fertility-related distress might be associated with decreased QoL, it is the fear of recurrence that mainly contributes to the perceived low levels of QoL among young women with cancer. Whilst the qualitative literature suggests that distress related to fertility issues in survivorship can have detrimental effect on young women's psychological well-being (see section 3.3.2), this effect could be of a qualitative rather than quantitative nature. This may be due to the fact that fear of recurrence is a direct consequence of cancer and is relevant to every cancer patient while fertility-related distress only involves certain groups of patients. In this study, almost 10% of the participants reported they did not experience any distress with respect to their post-cancer fertility status (scored 0 on the IES-R), while at the same time only 0.6% declared the complete absence of worries regarding the possibility of cancer recurrence.

5.4.1.4. Research question 4 – predicting relationship satisfaction and dating experience

The final research question in this study sought to clarify whether fertility-related distress predicted post-cancer relationship satisfaction among partnered women or dating experience among single women. The results suggest that neither was determined by fertility-related distress, which is in line with the existing quantitative evidence (see section 3.3.2.1.2).

Although the qualitative literature suggests that partnered women might feel guilty towards their partners for not being able to provide them with a biological child post-

cancer treatment and single women find their fertility issues to be a barrier to dating and getting involved with potential partners (see section 3.3.2.2.1.3), these findings are generally not supported by the quantitative evidence or the results of this study. As with QoL, it may that the prevalence of fertility issues and/or their intensity among the study participants were too low to detect any impact on relationship quality or dating experience. Whilst this does not seem a plausible explanation in the light of the existing quantitative evidence, this evidence is relatively limited with only two studies investigating these associations, therefore further research is warranted. Focusing on women who are particularly affected by the fertility-related distress should be a priority.

5.4.2. Limitations

Although this study possesses strengths in that it is one of the few to investigate fertility-issues among young gynaecological and breast cancer patients from a theory-driven perspective and to include the cross-cultural aspect, being the first to compare two distinct European populations –British and Polish, it is not free of limitations threfore its results should be interpreted with caution.

Whilst this was a multi-centre study with recruitment strategy designed to provide a diverse sample and an adequate sample size, the latter remained relatively small. This should be noted particularly when interpreting the results derived from the Polish subset of data which contained only 42 participants.

The overall small sample size also prevents from drawing unequivocal conclusions, particularly with respect to the conducted mediation analyses. While a path analysis might have been more appropriate to conduct the exploratory mediation and moderation analyses, the overall sample size was deemed insufficient to use this approach.

The results of the exploratory mediation and moderation analyses should also be treated with caution as these were driven by statistical criteria in the absence of empirical research. Although this is the first analysis of this type, it proved impossible to cross-validate the obtained model due to an insufficient sample size. The results need to be verified through a larger study.

As with all self-report studies, it is possible that some of the questions could have been sensitive to recollection bias (e.g., desire to have children at the time of diagnosis),

however, it was impossible to measure some of the constructs by other means. Another problem inherent to self-report is the potential response bias. To avoid it, the negative affect scale was used. Its score was subsequently introduced into the models as a control variable to eliminate effects due to participant's tendency to score high on instruments measuring distress and QoL.

5.4.3. Conclusions

Recent progress in cancer treatment has translated into increased survival rates among cancer patients (12). Despite this, cancer diagnosis and treatment are not indifferent to the lives of the patients who often struggle with both the emotional and physical consequences of cancer. While some of these such as fear of recurrence, QoL, and relationship satisfaction or dating experience are universal, others including fertility-related distress are age-specific. This study contributes to the growing field of research focusing on these issues which are commonly faced by young women diagnosed with cancer and adds to their understanding.

First, the results of this study suggest that the three psychosocial outcomes investigated – the distress related to fertility, fear of recurrence, and QoL – follow the assumptions of the CSM in that they are all determined by the way one conceptualises one's illness rather than by objective cancer characteristics. While fertility-related distress and fear of cancer recurrence appear to be contingent on the emotional representation of illness, QoL depends more on the cognitive representation. Hence, interventions tackling the process of conceptualising illness among young women could potentially improve their psychosocial outcomes in the survivorship period.

Fertility-related distress was determined by the desire to have children and treatment-related regret. While the former is a rather non-modifiable factor, if addressed early through open physician-patient communication, it could guide cancer treatment and FP decisions which could in turn potentially prevent the latter. However, as this study suggests there might be cross-cultural differences with respect to fertility-related distress as well as its determinants. Therefore, solutions and preventative measures effective among a particular group of patients might not necessarily apply to a culturally different group. This may prove a challenge to physicians working in multicultural societies, however, more evidence still needs to be gathered.

Although fertility-related distress might be important to many young women diagnosed with cancer, it does not necessarily affect all of them. Fear of recurrence, on the other hand, does and in this study it was the most important determinant of young women's QoL. More effort, therefore, should be made to tackle fear of recurrence, including interventions focusing on the way women conceptualise their illness.

Finally, fertility-related distress was shown not to have a detrimental effect on relationship satisfaction among partnered participants or dating experience among the single ones. This is a positive finding indicating that women generally do not perceive their reproductive concerns as a barrier to maintaining satisfactory close relationships or entering the new ones. Based on the qualitative evidence, however, an individualised approach might be necessary to identify women who might struggle with relationships because of their fertility-issues post-cancer.

Chapter 6 General discussion

This chapter summarises the main points of this PhD thesis and provides a synthesis of the qualitative and quantitative components of this project. First, research objectives as outlined in section 1.8 and the way they were addressed are discussed briefly in section 6.2. Section 6.2.1 provides a summary of the introductory chapter, section 6.2.2 briefly reviews the theoretical considerations, section 6.2.3 concentrates on the systematic review of literature, and sections 6.2.4 to 6.2.6 give an overview of the main findings of the qualitative and quantitative studies. Next, the synthesis of the results from both of the studies is presented, with reference to the theories used throughout the project (section 6.3). Thesis limitations, as well as implications for further research resulting from them are described in section 6.4. The chapter concludes with some practical implications of this project for both healthcare professionals and health psychologists (section 6.5) and the general conclusions of the thesis (section 6.6).

6.1. Introduction

The aim of this thesis was to investigate the role that fertility and reproductive issues played in the lives of young women diagnosed with gynaecological or breast cancer. The research objectives established to achieve this aim are discussed below with an emphasis placed on the synthesis of the findings from the qualitative and quantitative components of this project. This is achieved by considering the results within the framework of the Common Sense and the Shared Decision Making models, and provides additional insights into the pehnomena studied throughout this PhD project.

6.2. Discussion of research objectives

6.2.1. To establish the importance of fertility issues and fear of disease recurrence among young female cancer patients

Although cancer is generally considered to be a disease of older people, it can occur at any age (6). Approximately 7% of all cancers are diagnosed among reproductive age women (360) with breast, cervical, and ovarian cancer accounting respectively for 45%, 9%, and 5% of all new cancer cases diagnosed in this age group (10).

Young people with cancer, and specifically young women, are a group of patients presenting with particular, age-related needs. Among them, fertility-related information

and counselling play an important role (1-3), however, research shows that these needs often remain unmet (1, 4).

Fertility might be important to young women diagnosed with breast or gynaecological cancer since various treatment modalities including surgery, radiotherapy, chemotherapy, and endocrine therapy can lead to post-cancer fertility impairment (18-22, 25, 26, 114). Additionally, due to the 'postponement transition' resulting from sociocultural changes including the introduction of reliable contraceptive methods as well as women joining workforce and pursuing educational and career goals, women nowadays tend to delay childbearing (31). While voluntary childlessness might be a choice, cancer treatments and subsequent inability to conceive might contribute to involuntary childlessness among women. Involuntary childlessness can have adverse psychological consequences (44) which can affect young female cancer survivors in addition to the issues related directly to their cancer diagnosis.

One of these issues is the fear of cancer recurrence. According to a systematic review of unmet supportive needs among the general cancer patient population, 'fear of cancer spreading or recurring' constituted the most frequently identified psychosocial issue in the treatment and post-treatment phases (5). Studies focusing specifically on young women diagnosed with cancer suggest that this population is at risk of experiencing high levels of fear of recurrence (114).

Given the evidence regarding important issues faced by young female cancer survivors, this project investigated the role of fertility concerns and fear of cancer recurrence at the time of treatment decision-making and in the survivorship phase through a systematic review of literature (see section 6.2.3) as well as through two studies – a qualitative (see section 6.2.4) and a quantitative (see sections 6.2.5. and 6.2.6) one. These studies used the CSM as an overreaching theoretical framework, and the Shared Decision Making model was also applied in the qualitative study to specifically explore treatment decision-making processes.

6.2.2. To understand how individuals perceive their illness and cope with it from the perspective of the CSM and how this model can be applied to young women dealing with cancer and fertility issues

The CSM is a theoretical framework explaining health and illness behaviours based on three general assumptions, namely that:

1. individuals are problem-solving agents who select coping strategies to manage health threats based on their own representation of illness;
2. problem-solving occurs in a particular socio-cultural context;
3. individuals base their health-related decisions based on what is recognised as the most urgent threat and these decisions are limited by the available resources and are evaluated according to the 'satisfaction rule' (64).

Central to the CSM are illness perceptions which constitute an individual's own understanding of illness (64). These include the cognitive representations such as identity, timeline, control (personal and treatment), causes, and consequences (68-70) as well as emotional representation (80). Illness representations are activated by both concrete and abstract stimuli received by an individual from the internal and external environment.

The symmetry rule purports that information from both levels needs to be integrated for an illness representation to be fully and properly formed (64). Since illness representations are responsible for determining the response to a health threat as well as the selection of strategies to cope with it, a failure to fully form an illness representation may lead to maladaptive coping strategies (72).

The interpretation of stimuli informing a health threat also depends on multiple factors including self-identities and the socio-cultural context in which an individual is embedded. Several important heuristics have been identified in relation to how people interpret health threats including age-illness and prevalence heuristics (see section 2.2). The socio-cultural context plays a role in forming illness representations, emotionally responding to health threat, and choosing appropriate coping strategies (75). In egocentric cultures such as the European or Northern American ones, individuals often turn to the healthcare system to manage a health threat they are faced with. While

healthcare professionals are responsible for accurately diagnosing and treating the condition, it is the patient who bears the consequences of an illness. Being involved in making treatment-related decisions as well as gathering information about a health threat have been identified as strategies to adapt to an illness, particularly among cancer patients (104-107). The gold standard of clinical care is to include patients in the decision-making (57). This can be done through adopting the Shared Decision Making model.

The described aspects of the CSM are used to explain the findings of each part of this project, as well as to synthesise the qualitative and quantitative results. The Shared Decision Making model is applied to structure and analyse the qualitative data specifically pertaining to treatment decision-making processes.

6.2.3. To update a systematic review of literature examining fertility issues in the population of young female cancer patients

An updated systematic review of literature was conducted to address three objectives:

1. To identify factors associated with fertility issues in women diagnosed with cancer during their reproductive years;
2. To characterise the relationship between fertility issues and psychological well-being of reproductive-age women diagnosed with cancer;
3. To explore how women diagnosed with cancer during their reproductive years make cancer treatment-related decisions which can affect their reproductive potential and outcomes in the future.

Both qualitative and quantitative literature were included in the review. The former was analysed using narrative synthesis since the heterogeneity of outcomes precluded a meta-analysis. Thematic synthesis (201) was used to analyse the latter.

In relation to objective 1, multiple sociodemographic and medical factors including gynaecological and cancer-related characteristics were investigated as potential predictors of reproductive concerns. However, only a few were found to be associated with fertility-related distress including being single, not having children, a wish to have a child or more children, fewer pregnancies prior to cancer, and possibly receiving gonadotoxic treatments (see sections 3.3.1 and 3.4.1.1).

In relation to objective 2, the literature provided an inconsistent picture of the impact of fertility issues on young women's psychological well-being. Quantitative studies seemed to suggest a relationship between higher level of fertility concerns and lower levels of QoL and sexual functioning. On the other hand, there were mixed results as to whether reproductive issues were related to depressive symptoms and anxiety. Finally, the quantitative evidence indicated that there was no association between fertility concerns and relationship functioning or dating experiences, as opposed to the qualitative literature. Qualitative synthesis also identified other consequences of post-cancer infertility namely the perception that infertility increases the psychological burden of the cancer experience (see section 3.3.2.2.1.1), the negative emotions that it incurs (see section 3.3.2.2.1.2), but also the positive (albeit rare) aspects (see section 3.3.2.2.1.4). An attempt to explain why women's psychological well-being post-cancer might be affected by infertility focused on the broader socio-cultural context that women lived in and which they could not escape. Surrounded by healthy female friends, women compared themselves to them and also to women in general and found it difficult to accept that these women could spontaneously have children while this decision had been taken from them. It appears that these negative comparisons stemmed from the fact that the concept of motherhood had been internalised by women and was perceived as a necessary part of female identity. Therefore, when the possibility of being a parent after cancer was denied, women found it difficult to go back to their normal lives.

In relation to objective 3, the quantitative literature revealed that 13% to 29% of young women diagnosed with cancer found fertility to be an important factor which affected their treatment-related decisions. These decisions involved refusing chemotherapy, opting for a less gonadotoxic chemotherapy regimen, discontinuing endocrine therapy and undergoing trachelectomy instead of hysterectomy for cervical cancer.

The process of making treatment decisions was explained by the qualitative literature. Women who considered fertility important at the time of diagnosis engaged in a process of value clarification, which involved weighing their desire to preserve their reproductive potential against their wish to survive their prognosis (see section

3.3.3.2.1). This process allowed them to clarify their priorities and engage in treatment decision-making.

Women stressed the importance of information and the preferred way in which it should be delivered (see section 3.3.3.2.2). They also emphasised the role of physicians in the decision-making and their wish to involve them in this process, particularly when the physician-patient relationship was supportive. By that women meant an environment in which there was time and space for open communication between the physician and the patient (see section 3.3.3.2.3.1.2). Physician's unwillingness to discuss women's fertility-related preferences was often perceived as a sign of arrogance on the part of physician who made assumptions about their patient's fertility-related plans or lack of thereof (see section 3.3.3.2.3.1.2). This, along with being at either end of the reproductive age spectrum, being single, institutional and cost issues, the timing of decisions and their psychological burden, were all seen as barriers to treatment decision-making (see section 3.3.3.2.3.2). The sense of hope for motherhood and a chance for a normal life post-cancer were seen as facilitators to making a decision to preserve fertility (see section 3.3.3.2.3.3). While both women who preserved and those who did not preserve fertility reported positive and negative consequences of their decisions, the latter were more likely to experience decision-related regret (see section 3.3.3.2.4).

This extensive literature review not only served as a synthesis of the existing evidence, but also provided an additional framework which guided the analysis of the qualitative data. The findings relating to objective 3 appear to suggest that young women preferred to make their treatment-related decisions in line with their own priorities but also in an informed way and with guidance from their physicians. These three components – professional involvement, information exchange and accounting for preferences – constitute the core of the Shared Decision Making model (115), which was applied to the qualitative data.

6.2.4. To investigate how women in the UK diagnosed with either gynaecological or breast cancer make treatment-related decisions which can affect their reproductive potential and whether fertility issues play a role in those decisions

This study involved 24 in-depth telephone interviews conducted with young women diagnosed with either breast or gynaecological cancer who were treated prior to study

participation. The purpose was to gain an in-depth understanding of cancer treatment decision-making processes and the reasons behind these decisions including the role played by fertility issues and fear of cancer recurrence.

The findings of this study suggest that women's initial reaction to the diagnosis, their choice of treatments, and their adaptation to post-treatment reality were all largely influenced by their own understanding of their illness – their own illness perceptions as understood by the CSM.

The representation that determined the initial reaction to diagnosis was illness identity and the way it was constructed by women using age-illness and prevalence heuristics. Women often perceived themselves as protected from a cancer diagnosis by their young age and if they experienced symptoms prior to diagnosis, they tended to normalise them by comparing themselves to other women with similar symptoms who suffered from benign conditions. The latter contributed to the failure in the proper formation of illness identity through the violation of the symmetry rule. The perceived lack of or presence of only minimal symptoms did not fit the label of cancer. This might have contributed to women's reaction of shock and surprise when faced with a diagnosis of a malignant disease (see section 4.3.2.1).

More importantly, an illness representation that frequently guided women's treatment decisions was the perception of consequences which for many women involved potential fertility issues brought about by cancer and its treatments. The application of the symmetry rule to this illness perception involved women learning about the impact of cancer on fertility (see section 4.3.2.2) and clarifying their own attitudes towards fertility in the context of cancer through the balancing-prioritising process (see section 4.3.2.3.3). While many women in this study had the opportunity to both receive information about the impact of cancer on fertility and consider the extent to which fertility was important to them at the time of diagnosis, the physician's resistance to discussing fertility could potentially impede these processes. Research suggests that physicians often have negative preconceptions about initiating fertility discussions in the cancer setting (4), which might preclude some women from taking steps to preserve their fertility even if their particular circumstances allow for it.

The importance of the healthcare providers' involvement in the treatment decision-making was widely acknowledged by the majority of women in the study (see section 4.3.2.4.2). In terms of decisions that implicated fertility, many women also wished to involve their significant others – partners if they were in relationships at the time of diagnosis, or sometimes their parents if they were single (see section 4.3.2.4.4). Participants equally emphasised the role of being properly informed about the treatment and FP options, albeit the extent to which they wanted to be informed differed among women (see section 4.3.2.4.3). Finally, the importance of one's own preferences with respect to treatment outcomes was discussed by participants, and the crucial role of the congruence between the patient's and physician's preferences was noted. Participants' preferences were the result of the balancing-prioritising process and their conceptualisation of what losing fertility to cancer would mean for them. If this process was not supported by the physicians through open communication and a willingness to take women's priorities into account while drawing a treatment plan, this sometimes resulted in women changing physicians or going against their advice (see section 4.3.2.4.5).

These results reflect the current literature (see section 6.2.3) and also encompass the main components of the Shared Decision Making model – the wish for professional involvement, information exchange, and respect for fertility-related preferences in treatment decision-making. It is important to acknowledge that compared to other treatment decision-making models such as paternalistic or informed, the Shared Decision Making model allows best for the preservation of patient autonomy through the process of value clarification which was key in relation to fertility in this study. As suggested by Emanuel, E.J. and L.L. Emanuel (117), shared decision-making creates a clinical situation where 'the patient is empowered not simply to follow unexamined preferences or values but to consider, through dialogue, alternative, health-related values, their worthiness and their implications for treatment' (p. 7). This is the reason why open communication with the clinical team is crucial in the decision-making process.

Since the majority of participants had the experience of a relatively supportive environment to make treatment decisions, they positively evaluated their choices. Only

a minority reported the feelings of regret, however, at least in one case that could have potentially been prevented had the clinical team appropriately addressed the participant's reproductive concerns (see section 4.4.1.4). This is of particular importance since in the case of cancer treatments women only have one chance at making the 'right' decision (see section 4.4.1.5).

While most participants were positive about their treatment decisions, this did not prevent them from having difficulties going back to a life as they knew it before their cancer diagnosis. Irrespective of whether women decided to preserve their fertility, most still had to face post-cancer fertility issues. This is because the context in which the women made their reproductive choices changed for all of them. Although they were still in charge of the ultimate decision of whether to have children at all (through assisted reproduction or alternative parenting), control over those choices did not lie entirely with them. It depended on other people including healthcare professionals, potential surrogate mothers, or social services (see section 4.3.2.6.1.1). Therefore, persistent fertility issues, to varying degrees, pertained to all the women who were concerned about fertility prior to treatment.

Some women described negative emotional consequences of reproductive issues post-treatment and related these to the fact that they felt different from their peers as their future and fertility-related plans needed to be put on hold while their friends were able to freely make reproductive choices. These feelings of dissimilarity corroborate evidence from the literature which additionally suggests that these perceptions might result from an internalised norm of motherhood being central to women's identity (see section 6.2.3).

Fertility issues understood as not being able to have children were not the only consequence of cancer treatment that women commented on. They also mentioned the menopausal symptoms they suffered from and a fear of cancer recurrence. These two were shaped by the women's illness perceptions, and conceptualisation of both relied on the identity women attached to the observed symptoms and their beliefs about the causes of cancer. These two illness representations also determined their coping strategies with both menopausal symptoms and fear of cancer recurrence (see section 4.4.1.5).

6.2.5. To identify the determinants of fertility issues and fear of cancer recurrence among young women diagnosed with gynaecological or breast cancer drawn from two populations –British and Polish

These investigations were part of the quantitative study which involved questionnaire data from 164 young women diagnosed with breast or gynaecological cancer and treated prior to study participation.

The findings of these investigations revealed that neither distress related to fertility nor fear of cancer recurrence were predicted by objective cancer characteristics such as type, stage, treatment modality, or time since diagnosis. They were both, however, determined by the personal conceptualisation of a health threat, notably by its emotional representation. This evidence is consistent with the assumptions of the CSM and also reflects the results of a recent systematic review of illness perceptions in women with breast cancer (361). This review found a clear association between illness perceptions and many major psychosocial outcomes (361).

Contrary to the literature review (see section 6.2.3), fertility-related distress was neither related to one's relationship nor to one's childbearing status. It was, however, associated with the desire to have children as well as treatment-related regret. The additional mediation analyses demonstrated that treatment-related regret, and emotional representation of illness potentially acted as mediators of the relationship between desire to have children and fertility-related distress. This means that women with a higher desire to have children also experienced more post-treatment regret and perceived their illness as more emotionally burdensome, and hence reported more fertility-related distress.Therefore it is important to identify patients who wish to have children at the time of their diagnosis and while it might be impossible to change one's desire to have children, both treatment-related regret and emotional representation of cancer are likely modifiable factors. The risk of regret could be reduced by FP (63), while cognitive behavioural therapy has shown potential in modifying maladaptive illness perceptions (361).

Finally, examination of the country of origin as a moderator of the relationship between desire to have children, treatment-related regret, and fertility-related distress showed that the association between various predictors and mediators might vary cross-

culturally. This means that interventions effective in reducing fertility-related distress in one group of patients might not be adequate in a culturally different one.

6.2.6. To examine whether fertility issues and fear of cancer recurrence are associated with QoL and relationship functioning among young women diagnosed with gynaecological or breast cancer drawn from two populations –British and Polish

These investigations were also part of the survey study involving 164 women diagnosed with breast or gynaecological cancer and treated prior to study participation.

Whilst QoL was associated with fertility-related distress in univariate analysis, this relationship did not remain significant in the multivariate analyses. Relationship satisfaction and dating experience were not at all associated with fertility-related distress. These results are consistent with the existing quantitative literature, however, less so with the qualitative literature (see section 3.3.2). The qualitative evidence suggests that particularly single women perceive their fertility issues post-cancer as a barrier to dating and entering new relationships (see section 3.3.2.2.1.3). The review also suggest that women report a variety of negative emotions related to fertility issues and recognise them as a factor impeding the process of going back to normal after cancer (see sections 3.3.2.2.2 and 3.3.2.2.3). Nonetheless, it might be that QoL questionnaires in general, and the one used in this study in particular, operationalise QoL in a different way to women themselves when they describe the process of adaptation to their lives after cancer. Because of this possible discrepancy in definitions, making comparisons between the quantitative and qualitative evidence might be problematic.

Factors that significantly determined young women's QoL included illness perceptions – particularly the cognitive components, and the fear of cancer recurrence. Unsurprisingly, QoL as yet another psychosocial outcome was not predicted by objective disease characteristics, but by one's own conceptualisation of illness. While both distress related to fertility and fear of recurrence were dependent upon one's emotional representation of cancer, QoL was determined by cognitive representation.

However, the strongest predictor of QoL proved to be the fear of recurrence. Thewes, B. et al. (52, 53) who investigated recurrence fears among young women with breast cancer concluded that it was a prevalent problem in this population. These findings were supported by the results of this study. Whilst approximately 10% of the participants did not report any distress related to fertility, only 0.6% declared the complete absence of worries regarding the possibility of cancer recurrence. Since there is growing evidence for a relationship between QoL and fear of recurrence (50), and recurrence fears also seem to be most prevalent in younger populations (50), interventions tackling this issue in young women with cancer could potentially improve their QoL.

6.3. Synthesis of the qualitative and quantitative findings

Whilst the focus of the qualitative part of the project was the process of treatment-related decision-making and the quantitative study primarily explored the impact of fertility issues in survivorship, the two are in many ways interlinked and synthesising their findings provides additional insights into the investigation of fertility issues among young gynaecological and breast cancer survivors.

By analysing the two studies together, it became apparent that illness perceptions played an important role in determining an initial reaction to cancer diagnosis (identity); coping mechanisms such as treatment decision-making (consequences), and dealing with menopausal symptoms and fear of cancer recurrence (identity and perceived causes of cancer); as well as psychosocial outcomes in survivorship including fertility-related distress and fear of cancer recurrence (emotional representation of illness), and QoL (cognitive representation of illness). Illness representations seem, therefore, to be key to understanding the process of young women's adaptation to the cancer diagnosis.

The qualitative study in particular stresses the importance of the symmetry rule in the formation of illness perceptions (see 6.2.4). A violation of this rule may lead to maladaptive coping strategies as suggested by Bradley, E.J. et al. (72). Although Bradley, E.J. et al. (72) give the issues in forming illness identity (label without symptoms) as an example of the violation of symmetry rule, this could potentially apply to other illness perceptions too.

Women in this study conceptualised fertility issues as a consequence of cancer. The development of this illness representation occurred mainly as a result of the following processes:

1. becoming aware that cancer treatments could affect one's fertility which depended on women's pre-existing knowledge about cancer but also information provided by the clinical team;
2. the balancing-prioritising process which could be facilitated by a supportive patient-doctor relationship and communication.

As suggested by the findings, the proper conceptualisation of fertility issues as a potential consequence of cancer was important because women only had one chance at making the 'right' decision for their particular circumstances. The decisions they made could not be taken back or amended post-treatment. Therefore, if the 'wrong' decision was made (as perceived by the patient), this could potentially lead to treatment-related regret.

The fact that treatment impacted on one's fertility was a reason for regret in one participant in the qualitative study and 34.8% of participants in the quantitative study. The latter also suggested that women with a high desire to have children at the time of diagnosis were at risk of increased treatment-related regret. Whilst it might not be possible to change one's wish to have children, the mere discussion about the issue could indicate to the clinical team which patients were at risk of treatment-related regret. This is a potentially modifiable factor that could be minimised by:

1. open communication and provision of an explanation why FP is not advised in cases where it is contraindicated;
2. provision of the option to undergo FP.

However, it is important to remember that even undergoing FP does not guarantee that women would not be faced with fertility issues in the survivorship phase. The qualitative study revealed that post-treatment fertility was constrained even among women who opted for FP because of the loss of reproductive control (see section 6.2.3). The extent to which this might be perceived as problematic and a cause for distress remains as yet unknown. The quantitative study which investigated fertility-related

distress did not directly inquire whether women preserved fertility in the course of cancer treatments. However, when the type of treatment a woman received was operationalised into two categories (treatments inducing sterility vs those rendering fertility uncertain), the final multivariate model revealed that distress did not vary based on the type of treatment received. This tentatively suggests that both women who preserved and those who did not preserve fertility in the course of cancer treatment might perceive their post-cancer fertility issues as a cause for distress.

The fertility-related distress reported by approximately 90% of participants in the quantitative study was predicted by the desire to have children, treatment-related regret, and emotional representation of illness. Additional insights into these associations can be gained from the qualitative investigations. Women who took part in the interviews reported feeling different from their peers as they could not freely realise their childbearing desires. This made them feel excluded from their peer groups. The existing evidence suggests that such feelings can arise due to the fact that many women internalise the social role of being a mother and find it central to their female identity (see section 3.3.2.2.3.1). Hence, the desire to become a mother seems to be as much an individual as it is a cultural concept, particularly in societies where motherhood is perceived as something that ought to happen (362). When it does not, this can then potentially lead to the perception of being excluded from one's social circles which, as suggested by the literature, can indeed be the cause of anxiety and distress (363, 364).

The quantitative study attempted to measure whether fertility-related distress was conditional on the socio-cultural background. Although the culture-specific variables proved to be non-significant in the final model, the country of origin remained significant with Polish women experiencing more fertility-related distress than the British participants. In line with the social norms theory (362), it is possible that Polish women, because of their cultural background (see sections 2.2.3.2.1 and 5.4.1.1), had internalised fertility-related norms to a greater extent than their British counterparts. This could have in turn led to higher levels of distress generated by potential post-cancer infertility among Polish participants.

Whilst fertility-related distress differed between the Polish and British participants, fear of cancer recurrence was prevalent among almost all women, regardless of their country

of origin, in both the qualitative and the quantitative study. The quantitative study suggested that one's emotional representation of illness determined the levels of recurrence fears while the qualitative study found that efforts to cope with fear of recurrence were driven by illness identity and perceived causes of cancer. This corroborates the available evidence positioning fear of recurrence within the framework of the CSM (see section 2.2.1.1.1.1) and provides a potential starting point to design interventions tackling fear of recurrence among young women diagnosed with cancer.

6.4. Limitations of the project and implications for research

The limitations of the qualitative and quantitative parts of this project were discussed in sections 4.4.2 and 5.4.2 and they provide a useful context to inform future research.

Although this is the first study to identify the mediators of the relationship between the desire to have children and fertility-related distress, these results need to be treated with caution due to a limited sample size and the lack of possibility to cross-validate the model. This calls for more robust studies which would examine the associations reported in this project. More broadly, future research should concentrate on mechanisms in which non-modifiable factors affect fertility-related distress and whether there exist any potentially modifiable factors which could act as anchor points to design interventions aimed at reducing fertility-related distress.

There is also a need for more cross-cultural studies focusing on post-cancer fertility-related distress. As this study suggests, modifiable factors which could be targets for interventions can vary among women with different socio-cultural backgrounds. It is important to identify them in order to properly tailor interventions to the potential recipients.

As indicated by the qualitative study, irrespective of whether women preserved their fertility, they can still be at risk of the psychological effects of post-cancer fertility issues. The extent to which the loss of control over one's fertility subsequent to cancer treatments is problematic needs to be investigated in depth. If future research shows that women who underwent FP equally suffer from distress related to reproductive issues, it might be necessary to provide them with additional support.

Finally, although the findings of the qualitative study suggest that women's preferred way of making treatment decisions that could affect their future reproductive outcomes is consistent with the Shared Decision Making model, extrapolation of these results might be problematic due to the study design. Therefore, it would be worth investigating this further through a larger quantitative study, focusing on the actual and preferred role in cancer treatments decision-making in the context of maintaining fertility. This would allow for the distinction between what women want to happen and what actually happens in terms of treatment decision-making within the clinical setting and subsequent adjustment of practice.

6.5. Implications for practice

Based on the results of this project, the following recommendations for medical practitioners and health psychologists can be suggested.

For medical practice:

- **Elicit patient's preferences with respect to fertility prior to cancer treatments early on following diagnosis.** This would allow patients the time to consider whether fertility is a factor they would want to account for in their treatment-related decisions. This occurs through the balancing-prioritising process as described in the qualitative part of this PhD project (see section 4.3.2.3.3). The evidence suggests that young women often feel they do not have enough time to make truly informed choices with respect to cancer treatments in the context of maintaining fertility (see section 3.3.3.2.3.2.5). A recent study by Kim, J. and J.E. Mersereau (271) found that discussing fertility and providing young women with options early on facilitates the decision-making process and decreases potential decisional conflict.
- **Discuss fertility even if options to preserve fertility are not viable.** Young women constitute a group of patients who often want to assume a more active role in the treatment decision-making process (113). The qualitative part of this PhD project corroborates this evidence in that it proposes a Shared Decision Making model as a standard to adopt in treatment-related decision-making in the context of maintaining fertility among young women diagnosed with cancer. However, this is only possible when women have a clear understanding of the options available to them. When, for various reasons such as cancer stage or type there are no viable FP

options, this needs to be clearly explained. While the lack of options has often been described as frustrating (177, 246), the existing evidence also suggests that the lack of explanation as to why options to preserve fertility are unavailable leads to deep dissatisfaction with the patient-physician relationship (189, 249, 251, 252) and could make treatment decisions more difficult.

- **Incorporate patient's preferences into the treatment plan where possible.** As suggested by the qualitative part of this PhD project, young women respect their physicians' advice with regards to cancer treatments. Recognising patient's preferences through open communication about fertility and including these preferences in the treatment plan if and where possible could facilitate the process of treatment decision-making. This particularly applies to women who are unsure about whether they wish to pursue FP as the literature indicates that they constitute the group who most often relies on physicians' advice with respect to preserving fertility (248).
- **Where possible, allow the patient to make a decision about FP but support the process through discussion and preference clarification.** Both the literature and the results of the qualitative part of this PhD project suggest that some women perceive FP as the only decision in the whole process of cancer treatment-related decision-making that is truly theirs (246). The importance of being in control of making decisions which have the potential to affect one's life in the long term has been described in section 3.3.3.2.2.3. The literature suggests that young women who are allowed to make decisions about maintaining fertility in the context of cancer regain the sense of agency over their lives (248). In order for this to happen, women need to be well informed about the options hence the role of their physicians in discussing fertility with them and facilitating the balancing-prioritising process.
- **Adapt treatment decision-making process to individual patients, while bearing in mind that young women often wish to assume a more active role**. The results of the qualitative part of this project (see Chapter 4), along with the findings of the literature review (see Chapter 3) suggest that young women wish to make their treatment-related decisions in the context of maintaining fertility in line with the Shared Decision Making model. Therefore, the importance of providing appropriate information regarding fertility and eliciting patient's views and preferences with

respect to fertility cannot be underestimated. While some women will take the responsibility for informing themselves, others might want to stay away from the publicly available information (for example online resources) therefore this responsibility lies with the clinical team.

- **Attempt to identify patients at risk of fertility-related distress and refer to the appropriate supportive services if needed**. Existing research has identified several factors associated with higher fertility-related distress including one's relationship status (single), childbearing status (not having any children), and the desire to have children at the time of cancer diagnosis (see sections 3.3.1 and 3.4.1.1). The quantitative part of this PhD project corroborates the existing evidence as to the importance of one's wish to have (more) children in determining one's fertility-related distress after cancer and also identifies new factors which might prove useful in determining one's risk of experiencing fertility-related distress. These include one's country of origin, the extent of regret one feels with respect to having undergone fertility-impairing treatment, and the way one conceptualises their illness – particularly in terms of its emotional impact (see section 5.3.3). While these determinants could be used by physicians to identify patients at risk of fertility-related distress, it should be noted that only some of them are information routinely elicited in the course of a consultation (e. g., relationship status, childbearing status, country of origin). Therefore to appropriately determine a patient's risk it is necessary for clinicians to establish good communication with their patients and inquire about their childbearing desires, attitudes towards treatment, and their own understanding of their illness.
- **Be mindful of potential cross-cultural differences and the consequences these might have for the psychosocial outcomes of patients with various social backgrounds**. As suggested by Greil, A.L. et al. (47), the perception of fertility issues might vary cross-culturally. In the quantitative part of this study, the differences in experienced distress related to fertility issues after cancer were found between the Polish and British patients. Physicians' awareness that socio-cultural background might affect one's psychosocial outcomes, particularly those related to fertility is crucial to the choice of appropriate treatment pathways and counselling.

- **Recognise patient's conceptualisation of illness and facilitate the formation of appropriate illness perceptions through discussion.** The CSM provides a useful framework to understand how lay people conceptualise their own illness (62, 64). It is important for physicians to be aware of the way their patients perceive their medical conditions since it has proved to affect one's compliance with treatment (365, 366) and hence the treatment outcomes. The qualitative part of this PhD project found that cancer-related fertility issues were conceptualised by women as a consequence of their illness and the conceptualisation process occurred through (1) becoming aware that cancer can affect one's fertility; and (2) balancing and prioritising one's wish to survive cancer diagnosis against one's desire to have children after cancer. Physicians play a crucial role in delivering information about cancer-related fertility issues to their patients and discussing patients' fertility concerns. Hence, they are in a position to influence and shape women's conceptualisation of fertility issues in the context of cancer diagnosis. The importance of an appropriate conceptualisation of fertility issues cannot be underestimated since it guides women's treatment decisions (see sections 4.3.2.2, 4.3.2.3.3 and 4.3.2.4.5), which due to the nature of cancer treatments, cannot be easily amended or reversed later.

For health psychologists:

- **Initiate fertility discussions with young female patients if seen early in the process of diagnosis in case the issue have not been addressed by the clinical team.** As suggested above, discussing fertility early on in the course of cancer diagnosis should lie within the remit of physician's responsibilities towards the patient. However, according to the research conducted with healthcare providers the topic of fertility was routinely broached in only 48 (367) to 69% (368) of clinical consultations. Health and clinical psychologists might therefore be in a position to initiate fertility discussions with patients if they are referred early on in their cancer diagnosis trajectory. While this might be a difficult topic to discuss, it is important to make sure that patients are aware of cancer treatment's impact on fertility to make informed decisions as to whether they wish to preserve their fertility. Another role to be played by health and clinical psychologists would be to liaise between patients

and physicians as well as support the patients in the process of talking to physicians about fertility issues.

- **Tackle illness perceptions as a potential target for psychosocial interventions to reduce distress related to fertility, and fear of recurrence as well as improve QoL.** Illness perceptions affect young women's fertility-related distress, fear of cancer recurrence, and QoL (see sections 5.3.3, 5.3.4, and 5.3.5), and hence they constitute a logical target for interventions to improve patients' psychosocial outcomes. In the case of both fertility-related distress and fear of cancer recurrence, potential interventions could focus on tackling the emotional dimension of illness representation. As young women's QoL depended more on the cognitive components of illness representations (e. g., consequences, personal control, and identity), it is recommended that they constitute a target for interventions aimed at improving QoL.
- **Focus on managing fear of recurrence as it might improve patient's QoL.** Women's QoL could be improved by targeting illness representations as suggested above. However, the quantitative part of this project found that the fear of cancer recurrence was the strongest independent predictor of young women's QoL. Therefore, it would be worthwhile to concentrate on recurrence fears as a target for interventions to ameliorate young women's QoL. Several trials have recently been designed and conducted to tackle the issue of recurrence fears among head and neck (369) and breast cancer patients (370). Should they prove effective, they could be adapted and used in the population of young women diagnosed with cancer.
- **Support the redefinition of femininity to address fertility related distress in survivorship.** As suggested by the existing evidence and the qualitative part of this project, women who were able to redefine their femininity in terms of life goals as an alternative to having biological children (e. g., finding meaning in their relationships, religion, professional development, or alternative ways of parenting) (see sections 3.3.2.2.3.3 and 4.3.2.6.1.2.3) were also better equipped to cope with the impact cancer had on their fertility. Supporting the redefinition of femininity to find life purpose outwith the context of motherhood could be one way to help women move on with their lives in survivorship. Women for whom parenthood is core to their identity should be given an opportunity to explore in depth their

attitudes towards alternative parenting (e.g., adoption, surrogacy, or gamete donation) and supported in pursuing these should they wish to do so.

6.6. General conclusion

Fertility concerns and fear of cancer recurrence proved to be important issues among young women diagnosed with cancer (1-3, 52, 53). This project supports the existing evidence as well as provides new insights into the role fertility issues and fear of recurrence play in the lives of young women diagnosed with breast or gynaecological cancer. It explains how fertility issues and fear of cancer recurrence interplay in determining women's treatment-related decisions. It also sheds light on the process of decision-making about treatments which can potentially affect young women's future reproductive outcomes. Finally, it defines the determinants of the distress related to fertility issues and fear of recurrence, and clarifies how these factors influence young women's QoL and close relationships in survivorship.

References

1. Zebrack, B. Information and service needs for young adult cancer patients. *Supportive Care in Cancer.* 2008, **16**(12), pp.1353-1360.
2. Zebrack, B. Information and service needs for young adult cancer survivors. *Supportive Care in Cancer.* 2009, **17**(4), pp.349-357.
3. Zebrack, B., Mills, J. and Weitzman, T. Health and supportive care needs of young adult cancer patients and survivors. *Journal of Cancer Survivorship.* 2007, **1**(2), pp.137-145.
4. Goossens, J., Delbaere, I., Van Lancker, A., Beeckman, D., Verhaeghe, S. and Van Hecke, A. Cancer patients' and professional caregivers' needs, preferences and factors associated with receiving and providing fertility-related information: a mixed-methods systematic review. *International Journal of Nursing Studies.* 2014, **51**(2), pp.300-319.
5. Harrison, J., Young, J., Price, M., Butow, P. and Solomon, M. What are the unmet supportive care needs of people with cancer? A systematic review. *Supportive Care in Cancer.* 2009, **17**(8), pp.1117-1128.
6. Cancer Research UK. *Cancer incidence by age.* [Online]. 2014. [Accessed 04/08/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Zero
7. Cancer Research UK. *Cancer incidence in teenagers and young adults aged 15-24.* [Online]. 2014. [Accessed 04/08/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Four
8. Cancer Research UK. *Teenagers' and young adults' cancer incidence: Carcinomas.* [Online]. 2014. [Accessed 04/08/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-Three
9. Cancer Research UK. *Teenagers' and young adults' cancer incidence: By age.* [Online]. 2014. [Accessed 04/08/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-Ten

10. Cancer Research UK. *Most common cancers by age in females.* [Online]. 2014. [Accessed 04/08/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Two
11. Wojciechowska, U. and Didkowska, J. *Zachorowania i zgony na nowotwory złośliwe w Polsce.* [Online]. [no date]. [Accessed 04/08/2015]. Available from: http://onkologia.org.pl/raporty/
12. Aziz, N.M. and Rowland, J.H. Trends and advances in cancer survivorship research: challenge and opportunity1. *Seminars in Radiation Oncology.* 2003, **13**(3), pp.248-266.
13. Holton, S., Kirkman, M., Rowe, H. and Fisher, J. The childbearing concerns and related information needs and preferences of women of reproductive age with a chronic, noncommunicable health condition: a systematic review. *Women's Health Issues.* 2012, **22**(6), pp.e541-e552.
14. Peate, M., Meiser, B., Hickey, M. and Friedlander, M. The fertility-related concerns, needs and preferences of younger women with breast cancer: a systematic review. *Breast Cancer Research and Treatment.* 2009, **116**(2), pp.215-223.
15. Lee, S.J., Schover, L.R., Partridge, A.H., Patrizio, P., Wallace, W.H., Hagerty, K., Beck, L.N., Brennan, L.V. and Oktay, K. American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients. *Journal of Clinical Oncology.* 2006, **24**(18), pp.2917-2931.
16. Loren, A.W., Mangu, P.B., Beck, L.N., Brennan, L., Magdalinski, A.J., Partridge, A.H., Quinn, G., Wallace, W.H. and Oktay, K. Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of Clinical Oncology.* 2013, **31**(19), pp.2500-2510.
17. National Institute for Health and Care Excellence. *Fertility: Assessment and treatment for people with fertility problems.* [Online]. 2013. [Accessed 04/08/2015]. Available from: https://www.nice.org.uk/guidance/cg156/chapter/recommendations#people-with-cancer-who-wish-to-preserve-fertility

18. Wallace, W.H., Anderson, R.A. and Irvine, D.S. Fertility preservation for young patients with cancer: who is at risk and what can be offered? *The Lancet Oncology.* 2005, **6**(4), pp.209-218.
19. Knobf, M.T. Reproductive and hormonal sequelae of chemotherapy in women. Premature menopause and impaired fertility can result, effects that are especially disturbing to young women. *The American Journal of Nursing.* 2006, **106**(3 Suppl), pp.60-65.
20. Duffy, C. and Allen, S. Medical and psychosocial aspects of fertility after cancer. *Cancer Journal.* 2009, **15**(1), pp.27-33.
21. Lee, M.C., Gray, J., Han, H.S. and Plosker, S. Fertility and reproductive considerations in premenopausal patients with breast cancer. *Cancer Control: Journal of the Moffitt Cancer Center.* 2010, **17**(3), pp.162-172.
22. Barthelmes, L. and Gateley, C.A. Tamoxifen and pregnancy. *The Breast.* 2004, **13**(6), pp.446-451.
23. Thewes, B., Meiser, B., Taylor, A., Phillips, K.A., Pendlebury, S., Capp, A., Dalley, D., Goldstein, D., Baber, R. and Friedlander, M.L. Fertility- and menopause-related information needs of younger women with a diagnosis of early breast cancer. *Journal of Clinical Oncology.* 2005, **23**(22), pp.5155-5165.
24. National Cancer Institute. *Breast Cancer Treatment (PDQ®).* [Online]. 2013. [Accessed 7/02/2013]. Available from: http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional/page6#Section_95
25. Davies, C., Pan, H., Godwin, J., Gray, R., Arriagada, R., Raina, V., Abraham, M., Alencar, V.H.M., Badran, A., Bonfill, X., Bradbury, J., Clarke, M., Collins, R., Davis, S.R., Delmestri, A., Forbes, J.F., Haddad, P., Hou, M.-F., Inbar, M., Khaled, H., Kielanowska, J., Kwan, W.-H., Mathew, B.S., Mittra, I., Müller, B., Nicolucci, A., Peralta, O., Pernas, F., Petruzelka, L., Pienkowski, T., Radhika, R., Rajan, B., Rubach, M.T., Tort, S., Urrútia, G., Valentini, M., Wang, Y. and Peto, R. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *The Lancet.* 2013, **381**(9869), pp.805-816.

26. Gray, R.G., Rea, D.W., Handley, K., Marshall, A., Pritchard, M.G., Perry, P., Earl, H.M., Poole, C.J., Salman, A., Lee, M. and a, T.C. aTTom (adjuvant Tamoxifen--To offer more?): Randomized trial of 10 versus 5 years of adjuvant tamoxifen among 6,934 women with estrogen receptor-positive (ER+) or ER untested breast cancer--Preliminary results. *ASCO Meeting Abstracts.* 2008, **26**(Suppl 15), p.513.
27. Birch, J.M., Alston, R.D., Kelsey, A.M., Quinn, M.J., Babb, P. and McNally, R.J.Q. Classification and incidence of cancers in adolescents and young adults in England 1979-1997. *British Journal of Cancer.* 2002, **87**(11), pp.1267-1274.
28. Cotterill, S.J., Parker, L., Malcolm, A.J., Reid, M., More, L. and Craft, A.W. Incidence and survival for cancer in children and young adults in the North of England, 1968–1995: a report from the Northern Region Young Persons' Malignant Disease Registry. *British Journal of Cancer.* 2000, **83**(3), pp.397-403.
29. Zebrack, B., Bleyer, A., Albritton, K., Medearis, S. and Tang, J. Assessing the health care needs of adolescent and young adult cancer patients and survivors. *Cancer.* 2006, **107**(12), pp.2915-2923.
30. Kohler, H.-P., Billari, F.C. and Ortega, J.A. The Emergence of Lowest-Low Fertility in Europe During the 1990s. *Population and Development Review.* 2002, **28**(4), pp.641-680.
31. Mills, M., Rindfuss, R.R., McDonald, P., te Velde, E., Reproduction, o.b.o.t.E. and Force, S.T. Why do people postpone parenthood? Reasons and social policy incentives. *Human Reproduction Update.* 2011, **17**(6), pp.848-860.
32. Office for National Statistics. *Live Births in England and Wales by Characteristics of Mother 1, 2012.* [Online]. 2013. [Accessed 04/08/2015]. Available from: http://www.ons.gov.uk/ons/rel/vsob1/characteristics-of-Mother-1--england-and-wales/2012/sb-characteristics-of-mother-1--2012.html#tab-Timing-of-childbearing
33. Główny Urząd Statystyczny. *Sytuacja demograficzna Polski.* [Online]. 2011. [Accessed 04/08/2015]. Available from: http://stat.gov.pl/cps/rde/xbcr/bip/BIP_raport_2010-2011.pdf
34. Bloom, D. and Pebley, A. Voluntary childlessness: A review of the evidence and implications. *Population Research and Policy Review.* 1982, **1**(3), pp.203-224.

35. Bongaarts, J. A method for the estimation of fecundability. *Demography.* 1975, **12**(4), pp.645-660.
36. Leridon, H. *Human fertility.* University of Chicago Press, 1977.
37. Wood, J.W. Fecundity and natural fertility in humans. *Oxford Reviews of Reproductive Biology.* 1989, **11**, pp.61-109.
38. Calhoun, L.G. and Selby, J.W. Voluntary Childlessness, Involuntary Childlessness, and Having Children: A Study of Social Perceptions. *Family Relations.* 1980, **29**(2), pp.181-183.
39. Gillespie, R. When no means no: Disbelief, disregard and deviance as discourses of voluntary childlessness. *Women's Studies International Forum.* 2000, **23**(2), pp.223-234.
40. Callan, V.J. The Personal and Marital Adjustment of Mothers and of Voluntarily and Involuntarily Childless Wives. *Journal of Marriage and Family.* 1987, **49**(4), pp.847-856.
41. Jeffries, S. and Konnert, C. Regret and Psychological Well-Being among Voluntarily and Involuntarily Childless Women and Mothers. *The International Journal of Aging and Human Development.* 2002, **54**(2), pp.89-106.
42. Basten, S. Voluntary childlessness and being Childfree. *The Future of Human Reproduction: Working Paper.* 2009, **5**, pp.1-23.
43. Gillespie, R. Childfree And Feminine: Understanding the Gender Identity of Voluntarily Childless Women. *Gender & Society.* 2003, **17**(1), pp.122-136.
44. Lechner, L., Bolman, C. and van Dalen, A. Definite involuntary childlessness: associations between coping, social support and psychological distress. *Human Reproduction.* 2007, **22**(1), pp.288-294.
45. Cockburn, J. and Pawson, M. *Psychological challenges to obstetrics and gynecology the clinical management.* [Online]. London : Springer, 2007. Available from: http://dx.doi.org/10.1007/978-1-84628-808-1
46. Cousineau, T.M. and Domar, A.D. Psychological impact of infertility. *Best Practice & Research Clinical Obstetrics & Gynaecology.* 2007, **21**(2), pp.293-308.

47. Greil, A.L., Slauson-Blevins, K. and McQuillan, J. The experience of infertility: a review of recent literature. *Sociology of Health & Illness.* 2010, **32**(1), pp.140-162.
48. Chachamovich, J.R., Chachamovich, E., Ezer, H., Fleck, M.P., Knauth, D. and Passos, E.P. Investigating quality of life and health-related quality of life in infertility: a systematic review. *Journal of Psychosomatic Obstetrics & Gynecology.* 2010, **31**(2), pp.101-110.
49. Ozakinci, G., Sobota, A. and Humphris, G. Fear of Cancer Recurrence Among Breast Cancer Survivors. *Current Breast Cancer Reports.* 2014, **6**(3), pp.219-225.
50. Simard, S., Thewes, B., Humphris, G., Dixon, M., Hayden, C., Mireskandari, S. and Ozakinci, G. Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. *Journal of Cancer Survivorship.* 2013, **7**(3), pp.300-322.
51. Lebel, S., Beattie, S., Arès, I. and Bielajew, C. Young and worried: Age and fear of recurrence in breast cancer survivors. *Health Psychology.* 2013, **32**(6), pp.695-705.
52. Thewes, B., Bell, M.L., Butow, P., Beith, J., Boyle, F., Friedlander, M. and McLachlan, S.A. Psychological morbidity and stress but not social factors influence level of fear of cancer recurrence in young women with early breast cancer: results of a cross-sectional study. *Psychooncology.* 2013, **22**(12), pp.2797-2806.
53. Thewes, B., Butow, P., Bell, M.L., Beith, J., Stuart-Harris, R., Grossi, M., Capp, A. and Dalley, D. Fear of cancer recurrence in young women with a history of early-stage breast cancer: a cross-sectional study of prevalence and association with health behaviours. *Supportive Care in Cancer.* 2012, **20**(11), pp.2651-2659.
54. Mehnert, A., Berg, P., Henrich, G. and Herschbach, P. Fear of cancer progression and cancer-related intrusive cognitions in breast cancer survivors. *Psychooncology.* 2009, **18**(12), pp.1273-1280.
55. Arès, I., Lebel, S. and Bielajew, C. The impact of motherhood on perceived stress, illness intrusiveness and fear of cancer recurrence in young breast cancer survivors over time. *Psychology & Health.* 2014, **29**(6), pp.651-670.

56. Howard-Anderson, J., Ganz, P.A., Bower, J.E. and Stanton, A.L. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. *Journal of the National Cancer Institute.* 2012, **104**(5), pp.386-405.
57. Gillick, M.R. Re-engineering shared decision-making. *Journal of Medical Ethics.* 2015, **41**(9), pp.785-788.
58. Walker, R. Models in health psychology: an introduction. *Journal of Diabetes Nursing.* 1999, **3**(6), pp.188-191.
59. Ogden, J. Health Psychology. In: Hewstone, M. et al. eds. *Psychology*. Malden (Mass.): Blackwell, 2005, pp.408-427.
60. Scheier, M.F. and Carver, C.S. Goals and confidence as self-regulatory elements. In: Cameron, L. and Leventhal, H. eds. *The Self regulation of health and illness behaviour*. Oxon: Routledge, 2003, pp.17-41.
61. Zimmerman, B.J. Attaining Self-Regulation. A social cognitive perspective. In: Boekaerts, M. et al. eds. *Handbook of self-regulation*. San Diego, Calif.: Academic Press, 2000, pp.13-41.
62. Leventhal, H., Meyer, D. and Nerenz, D. *The common sense representation of illness danger.* Oxford: Pergamon Press, 1980.
63. Sobota, A. and Ozakinci, G. Fertility and parenthood issues in young female cancer patients—a systematic review. *Journal of Cancer Survivorship.* 2014, **8**(4), pp.707-721.
64. Leventhal, H., Leventhal, E.A. and Contrada, R.J. Self-regulation, health, and behavior: A perceptual-cognitive approach. *Psychology & Health.* 1998, **13**(4), pp.717-733.
65. Leventhal, H., Brissette, I. and Leventhal, E.A. The common-sense model of self-regulation of health and illness. In: Cameron, L. and Leventhal, H. eds. *The Self regulation of health and illness behaviour*. Oxon: Routledge, 2003, pp.42-65.
66. Leventhal, H. Findings and theory in the study of fear communications. *Advances in Experimental Social Psychology.* 1970, **5**, pp.78-86.
67. Leventhal, H., Halm, E., Horowitz, C., Leventhal, E.A. and Ozakinci, G. Living with Chronic Illness: A Contextualized, Self-Regulation Approach. In: *The*

SAGE handbook of health psychology. Sutton Stephen, Baum Andrew, Johnston Marie ed. London: Thousand Oaks, Calif. : SAGE Publications, 2004, pp.197-240.

68. Hagger, M.S. and Orbell, S. A meta-analytic review of the common-sense model of illness representations. *Psychology & Health.* 2003, **18**(2), pp.141-184.
69. Benyamini, Y., Leventhal, H. and Leventhal, E.A. Attributions and health. In: Ayers, S. et al. eds. *Cambridge handbook of psychology, health, and medicine*. Cambridge; New York: Cambridge University Press, 2007, pp.26-33.
70. Lau, R.R. and Hartman, K.A. Common sense representations of common illnesses. *Health Psychology.* 1983, **2**(2), pp.167-185.
71. Benyamini, Y., Gozlan, M. and Kokia, E. On the self-regulation of a health threat: Cognitions, coping, and emotions among women undergoing treatment for infertility. *Cognitive Therapy and Research.* 2004, **28**(5), pp.577-592.
72. Bradley, E.J., Calvert, E., Pitts, M.K. and Redman, C.W.E. Illness Identity and the Self-regulatory Model in Recovery from Early Stage Gynaecological Cancer. *Journal of Health Psychology.* 2001, **6**(5), pp.511-521.
73. Contrada, R.J. and Coups, E.J. Personality and self-regulation in health and disease. In: Cameron, L. and Leventhal, H. eds. *The Self regulation of health and illness behaviour*. Oxon: Routledge, 2003, pp.66-94.
74. Eysenck, M.W. and Keane, M.T. *Cognitive psychology : a student's handbook.* Hove, Eng.; New York: Psychology Press, 2010.
75. Baumann, L.C. Culture and illness representation. In: Cameron, L. and Leventhal, H. eds. *The Self regulation of health and illness behaviour*. Oxon: Routledge, 2003, pp.242-253.
76. Giger, J.N. and Davidhizar, R.E. *Transcultural nursing : assessment and intervention.* St. Louis: Mosby, 1999.
77. Eysenbach, G., Powell, J., Englesakis, M., Rizo, C. and Stern, A. Health related virtual communities and electronic support groups: systematic review of the effects of online peer to peer interactions. *BMJ: British Medical Journal.* 2004, **328**(7449), pp.1166-1166.

78. Klemm, P., Bunnell, D., Cullen, M., Soneji, R., Gibbons, P. and Holecek, A. Online Cancer Support Groups: A Review of the Research Literature. *Computers Informatics Nursing.* 2003, **21**(3), pp.136-142.
79. Weinman, J., Petrie, K.J., Moss-Morris, R. and Horne, R. The illness perception questionnaire: a new method for assessing the cognitive representation of illness. *Psychology & Health.* 1996, **11**(3), pp.431-445.
80. Moss-Morris, R., Weinman, J., Petrie, K., Horne, R., Cameron, L. and Buick, D. The revised illness perception questionnaire (IPQ-R). *Psychology & Health.* 2002, **17**(1), pp.1-16.
81. Dempster, M., McCorry, N.K., Brennan, E., Donnelly, M., Murray, L.J. and Johnston, B.T. Illness perceptions among carer-survivor dyads are related to psychological distress among Oesophageal cancer survivors. *Journal of Psychosomatic Research.* 2011, **70**(5), pp.432-439.
82. Dempster, M., McCorry, N.K., Brennan, E., Donnelly, M., Murray, L.J. and Johnston, B.T. Do changes in illness perceptions predict changes in psychological distress among oesophageal cancer survivors? *Journal of Health Psychology.* 2011, **16**(3), pp.500-509.
83. Fischer, M.J., Wiesenhaan, M.E., Heijer, A.D., Kleijn, W.C., Nortier, J.W. and Kaptein, A.A. From despair to hope: A longitudinal study of illness perceptions and coping in a psycho-educational group intervention for women with breast cancer. *British Journal of Health Psychology.* 2013, **18**(3), pp.526-545.
84. Gould, R.V., Brown, S.L. and Bramwell, R. Psychological adjustment to gynaecological cancer: Patients' illness representations, coping strategies and mood disturbance. *Psychology & Health.* 2010, **25**(5), pp.633-646.
85. Jorgensen, I.L., Frederiksen, K., Boesen, E., Elsass, P. and Johansen, C. An exploratory study of associations between illness perceptions and adjustment and changes after psychosocial rehabilitation in survivors of breast cancer. *Acta Oncologica.* 2009, **48**(8), pp.1119-1127.
86. Lehto, R.H. Causal attributions in individuals with suspected lung cancer: relationships to illness coherence and emotional responses. *Journal of the American Psychiatric Nurses Association.* 2007, **13**(2), pp.109-115.

87. Millar, K., Purushotham, A.D., McLatchie, E., George, W.D. and Murray, G.D. A 1-year prospective study of individual variation in distress, and illness perceptions, after treatment for breast cancer. *Journal of Psychosomatic Research.* 2005, **58**(4), pp.335-342.
88. Vurnek Zivkovic, M., Buljan, M., Blajic, I. and Situm, M. Psychological status and illness perceptions in patients with melanoma. *Collegium Antropologicum.* 2008, **32 Suppl 2**, pp.75-78.
89. Llewellyn, C.D., McGurk, M. and Weinman, J. Illness and treatment beliefs in head and neck cancer: is Leventhal's common sense model a useful framework for determining changes in outcomes over time? *Journal of Psychosomatic Research.* 2007, **63**(1), pp.17-26.
90. Dempster, M., McCorry, N.K., Brennan, E., Donnelly, M., Murray, L. and Johnston, B.T. Psychological distress among survivors of esophageal cancer: the role of illness cognitions and coping. *Diseases of the Esophagus.* 2012, **25**(3), pp.222-227.
91. McCorry, N.K., Dempster, M., Quinn, J., Hogg, A., Newell, J., Moore, M., Kelly, S. and Kirk, S.J. Illness perception clusters at diagnosis predict psychological distress among women with breast cancer at 6 months post diagnosis. *Psychooncology.* 2013, **22**(3), pp.692-698.
92. Corter, A.L., Findlay, M., Broom, R., Porter, D. and Petrie, K.J. Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology.* 2013, **18**(1), pp.168-181.
93. Llewellyn, C.D., Weinman, J., McGurk, M. and Humphris, G. Can we predict which head and neck cancer survivors develop fears of recurrence? *Journal of Psychosomatic Research.* 2008, **65**(6), pp.525-532.
94. Llewellyn, C., McGurk, M. and Weinman, J. The relationship between the Patient Generated Index (PGI) and measures of HR-QoL following diagnosis with head and neck cancer: are illness and treatment perceptions determinants of judgment-based outcomes? *British Journal of Health Psychology.* 2007, **12**(Pt 3), pp.421-437.

95. Llewellyn, C.D., McGurk, M. and Weinman, J. Head and neck cancer: to what extent can psychological factors explain differences between health-related quality of life and individual quality of life? *British Journal of Oral and Maxillofacial Surgery.* 2006, **44**(5), pp.351-357.
96. Scharloo, M., Baatenburg de Jong, R.J., Langeveld, T.P., van Velzen-Verkaik, E., Doorn-Op den Akker, M.M. and Kaptein, A.A. Illness cognitions in head and neck squamous cell carcinoma: predicting quality of life outcome. *Supportive Care in Cancer.* 2010, **18**(9), pp.1137-1145.
97. Rozema, H., Vollink, T. and Lechner, L. The role of illness representations in coping and health of patients treated for breast cancer. *Psychooncology.* 2009, **18**(8), pp.849-857.
98. Scharloo, M., Baatenburg de Jong, R.J., Langeveld, T.P., van Velzen-Verkaik, E., Doorn-op den Akker, M.M. and Kaptein, A.A. Quality of life and illness perceptions in patients with recently diagnosed head and neck cancer. *Head & Neck.* 2005, **27**(10), pp.857-863.
99. Llewellyn, C.D., McGurk, M. and Weinman, J. The relationship between the Patient Generated Index (PGI) and measures of HR-QoL following diagnosis with head and neck cancer: Are illness and treatment perceptions determinants of judgment-based outcomes? *British Journal of Health Psychology.* 2007, **12**(3), pp.421-437.
100. Traeger, L., Penedo, F.J., Gonzalez, J.S., Dahn, J.R., Lechner, S.C., Schneiderman, N. and Antoni, M.H. Illness perceptions and emotional well-being in men treated for localized prostate cancer. *Journal of Psychosomatic Research.* 2009, **67**(5), pp.389-397.
101. Benyamini, Y., Gozlan, M. and Kokia, E. Women's and men's perceptions of infertility and their associations with psychological adjustment: a dyadic approach. *British Journal of Health Psychology.* 2009, **14**(Pt 1), pp.1-16.
102. Lord, S. and Robertson, N. Illness representations, coping and psychological morbidity in infertility. *Proceedings of the 14th International Conference of Psychosomatic Obstetrics and Gynaecology.* 2004, pp.201-206.
103. Hofstede, G. Dimensionalizing cultures: The Hofstede model in context. *Online Readings in Psychology and Culture.* 2011, **2**(1), p.8.

104. Henman, M., Butow, P., Boyle, F. and Tattersall, M. Lay constructions of decision-making in cancer. *Psychooncology.* 2002, **11**(4), pp.295-306.
105. Rutten, L.J.F., Arora, N.K., Bakos, A.D., Aziz, N. and Rowland, J. Information needs and sources of information among cancer patients: a systematic review of research (1980–2003). *Patient Education and Counseling.* 2005, **57**(3), pp.250-261.
106. van der Molen, B. Relating information needs to the cancer experience: 1. Information as a key coping strategy. *European Journal of Cancer Care.* 1999, **8**(4), pp.238-244.
107. Whitney, S.N., McGuire, A.L. and McCullough, L.B. A typology of shared decision making, informed consent, and simple consent. *Annals of Internal Medicine.* 2004, **140**(1), pp.54-59.
108. Jenkins, V., Fallowfield, L. and Saul, J. Information needs of patients with cancer: results from a large study in UK cancer centres. *British Journal of Cancer.* 2001, **84**(1), pp.48-51.
109. Mills, M.E. and Sullivan, K. The importance of information giving for patients newly diagnosed with cancer: a review of the literature. *Journal of Clinical Nursing.* 1999, **8**(6), pp.631-642.
110. Degner, L.F. and Sloan, J.A. Decision making during serious illness: what role do patients really want to play? *Journal of Clinical Epidemiology.* 1992, **45**(9), pp.941-950.
111. Beaver, K., Luker, K.A., Owens, R.G., Leinster, S.J., Degner, L.F. and Sloan, J.A. Treatment decision making in women newly diagnosed with breast cancer. *Cancer Nursing.* 1996, **19**(1), pp.8-19.
112. Singh, J.A., Sloan, J.A., Atherton, P.J., Smith, T., Hack, T.F., Huschka, M.M., Rummans, T.A., Clark, M.M., Diekmann, B. and Degner, L.F. Preferred Roles in Treatment Decision Making Among Patients With Cancer: A Pooled Analysis of Studies Using the Control Preferences Scale. *The American Journal of Managed Care.* 2010, **16**(9), pp.688-696.
113. Say, R., Murtagh, M. and Thomson, R. Patients' preference for involvement in medical decision making: A narrative review. *Patient Education and Counseling.* 2006, **60**(2), pp.102-114.

114. Thewes, B., Meiser, B., Taylor, A., Phillips, K.A., Pendlebury, S., Capp, A., Dalley, D., Goldstein, D., Baber, R. and Friedlander, M.L. Fertility- and Menopause-Related Information Needs of Younger Women With a Diagnosis of Early Breast Cancer. *Journal of Clinical Oncology.* 2005, **23**(22), pp.5155-5165.
115. Charles, C., Gafni, A. and Whelan, T. Shared decision-making in the medical encounter: what does it mean?(or it takes at least two to tango). *Social Science & Medicine.* 1997, **44**(5), pp.681-692.
116. Charles, C., Gafni, A. and Whelan, T. Decision-making in the physician–patient encounter: revisiting the shared treatment decision-making model. *Social Science & Medicine.* 1999, **49**(5), pp.651-661.
117. Emanuel, E.J. and Emanuel, L.L. Four models of the physician-patient relationship. *JAMA: The Journal of the American Medical Association* 1992, **267**(16), pp.2221-2226.
118. Gafni, A., Charles, C. and Whelan, T. The physician–patient encounter: the physician as a perfect agent for the patient versus the informed treatment decision-making model. *Social Science & Medicine.* 1998, **47**(3), pp.347-354.
119. Beauchamp, T.L. and Childress, J.F. *Principles of biomedical ethics.* New York, N.Y: Oxford University Press, 2001.
120. Gillon, R. Medical ethics: four principles plus attention to scope. *BMJ: British Medical Journal.* 1994, **309**(6948), p.184.
121. Gillon, R. Ethics needs principles—four can encompass the rest—and respect for autonomy should be "first among equals". *Journal of Medical Ethics.* 2003, **29**(5), pp.307-312.
122. Haug, M.R. and Lavin, B. *Consumerism in medicine : challenging physician authority.* Beverly Hills: Sage Publications, 1983.
123. Makoul, G. and Clayman, M.L. An integrative model of shared decision making in medical encounters. *Patient Education and Counseling.* 2006, **60**(3), pp.301-312.
124. Stacey, D., Samant, R. and Bennett, C. Decision making in oncology: a review of patient decision aids to support patient participation. *CA: A Cancer Journal for Clinicians.* 2008, **58**(5), pp.293-304.

125. Joosten, E.A.G., DeFuentes-Merillas, L., de Weert, G.H., Sensky, T., van der Staak, C.P.F. and de Jong, C.A.J. Systematic Review of the Effects of Shared Decision-Making on Patient Satisfaction, Treatment Adherence and Health Status. *Psychotherapy and Psychosomatics.* 2008, **77**(4), pp.219-226.
126. Charles, C., Whelan, T., Gafni, A., Reyno, L. and Redko, C. Doing Nothing is No Choice: Lay Constructions of Treatment Decision-making Among Women with Early-stage Breast Cancer. *Sociology of Health & Illness.* 1998, **20**(1), pp.71-95.
127. Kiesler, D.J. and Auerbach, S.M. Optimal matches of patient preferences for information, decision-making and interpersonal behavior: Evidence, models and interventions. *Patient Education and Counseling.* 2006, **61**(3), pp.319-341.
128. Brehaut, J.C., O'Connor, A.M., Wood, T.J., Hack, T.F., Siminoff, L., Gordon, E. and Feldman-Stewart, D. Validation of a decision regret scale. *Medical Decision Making.* 2003, **23**(4), pp.281-292.
129. Connolly, T. and Reb, J. Regret in cancer-related decisions. *Health Psychology.* 2005, **24**(4, Suppl), pp.S29-S34.
130. Joseph-Williams, N., Edwards, A. and Elwyn, G. The importance and complexity of regret in the measurement of 'good'decisions: a systematic review and a content analysis of existing assessment instruments. *Health Expectations.* 2011, **14**(1), pp.59-83.
131. Zeelenberg, M. and Pieters, R. A theory of regret regulation 1.0. *Journal of Consumer Psychology.* 2007, **17**(1), pp.3-18.
132. Hack, T.F., Degner, L.F., Watson, P. and Sinha, L. Do patients benefit from participating in medical decision making? Longitudinal follow-up of women with breast cancer. *Psychooncology.* 2006, **15**(1), pp.9-19.
133. Clark, J.A., Wray, N.P. and Ashton, C.M. Living with treatment decisions: regrets and quality of life among men treated for metastatic prostate cancer. *Journal of Clinical Oncology.* 2001, **19**(1), pp.72-80.
134. Kaptein, A.A., Yamaoka, K., Snoei, L., Kobayashi, K., Uchida, Y., van der Kloot, W.A., Tabei, T., Kleijn, W.C., Koster, M. and Wijnands, G. Illness perceptions and quality of life in Japanese and Dutch patients with non-small-cell lung cancer. *Lung Cancer.* 2011, **72**(3), pp.384-390.

135. Kaptein, A.A., Yamaoka, K., Snoei, L., Van der Kloot, W.A., Inoue, K., Tabei, T., Kroep, J.R., Krol-Warmerdam, E., Ranke, G. and Meirink, C. Illness Perceptions and Quality of Life in Japanese and Dutch Women with Breast Cancer. *Journal of Psychosocial Oncology.* 2013, **31**(1), pp.83-102.
136. Hynie, M. and Burns, L.H. Cross-Cultural Issues in Infertility Counseling. In: Covington, S.N. and Hammer, B.L. eds. *Infertility Counseling A Comprehensive Handbook for Clinicians*. Cambridge: Cambridge University Press, 2006, pp.61-82.
137. Trommsdorff, G. and Nauck, B. *The Value of Children in Cross-Cultural Perspective: Case Studies From Eight Societies.* Lengerich: Pabst Science, 2005.
138. Hoffman, L.W. and Hoffman, M.L. The value of children to parents. In: Fawcett, J.T. ed. *Psychological Perspectives on Population*. New York: Basic Books, 1973, pp.19-76.
139. Hoffman, L.W. The value of children to parents and the decrease in family size. *Proceedings of the American Philosophical Society.* 1975, **119**(6), pp.430-438.
140. Suckow, J. and Klaus, D. *Value of Children in Six Cultures*. Faculty of Social Studies, Masaryk University Brno. 2002.
141. Kagitcibasi, C. and Ataca, B. Value of Children and Family Change: A Three-Decade Portrait From Turkey. *Applied Psychology.* 2005, **54**(3), pp.317-337.
142. Trommsdorff, G. Cultural and Developmental Aspects of Values of Children. In: Sciences, G.-J.S.f.S. ed. *Social and psychological change of Japan and Germany : the last decade of the 20th century*. Tokyo: Waseda Univ. Pr., 1999, pp.209-229.
143. Zheng, G. and Shi, S. Intercultural and intracultural differences in the value of children: comparisons between four countries and the urban, rural, and floating populations in China. In: Zheng, G. et al. eds. *Perspectives and progress in contemporary cross-cultural psychology. Online edition.* [Online]. 2004, pp.129-148. Available from: http://ebooks.iaccp.org/xian/PDFs/3_7Zheng.pdf
144. Merz, E.-M. and Liefbroer, A.C. The Attitude Toward Voluntary Childlessness in Europe: Cultural and Institutional Explanations. *Journal of Marriage and Family.* 2012, **74**(3), pp.587-600.

145. Huijts, T., Kraaykamp, G. and Subramanian, S.V. Childlessness and Psychological Well-Being in Context: A Multilevel Study on 24 European Countries. *European Sociological Review.* 2011, p.jcr037.
146. Przybył, I. Naznaczanie społeczne i samonaznaczanie osób niepłodnych. *Roczniki Socjologii Rodzinnej.* 2003, **15**, pp.47-61.
147. Remennick, L. Childless in the Land of Imperative Motherhood: Stigma and Coping Among Infertile Israeli Women. *Sex Roles.* 2000, **43**(11), p.821.
148. Van De Kaa, D.J. Europe's second demographic transition. *Population Bulletin.* 1987, **42**(1), pp.1-59.
149. The Hofstede Centre. *United Kingdom.* [Online]. 2012. [Accessed 22/08/2013]. Available from: http://geert-hofstede.com/united-kingdom.html
150. Hofstede, G. The cultural relativity of organizational practices and theories. *Journal of International Business Studies.* 1983, **14**(2), pp.75-89.
151. Mynarska, M. Deadline for Parenthood: Fertility Postponement and Age Norms in Poland. *European Journal of Population / Revue européenne de Démographie.* 2010, **26**(3), pp.351-373.
152. Główny Urząd Statystyczny. *Ludność. Stan i struktura demograficzno-społeczna. Narodowy Spis Powszechny Ludności i Mieszkań 2011.* [Online]. 2013. [Accessed 20/08/2013]. Available from: http://www.stat.gov.pl/cps/rde/xbcr/gus/LUD_ludnosc_stan_str_dem_spo_NSP2011.pdf
153. National Records of Scotland. *Scotland's Census 2011 - National Records of Scotland, Table DC2107SC - Religion by sex by age, All people.* [Online]. 2011. [Accessed 27/07/2015]. Available from: http://www.scotlandscensus.gov.uk/ods-analyser/jsf/tableView/tableView.xhtml
154. Office for National Statistics. *Religion in England and Wales 2011.* [Online]. 2012. [Accessed 27/07/2015]. Available from: http://www.ons.gov.uk/ons/dcp171776_290510.pdf
155. Radkowska-Walkowicz, M. The creation of "monsters": the discourse of opposition to in vitro fertilization in Poland. *Reproductive Health Matters.* 2012, **20**(40), pp.30-37.

156. McQuillan, K. When Does Religion Influence Fertility? *Population and Development Review.* 2004, **30**(1), pp.25-56.

157. Conlon, C., O'Connor, J. and Ni Chathain, S. *Attitudes to Fertility, Sexual Health, and Motherhood Amongst a Sample of Non-Irish National Minority Ethnic Women Living in Ireland.* [Online]. 2012. [Accessed 20/08/2013]. Available from: http://crisispregnancy.ie/wp-content/uploads/2012/06/migrant-women-report.pdf

158. Office for National Statistics. *Polish People in the UK - Half a million Polish Residents.* [Online]. 2011. [Accessed 22/08/2013]. Available from: http://www.ons.gov.uk/ons/dcp171780_229910.pdf

159. Davidoff, F., Haynes, B., Sackett, D. and Smith, R. Evidence based medicine. *BMJ: British Medical Journal.* 1995, **310**(6987), p.1085.

160. Sackett, D.L. Evidence-based medicine. *Seminars in Perinatology.* 1997, **21**(1), pp.3-5.

161. American Psychological Association. Evidence-based practice in psychology. *American Psychologist.* 2006, **61**(4), pp.271-285.

162. Adams, E., McCann, L., Armes, J., Richardson, A., Stark, D., Watson, E. and Hubbard, G. The experiences, needs and concerns of younger women with breast cancer: a meta-ethnography. *Psychooncology.* 2011, **20**(8), pp.851-861.

163. Gonçalves, V., Sehovic, I. and Quinn, G. Childbearing attitudes and decisions of young breast cancer survivors: a systematic review. *Human Reproduction Update.* 2014, **20**(2), pp.279-292.

164. Dixon-Woods, M., Bonas, S., Booth, A., Jones, D.R., Miller, T., Sutton, A.J., Shaw, R.L., Smith, J.A. and Young, B. How can systematic reviews incorporate qualitative research? A critical perspective. *Qualitative Research.* 2006, **6**(1), pp.27-44.

165. Tong, A., Flemming, K., McInnes, E., Oliver, S. and Craig, J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology.* 2012, **12**(1), p.181.

166. Walsh, D. and Downe, S. Meta-synthesis method for qualitative research: a literature review. *Journal of Advanced Nursing.* 2005, **50**(2), pp.204-211.

167. Wenzel, L., Dogan-Ates, A., Habbal, R., Berkowitz, R., Goldstein, D.P., Bernstein, M., Kluhsman, B.C., Osann, K., Newlands, E., Seckl, M.J., Hancock, B. and Cella, D. Defining and Measuring Reproductive Concerns of Female Cancer Survivors. *Journal of the National Cancer Institute. Monographs.* 2005, **2005**(34), pp.94-98.

168. De Vos, M., Smitz, J. and Woodruff, T.K. Fertility preservation in women with cancer. *The Lancet.* **384**(9950), pp.1302-1310.

169. Turner, N.H., Partridge, A., Sanna, G., Di Leo, A. and Biganzoli, L. Utility of gonadotropin-releasing hormone agonists for fertility preservation in young breast cancer patients: the benefit remains uncertain. *Annals of Oncology.* 2013, **24**(9), pp.2224-2235.

170. Blumenfeld, Z. How to Preserve Fertility in Young Women Exposed to Chemotherapy? The Role of GnRH Agonist Cotreatment in Addition to Cryopreservation of Embrya, Oocytes, or Ovaries. *The Oncologist.* 2007, **12**(9), pp.1044-1054.

171. Dargent, D., Martin, X., Sacchetoni, A. and Mathevet, P. Laparoscopic vaginal radical trachelectomy. *Cancer.* 2000, **88**(8), pp.1877-1882.

172. Kim, Y.B., Holschneider, C.H., Ghosh, K., Nieberg, R.K. and Montz, F.J. Progestin alone as primary treatment of endometrial carcinoma in premenopausal women. *Cancer.* 1997, **79**(2), pp.320-327.

173. Fruscio, R., Corso, S., Ceppi, L., Garavaglia, D., Garbi, A., Floriani, I., Franchi, D., Cantù, M.G., Bonazzi, C.M., Milani, R., Mangioni, C. and Colombo, N. Conservative management of early-stage epithelial ovarian cancer: results of a large retrospective series. *Annals of Oncology.* 2013, **24**(1), pp.138-144.

174. Morice, P., Camatte, S., El Hassan, J., Pautier, P., Duvillard, P. and Castaigne, D. Clinical outcomes and fertility after conservative treatment of ovarian borderline tumors. *Fertility and Sterility.* 2001, **75**(1), pp.92-96.

175. Thomas, F., Renaud, F., Benefice, E., de Meeus, T. and Guegan, J.F. International variability of ages at menarche and menopause: patterns and main determinants. *Human Biology.* 2001, **73**(2), pp.271-290.

176. Dursun, P., LeBlanc, E. and Nogueira, M.C. Radical vaginal trachelectomy (Dargent's operation): A critical review of the literature. *European Journal of Surgical Oncology.* **33**(8), pp.933-941.
177. Gorman, J.R., Bailey, S., Pierce, J.P. and Su, H.I. How do you feel about fertility and parenthood? The voices of young female cancer survivors. *Journal of Cancer Survivorship.* 2012, **6**(2), pp.200-209.
178. Gorman, J.R., Su, H.I., Pierce, J.P., Roberts, S.C., Dominick, S.A. and Malcarne, V.L. A multidimensional scale to measure the reproductive concerns of young adult female cancer survivors. *Journal of Cancer Survivorship.* 2014, **8**(2), pp.218-228.
179. Perz, J., Ussher, J. and Gilbert, E. Loss, uncertainty, or acceptance: subjective experience of changes to fertility after breast cancer. *European Journal of Cancer Care.* 2014, **23**(4), pp.514-522.
180. Ferrell, B., Smith, S., Cullinane, C. and Melancon, C. Symptom Concerns of Women with Ovarian Cancer. *Journal of Pain and Symptom Management.* 2003, **25**(6), pp.528-538.
181. Molassiotis, A., Chan, C.W., Yam, B.M., Chan, E.S. and Lam, C.S. Life after cancer: adaptation issues faced by Chinese gynaecological cancer survivors in Hong Kong. *Psychooncology.* 2002, **11**(2), pp.114-123.
182. Reis, N., Beji, N.K. and Coskun, A. Quality of life and sexual functioning in gynecological cancer patients: results from quantitative and qualitative data. *European Journal of Oncology Nursing.* 2010, **14**(2), pp.137-146.
183. Bastings, L., Baysal, O., Beerendonk, C.C., IntHout, J., Traas, M.A., Verhaak, C.M., Braat, D.D. and Nelen, W.L. Deciding about fertility preservation after specialist counselling. *Human Reproduction.* 2014, **29**(8), pp.1721-1729.
184. Bell, R.J., Fradkin, P., Schwarz, M. and Davis, S.R. Understanding discontinuation of oral adjuvant endocrine therapy by women with hormone receptor-positive invasive breast cancer nearly 4 years from diagnosis. *Menopause.* 2013, **20**(1), pp.15-21.
185. Letourneau, J.M., Ebbel, E.E., Katz, P.P., Katz, A., Ai, W.Z., Chien, A.J., Melisko, M.E., Cedars, M.I. and Rosen, M.P. Pretreatment fertility counseling

and fertility preservation improve quality of life in reproductive age women with cancer. *Cancer.* 2012, **118**(6), pp.1710-1717.

186. Letourneau, J.M., Smith, J.F., Ebbel, E.E., Craig, A., Katz, P.P., Cedars, M.I. and Rosen, M.P. Racial, socioeconomic, and demographic disparities in access to fertility preservation in young women diagnosed with cancer. *Cancer.* 2012, **118**(18), pp.4579-4588.
187. Hershberger, P.E., Finnegan, L., Altfeld, S., Lake, S. and Hirshfeld-Cytron, J. Toward theoretical understanding of the fertility preservation decision-making process: Examining information processing among young women with cancer. *Research and Theory for Nursing Practice.* 2013, **27**(4), pp.257-275.
188. Hershberger, P.E., Finnegan, L., Pierce, P.F. and Scoccia, B. The decision-making process of young adult women with cancer who considered fertility cryopreservation. *Journal of Obstetric, Gynecologic, and Neonatal Nursing : JOGNN / NAACOG.* 2013, **42**(1), pp.59-69.
189. Corney, R., Puthussery, S. and Swinglehurst, J. The stressors and vulnerabilities of young single childless women with breast cancer: a qualitative study. *European Journal of Oncology Nursing.* 2014, **18**(1), pp.17-22.
190. Corney, R.H. and Swinglehurst, A.J. Young childless women with breast cancer in the UK: a qualitative study of their fertility-related experiences, options, and the information given by health professionals. *Psychooncology.* 2014, **23**(1), pp.20-26.
191. Halliday, L.E., Boughton, M.A. and Kerridge, I. Mothering and self-othering: the impact of uncertain reproductive capability in young women after hematological malignancy. *Health Care for Women International.* 2014, **35**(3), pp.249-265.
192. Halliday, L.E., Boughton, M.A. and Kerridge, I. Liminal reproductive experiences after therapies for hematological malignancy. *Qualitative Health Research.* 2015, **25**(3), pp.408-416.
193. Kirkman, M., Stern, C., Neil, S., Winship, I., Mann, G.B., Shanahan, K., Missen, D., Shepherd, H. and Fisher, J.R. Fertility management after breast cancer diagnosis: a qualitative investigation of women's experiences of and

recommendations for professional care. *Health Care for Women International.* 2013, **34**(1), pp.50-67.

194. Kirkman, M., Winship, I., Stern, C., Neil, S., Mann, G.B. and Fisher, J.R. Women's reflections on fertility and motherhood after breast cancer and its treatment. *European Journal of Cancer Care.* 2014, **23**(4), pp.502-513.

195. Cluze, C., Rey, D., Huiart, L., BenDiane, M.K., Bouhnik, A.D., Berenger, C., Carrieri, M.P. and Giorgi, R. Adjuvant endocrine therapy with tamoxifen in young women with breast cancer: determinants of interruptions vary over time. *Annals of Oncology.* 2012, **23**(4), pp.882-890.

196. Huiart, L., Bouhnik, A.D., Rey, D., Tarpin, C., Cluze, C., Bendiane, M.K., Viens, P. and Giorgi, R. Early discontinuation of tamoxifen intake in younger women with breast cancer: is it time to rethink the way it is prescribed? *European Journal of Cancer.* 2012, **48**(13), pp.1939-1946.

197. Carter, J., Sonoda, Y. and Abu-Rustum, N.R. Reproductive concerns of women treated with radical trachelectomy for cervical cancer. *Gynecologic Oncology.* 2007, **105**(1), pp.13-16.

198. Carter, J., Sonoda, Y., Baser, R.E., Raviv, L., Chi, D.S., Barakat, R.R., Iasonos, A., Brown, C.L. and Abu-Rustum, N.R. A 2-year prospective study assessing the emotional, sexual, and quality of life concerns of women undergoing radical trachelectomy versus radical hysterectomy for treatment of early-stage cervical cancer. *Gynecologic Oncology.* 2010, **119**(2), pp.358-365.

199. *NVivo qualitative data analysis Software.* 2012.

200. Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., Britten, N., Roen, K. and Duffy, S. Guidance on the conduct of narrative synthesis in systematic reviews. *A product from the ESRC methods programme.* 2006, **1**.

201. Thomas, J. and Harden, A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology.* 2008, **8**(1), p.45.

202. Harden, A., Brunton, G., Fletcher, A., Oakley, A., Burchett, H. and Backhans, M. *Young people, pregnancy and social exclusion: A systematic synthesis of research evidence to identify effective, appropriate and promising approaches*

for prevention and support. EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, 2006.

203. Harden, A., Garcia, J., Oliver, S., Rees, R., Shepherd, J., Brunton, G. and Oakley, A. Applying systematic review methods to studies of people's views: an example from public health research. *Journal of Epidemiology & Community Health.* 2004, **58**(9), pp.794-800.

204. Thomas, J., Kavanagh, J., Tucker, H., Burchett, H., Tripney, J. and Oakley, A. *Accidental injury, risk-taking behaviour and the social circumstances in which young people live: a systematic review.* London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, 2007.

205. Thomas, J., Sutcliffe, K., Harden, A., Oakley, A., Oliver, S., Rees, R., Brunton, G. and Kavanagh, J. *Children and healthy eating: a systematic review of barriers and facilitators.* London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, 2003.

206. Kmet, L., Lee, R. and Cook, L. *Standard Quality Assessment Criteria for Evaluating Primary Research Papers from A Variety of Fields* [Online]. 2004. [Accessed 7/02/2014]. Available from: http://www.ihe.ca/documents/HTA-FR13.pdf

207. Greenland, S. and O'Rourke, K. On the bias produced by quality scores in meta-analysis, and a hierarchical view of proposed solutions. *Biostatistics.* 2001, **2**(4), pp.463-471.

208. Canada, A.L. and Schover, L.R. The psychosocial impact of interrupted childbearing in long-term female cancer survivors. *Psychooncology.* 2012, **21**(2), pp.134-143.

209. Gorman, J.R., Malcarne, V.L., Roesch, S.C., Madlensky, L. and Pierce, J.P. Depressive symptoms among young breast cancer survivors: the importance of reproductive concerns. *Breast Cancer Research and Treatment.* 2010, **123**(2), pp.477-485.

210. Partridge, A.H., Gelber, S., Peppercorn, J., Sampson, E., Knudsen, K., Laufer, M., Rosenberg, R., Przypyszny, M., Rein, A. and Winer, E.P. Web-based survey of fertility issues in young women with breast cancer. *Journal of Clinical Oncology.* 2004, **22**(20), pp.4174-4183.

211. Ruddy, K.J., Gelber, S.I., Tamimi, R.M., Ginsburg, E.S., Schapira, L., Come, S.E., Borges, V.F., Meyer, M.E. and Partridge, A.H. Prospective study of fertility concerns and preservation strategies in young women with breast cancer. *Journal of Clinical Oncology.* 2014, **32**(11), pp.1151-1156.
212. Mancini, J., Rey, D., Preau, M., Malavolti, L. and Moatti, J.P. Infertility induced by cancer treatment: inappropriate or no information provided to majority of French survivors of cancer. *Fertility and Sterility.* 2008, **90**(5), pp.1616-1625.
213. Wenzel, L., DeAlba, I., Habbal, R., Kluhsman, B.C., Fairclough, D., Krebs, L.U., Anton-Culver, H., Berkowitz, R. and Aziz, N. Quality of life in long-term cervical cancer survivors. *Gynecologic Oncology.* 2005, **97**(2), pp.310-317.
214. Ferrell, B.R., Dow, K.H., Leigh, S., Ly, J. and Gulasekaram, P. Quality of life in long-term cancer survivors. *Oncology Nursing Forum.* 1995, **22**(6), pp.915-922.
215. Carey, M.P., Spector, I.P., Lantinga, L.J. and Krauss, D.J. Reliability of the Dyadic Adjustment Scale. *Psychological Assessment.* 1993, **5**(2), pp.238-240.
216. Schag, C.A., Heinrich, R.L., Aadland, R.L. and Ganz, P.A. Assessing problems of cancer patients: psychometric properties of the cancer inventory of problem situations. *Health Psychology.* 1990, **9**(1), pp.83-102.
217. Eeltink, C.M., Incrocci, L., Witte, B.I., Meurs, S., Visser, O., Huijgens, P. and Verdonck-de Leeuw, I.M. Fertility and sexual function in female Hodgkin lymphoma survivors of reproductive age. *Journal of Clinical Nursing.* 2013, **22**(23-24), pp.3513-3521.
218. Brånvall, E., Derolf, Å.R., Johansson, E., Hultcrantz, M., Bergmark, K. and Björkholm, M. Self-reported fertility in long-term survivors of acute myeloid leukemia. *Annals of Hematology.* 2014, **93**(9), pp.1491-1498.
219. Gorman, J.R., Usita, P.M., Madlensky, L. and Pierce, J.P. Young breast cancer survivors: their perspectives on treatment decisions and fertility concerns. *Cancer Nursing.* 2011, **34**(1), pp.32-40.
220. Keim-Malpass, J., Baernholdt, M., Erickson, J.M., Ropka, M.E., Schroen, A.T. and Steeves, R.H. Blogging through cancer: young women's persistent problems shared online. *Cancer Nursing.* 2013, **36**(2), pp.163-172.

221. Schaefer, K.M., Ladd, E.C., Lammers, S.E. and Echenberg, R.J. In Your Skin You are Different: Women Living with Ovarian Cancer During Childbearing Years. *Qualitative Health Research.* 1999, **9**(2), pp.227-242.
222. Siegel, K., Gluhoski, V. and Gorey, E. Age-Related Distress Among Young Women with Breast Cancer. *Journal of Psychosocial Oncology.* 1999, **17**(1), pp.1-20.
223. Venturini, E., Giacomoni, C., Hoarau, H. and Conri, V. Impact du cancer gynécologique sur la sexualité féminine. *Psycho-Oncologie.* 2012, **6**(3), pp.151-162.
224. Yee, S., Abrol, K., McDonald, M., Tonelli, M. and Liu, K.E. Addressing oncofertility needs: views of female cancer patients in fertility preservation. *Journal of Psychosocial Oncology.* 2012, **30**(3), pp.331-346.
225. Carter, J., Rowland, K., Chi, D., Brown, C., Abu-Rustum, N., Castiel, M. and Barakat, R. Gynecologic cancer treatment and the impact of cancer-related infertility. *Gynecologic Oncology.* 2005, **97**(1), pp.90-95.
226. Thewes, B., Meiser, B., Rickard, J. and Friedlander, M. The fertility- and menopause-related information needs of younger women with a diagnosis of breast cancer: a qualitative study. *Psychooncology.* 2003, **12**(5), pp.500-511.
227. Doka, K.J. *Disenfranchised grief: Recognizing hidden sorrow.* Lexington [etc.]: Lexington Books 1989.
228. Tschudin, S., Bunting, L., Abraham, J., Gallop-Evans, E., Fiander, A. and Boivin, J. Correlates of fertility issues in an internet survey of cancer survivors. *Journal of Psychosomatic Obstetrics & Gynecology.* 2010, **31**(3), pp.150-157.
229. Dryden, A., Ussher, J.M. and Perz, J. Young women's construction of their post-cancer fertility. *Psychology & Health.* 2014, **29**(11), pp.1341-1360.
230. Avis, N.E., Crawford, S. and Manuel, J. Psychosocial problems among younger women with breast cancer. *Psychooncology.* 2004, **13**(5), pp.295-308.
231. Scanlon, M., Blaes, A., Geller, M., Majhail, N.S., Lindgren, B. and Haddad, T. Patient Satisfaction with Physician Discussions of Treatment Impact on Fertility, Menopause and Sexual Health among Pre-menopausal Women with Cancer. *Journal of Cancer.* 2012, **3**, pp.217-225.

232. Campos, S.M., Berlin, S., Matulonis, U.A., Muto, M.G., Pereira, L., Mosquera, M.M. and Horowitz, N. Young women diagnosed with early-stage ovarian cancer or borderline malignancy of the ovary: a focus on fertility and sexual function. *Journal of Psychosocial Oncology.* 2012, **30**(4), pp.387-401.

233. Senkus, E., Gomez, H., Dirix, L., Jerusalem, G., Murray, E., Van Tienhoven, G., Westenberg, A.H., Bottomley, A., Rapion, J., Bogaerts, J., Di Leo, A. and Neskovic-Konstantinovic, Z. Attitudes of young patients with breast cancer toward fertility loss related to adjuvant systemic therapies. EORTC study 10002 BIG 3-98. *Psychooncology.* 2014, **23**(2), pp.173-182.

234. Bramwell, V.H., Pritchard, K.I., Tu, D., Tonkin, K., Vachhrajani, H., Vandenberg, T.A., Robert, J., Arnold, A., O'Reilly, S.E., Graham, B. and Shepherd, L. A randomized placebo-controlled study of tamoxifen after adjuvant chemotherapy in premenopausal women with early breast cancer (National Cancer Institute of Canada--Clinical Trials Group Trial, MA.12). *Annals of Oncology.* 2010, **21**(2), pp.283-290.

235. Güth, U., Myrick, M.E., Kilic, N., Eppenberger-Castori, S. and Schmid, S.M. Compliance and persistence of endocrine adjuvant breast cancer therapy. *Breast Cancer Research and Treatment.* 2012, **131**(2), pp.491-499.

236. Rippy, E.E., Karat, I.F. and Kissin, M.W. Pregnancy after breast cancer: the importance of active counselling and planning. *Breast.* 2009, **18**(6), pp.345-350.

237. Hill, K.A., Nadler, T., Mandel, R., Burlein-Hall, S., Librach, C., Glass, K. and Warner, E. Experience of young women diagnosed with breast cancer who undergo fertility preservation consultation. *Clinical Breast Cancer.* 2012, **12**(2), pp.127-132.

238. Huyghe, E., Sui, D., Odensky, E. and Schover, L.R. Needs assessment survey to justify establishing a reproductive health clinic at a comprehensive cancer center. *The Journal of Sexual Medicine.* 2009, **6**(1), pp.149-163.

239. Kim, J., Deal, A.M., Balthazar, U., Kondapalli, L.A., Gracia, C. and Mersereau, J.E. Fertility preservation consultation for women with cancer: are we helping patients make high-quality decisions? *Reproductive BioMedicine Online.* 2013, **27**(1), pp.96-103.

240. Kim, J., Oktay, K., Gracia, C., Lee, S., Morse, C. and Mersereau, J.E. Which patients pursue fertility preservation treatments? A multicenter analysis of the predictors of fertility preservation in women with breast cancer. *Fertility and Sterility.* 2012, **97**(3), pp.671-676.

241. Mersereau, J.E., Goodman, L.R., Deal, A.M., Gorman, J.R., Whitcomb, B.W. and Su, H.I. To preserve or not to preserve: how difficult is the decision about fertility preservation? *Cancer.* 2013, **119**(22), pp.4044-4050.

242. Peate, M., Meiser, B., Friedlander, M., Zorbas, H., Rovelli, S., Sansom-Daly, U., Sangster, J., Hadzi-Pavlovic, D. and Hickey, M. It's now or never: fertility-related knowledge, decision-making preferences, and treatment intentions in young women with breast cancer--an Australian fertility decision aid collaborative group study. *Journal of Clinical Oncology.* 2011, **29**(13), pp.1670-1677.

243. Razzano, A., Revelli, A., Delle Piane, L., Salvagno, F., Casano, S., Randaccio, S. and Benedetto, C. Fertility preservation program before ovarotoxic oncostatic treatments: role of the psychological support in managing emotional aspects. *Gynecological Endocrinology.* 2014, **30**(11), pp.822-824.

244. Reh, A.E., Lu, L., Weinerman, R., Grifo, J., Krey, L. and Noyes, N. Treatment outcomes and quality-of-life assessment in a university-based fertility preservation program: results of a registry of female cancer patients at 2 years. *Journal of Assisted Reproduction and Genetics.* 2011, **28**(7), pp.635-641.

245. Treves, R., Grynberg, M., Parco, S., Finet, A., Poulain, M. and Fanchin, R. Female fertility preservation in cancer patients: an instrumental tool for the envisioning a postdisease life. *Future Oncology.* 2014, **10**(6), pp.969-974.

246. Garvelink, M.M., Ter Kuile, M.M., Bakker, R.M., Geense, W.J., Jenninga, E., Louwe, L.A., Hilders, C.G. and Stiggelbout, A.M. Women's experiences with information provision and deciding about fertility preservation in the Netherlands: 'satisfaction in general, but unmet needs'. *Health Expectations.* 2015, **18**(5), pp.956-968.

247. Lee, R.J., Wakefield, A., Foy, S., Howell, S.J., Wardley, A.M. and Armstrong, A.C. Facilitating reproductive choices: the impact of health services on the

experiences of young women with breast cancer. *Psychooncology.* 2011, **20**(10), pp.1044-1052.

248. Snyder, K.A. and Tate, A.L. What to do now? How women with breast cancer make fertility preservation decisions. *Journal of Family Planning and Reproductive Health Care.* 2013, **39**(3), pp.172-178.

249. Niemasik, E.E., Letourneau, J., Dohan, D., Katz, A., Melisko, M., Rugo, H. and Rosen, M. Patient perceptions of reproductive health counseling at the time of cancer diagnosis: a qualitative study of female California cancer survivors. *Journal of Cancer Survivorship.* 2012, **6**(3), pp.324-332.

250. Pellegrini, I., Sarradon-Eck, A., Soussan, P.B., Lacour, A.C., Largillier, R., Tallet, A., Tarpin, C. and Julian-Reynier, C. Women's perceptions and experience of adjuvant tamoxifen therapy account for their adherence: breast cancer patients' point of view. *Psychooncology.* 2010, **19**(5), pp.472-479.

251. Wright, C.I., Coad, J., Morgan, S., Stark, D. and Cable, M. 'Just in case': the fertility information needs of teenagers and young adults with cancer. *European Journal of Cancer Care.* 2014, **23**(2), pp.189-198.

252. Wilkes, S., Coulson, S., Crosland, A., Rubin, G. and Stewart, J. Experience of fertility preservation among younger people diagnosed with cancer. *Human Fertility.* 2010, **13**(3), pp.151-158.

253. Ruddy, K.J., Greaney, M.L., Sprunck-Harrild, K., Meyer, M.E., Emmons, K.M. and Partridge, A.H. Young women with breast cancer: a focus group study of unmet needs. *Journal of Adolescent and Young Adult Oncology.* 2013, **2**(4), pp.153-160.

254. Agledahl, K.M., Førde, R. and Wifstad, Å. Choice is not the issue. The misrepresentation of healthcare in bioethical discourse. *Journal of Medical Ethics.* 2011, **37**(4), pp.212-215.

255. Lloyd, P.A., Briggs, E.V., Kane, N., Jeyarajah, A.R. and Shepherd, J.H. Women's experiences after a radical vaginal trachelectomy for early stage cervical cancer. A descriptive phenomenological study. *European Journal of Oncology Nursing.* 2014, **18**(4), pp.362-371.

256. Crawshaw, M.A., Glaser, A.W., Hale, J.P. and Sloper, P. Male and female experiences of having fertility matters raised alongside a cancer diagnosis during

the teenage and young adult years. *European Journal of Cancer Care.* 2009, **18**(4), pp.381-390.

257. Connell, S., Patterson, C. and Newman, B. A qualitative analysis of reproductive issues raised by young Australian women with breast cancer. *Health Care for Women International.* 2006, **27**(1), pp.94-110.

258. Bukberg, J., Penman, D. and Holland, J.C. Depression in hospitalized cancer patients. *Psychosomatic Medicine.* 1984, **46**(3), pp.199-212.

259. Cella, D.F., Orofiamma, B., Holland, J.C., Silberfarb, P.M., Tross, S., Feldstein, M., Perry, M., Maurer, L.H., Comis, R. and Orav, E.J. The relationship of psychological distress, extent of disease, and performance status in patients with lung cancer. *Cancer.* 1987, **60**(7), pp.1661-1667.

260. Allen, J.D., Savadatti, S. and Gurmankin Levy, A. The transition from breast cancer 'patient' to 'survivor'. *Psychooncology.* 2009, **18**(1), pp.71-78.

261. Jefford, M., Karahalios, E., Pollard, A., Baravelli, C., Carey, M., Franklin, J., Aranda, S. and Schofield, P. Survivorship issues following treatment completion—results from focus groups with Australian cancer survivors and health professionals. *Journal of Cancer Survivorship.* 2008, **2**(1), pp.20-32.

262. Woodgate, R.L. Life is never the same: childhood cancer narratives. *European Journal of Cancer Care.* 2006, **15**(1), pp.8-18.

263. Lichtman, R.R. and Taylor, S.E. Close Relationships and the Female Cancer Patient. In: Andersen, B. ed. *Women with Cancer*. New York: Springer New York, 1986, pp.233-256.

264. Ochsenkuhn, R., Hermelink, K., Clayton, A.H., von Schonfeldt, V., Gallwas, J., Ditsch, N., Rogenhofer, N. and Kahlert, S. Menopausal status in breast cancer patients with past chemotherapy determines long-term hypoactive sexual desire disorder. *The Journal of Sexual Medicine.* 2011, **8**(5), pp.1486-1494.

265. Rosenberg, S.M., Tamimi, R.M., Gelber, S., Ruddy, K.J., Bober, S.L., Kereakoglow, S., Borges, V.F., Come, S.E., Schapira, L. and Partridge, A.H. Treatment-related amenorrhea and sexual functioning in young breast cancer survivors. *Cancer.* 2014, **120**(15), pp.2264-2271.

266. Gershenson, D.M., Miller, A.M., Champion, V.L., Monahan, P.O., Zhao, Q., Cella, D. and Williams, S.D. Reproductive and sexual function after platinum-

based chemotherapy in long-term ovarian germ cell tumor survivors: a Gynecologic Oncology Group Study. *Journal of Clinical Oncology.* 2007, **25**(19), pp.2792-2797.

267. Avis, N.E., Stellato, R., Crawford, S., Johannes, C. and Longcope, C. Is there an association between menopause status and sexual functioning? *Menopause.* 2000, **7**(5), pp.297-309.

268. Dennerstein, L., Lehert, P., Burger, H. and Dudley, E. Factors affecting sexual functioning of women in the mid-life years. *Climacteric.* 1999, **2**(4), pp.254-262.

269. Redmond, G.P. Hormones and sexual function. *International Journal of Fertility and Women's Medicine.* 1999, **44**(4), pp.193-197.

270. Stacey, D., Légaré, F., Col Nananda, F., Bennett Carol, L., Barry Michael, J., Eden Karen, B., Holmes-Rovner, M., Llewellyn-Thomas, H., Lyddiatt, A., Thomson, R., Trevena, L. and Wu Julie, H.C. Decision aids for people facing health treatment or screening decisions. *Cochrane Database of Systematic Reviews.* [Online]. 2014, (1). Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001431.pub4/abstract

271. Kim, J. and Mersereau, J.E. Early referral makes the decision-making about fertility preservation easier: a pilot survey study of young female cancer survivors. *Supportive Care in Cancer.* 2015, **23**(6), pp.1663-1667.

272. Snyder, K.A. and Pearse, W. How Do Cancer Patients Learn About Fertility Preservation? Five Trajectories of Experience. In: Woodruff, T.K. et al. eds. *Oncofertility Communication*. New York: Springer New York, 2014, pp.3-17.

273. Carter, J., Raviv, L., Applegarth, L., Ford, J., Josephs, L., Grill, E., Sklar, C., Sonoda, Y., Baser, R. and Barakat, R. A cross-sectional study of the psychosexual impact of cancer-related infertility in women: third-party reproductive assistance. *Journal of Cancer Survivorship.* 2010, **4**(3), pp.236-246.

274. Balthazar, U., Fritz, M.A. and Mersereau, J.E. Fertility preservation: a pilot study to assess previsit patient knowledge quantitatively. *Fertility and Sterility.* 2011, **95**(6), pp.1913-1916.

275. Goldfarb, J., Austin, C., Lisbona, H., de Mola, R., Peskin, B. and Stewart, S. Factors influencing patients' decision not to repeat IVF. *Journal of Assisted Reproduction and Genetics.* 1997, **14**(7), pp.381-384.

276. Blakely, L.J., Buzdar, A.U., Lozada, J.A., Shullaih, S.A., Hoy, E., Smith, T.L. and Hortobagyi, G.N. Effects of pregnancy after treatment for breast carcinoma on survival and risk of recurrence. *Cancer.* 2004, **100**(3), pp.465-469.

277. Gelber, S., Coates, A.S., Goldhirsch, A., Castiglione-Gertsch, M., Marini, G., Lindtner, J., Edelmann, D.Z., Gudgeon, A., Harvey, V. and Gelber, R.D. Effect of pregnancy on overall survival after the diagnosis of early-stage breast cancer. *Journal of Clinical Oncology.* 2001, **19**(6), pp.1671-1675.

278. Ives, A., Saunders, C., Bulsara, M. and Semmens, J. Pregnancy after breast cancer: population based study. *British Medical Journal.* 2007, **334**(7586), p.194.

279. Fossa, S.D., Magelssen, H., Melve, K., Jacobsen, A.B., Langmark, F. and Skjaerven, R. Parenthood in survivors after adulthood cancer and perinatal health in their offspring: a preliminary report. *Journal of the National Cancer Institute. Monographs.* 2005, (34), pp.77-82.

280. Kenney, L.B., Nicholson, H.S., Brasseux, C., Mills, J.L., Robison, L.L., Zeltzer, L.K., Meadows, A.T., Reaman, G.H. and Byrne, J. Birth defects in offspring of adult survivors of childhood acute lymphoblastic leukemia. A Childrens Cancer Group/National Institutes of Health Report. *Cancer.* 1996, **78**(1), pp.169-176.

281. Cvancarova, M., Samuelsen, S.O., Magelssen, H. and Fossa, S.D. Reproduction rates after cancer treatment: experience from the Norwegian radium hospital. *Journal of Clinical Oncology.* 2009, **27**(3), pp.334-343.

282. Green, D.M., Kawashima, T., Stovall, M., Leisenring, W., Sklar, C.A., Mertens, A.C., Donaldson, S.S., Byrne, J. and Robison, L.L. Fertility of female survivors of childhood cancer: a report from the childhood cancer survivor study. *Journal of Clinical Oncology.* 2009, **27**(16), pp.2677-2685.

283. Magelssen, H., Melve, K.K., Skjaerven, R. and Fossa, S.D. Parenthood probability and pregnancy outcome in patients with a cancer diagnosis during adolescence and young adulthood. *Human Reproduction.* 2008, **23**(1), pp.178-186.

284. Pivetta, E., Maule, M.M., Pisani, P., Zugna, D., Haupt, R., Jankovic, M., Arico, M., Casale, F., Clerico, A., Cordero di Montezemolo, L., Kiren, V., Locatelli, F., Palumbo, G., Pession, A., Pillon, M., Santoro, N., Terenziani, M., Valsecchi, M.G., Dama, E., Magnani, C., Merletti, F. and Pastore, G. Marriage and parenthood among childhood cancer survivors: a report from the Italian AIEOP Off-Therapy Registry. *Haematologica.* 2011, **96**(5), pp.744-751.

285. Reulen, R.C., Zeegers, M.P., Wallace, W.H.B., Frobisher, C., Taylor, A.J., Lancashire, E.R., Winter, D.L., Hawkins, M.M. and Study, o.b.o.t.B.C.C.S. Pregnancy Outcomes among Adult Survivors of Childhood Cancer in the British Childhood Cancer Survivor Study. *Cancer Epidemiology Biomarkers & Prevention.* 2009, **18**(8), pp.2239-2247.

286. Syse, A., Kravdal, O. and Tretli, S. Parenthood after cancer - a population-based study. *Psychooncology.* 2007, **16**(10), pp.920-927.

287. Moffat, R. and Güth, U. Preserving fertility in patients undergoing treatment for breast cancer: current perspectives. *Breast Cancer : Targets and Therapy.* 2014, **6**, pp.93-101.

288. Cardozo, E., Thomson, A., Karmon, A., Dickinson, K., Wright, D. and Sabatini, M. Ovarian stimulation and in-vitro fertilization outcomes of cancer patients undergoing fertility preservation compared to age matched controls: a 17-year experience. *Journal of Assisted Reproduction and Genetics.* 2015, **32**(4), pp.587-596.

289. Dolmans, M.M., Hollanders de Ouderaen, S., Demylle, D. and Pirard, C. Utilization rates and results of long-term embryo cryopreservation before gonadotoxic treatment. *Journal of Assisted Reproduction and Genetics.* 2015, **32**(8), pp.1233-1237.

290. Robertson, A.D., Missmer, S.A. and Ginsburg, E.S. Embryo yield after in vitro fertilization in women undergoing embryo banking for fertility preservation before chemotherapy. *Fertility and Sterility.* 2011, **95**(2), pp.588-591.

291. Dominick, S.A., Whitcomb, B.W., Gorman, J.R., Mersereau, J.E., Chung, K. and Su, H.I. Factors associated with pregnancy attempts among female young adult cancer survivors. *Journal of Cancer Survivorship.* 2014, **8**(4), pp.571-579.

292. Hammarberg, K., Astbury, J. and Baker, H.W.G. Women's experience of IVF: a follow-up study. *Human Reproduction.* 2001, **16**(2), pp.374-383.
293. Malin, M., Hemminki, E., Räikkönen, O., Sihvo, S. and Perälä, M.L. What do women want? Women's experiences of infertility treatment. *Social Science & Medicine.* 2001, **53**(1), pp.123-133.
294. Gwyn, K. and Theriault, R. Breast cancer during pregnancy. *Oncology (Williston Park, NY).* 2001, **15**(1), pp.39-46.
295. Petrek, J.A. Pregnancy safety after breast cancer. *Cancer.* 1994, **74**(S1), pp.528-531.
296. Azim, A.A., Costantini-Ferrando, M. and Oktay, K. Safety of Fertility Preservation by Ovarian Stimulation With Letrozole and Gonadotropins in Patients With Breast Cancer: A Prospective Controlled Study. *Journal of Clinical Oncology.* 2008, **26**(16), pp.2630-2635.
297. Marshall, M.N. Sampling for qualitative research. *Family Practice.* 1996, **13**(6), pp.522-526.
298. Malterud, K. Qualitative research: standards, challenges, and guidelines. *The Lancet.* 2001, **358**(9280), pp.483-488.
299. The Hofstede Centre. *Poland.* [Online]. 2012. [Accessed 16/07/2016]. Available from: https://geert-hofstede.com/poland.html
300. Macfarlane, A. and O'Reilly-de Brun, M. Using a theory-driven conceptual framework in qualitative health research. *Qualitative Health Research.* 2012, **22**(5), pp.607-618.
301. Maxwell, J.A. Designing a Qualitative Study. In: Bickman, L. and Rog, D.J. eds. *The SAGE handbook of applied social research methods*. Los Angeles: Sage Publications, 2009, pp.214-253.
302. Miller, R.L. *Researching life stories and family histories.* London: Sage Publications, 2000.
303. Calman, L., Brunton, L. and Molassiotis, A. Developing longitudinal qualitative designs: lessons learned and recommendations for health services research. *BMC Medical Research Methodology.* 2013, **13**(1), p.14.

304. McCoyd, J.L.M. and Kerson, T.S. Conducting Intensive Interviews Using Email: A Serendipitous Comparative Opportunity. *Qualitative Social Work.* 2006, **5**(3), pp.389-406.
305. Novick, G. Is there a bias against telephone interviews in qualitative research? *Research in Nursing & Health.* 2008, **31**(4), pp.391-398.
306. Braun, V. and Clarke, V. Using thematic analysis in psychology. *Qualitative Research in Psychology.* 2006, **3**(2), pp.77-101.
307. Smith, J.A. Beyond the divide between cognition and discourse: Using interpretative phenomenological analysis in health psychology. *Psychology & Health.* 1996, **11**(2), pp.261-271.
308. Charmaz, K. *Constructing grounded theory: a practical guide through qualitative analysis.* London: Sage Publications, 2006.
309. Yardley, L. and Murray, M. Qualitative analysis of talk and text: Discourse and narrative analysis. *Research Methods for Clinical and Health Psychology.* 2003, pp.90-101.
310. Saldana, J. *Coding manual for qualitative researchers.* Los Angeles, Calif.: Sage Publications, 2008.
311. Levinson, D.J. A conception of adult development. *American Psychologist.* 1986, **41**(1), pp.3-13.
312. Pacheco Palha, A. and Lourenco, M.F. Psychological and cross-cultural aspects of infertility and human sexuality. *Advances in Psychosomatic Medicine.* 2011, **31**, pp.164-183.
313. Jansen, S., Otten, W., Van de Velde, C., Nortier, J. and Stiggelbout, A. The impact of the perception of treatment choice on satisfaction with treatment, experienced chemotherapy burden and current quality of life. *British Journal of Cancer.* 2004, **91**(1), pp.56-61.
314. Street, R.L. and Voigt, B. Patient Participation in Deciding Breast Cancer Treatment and Subsequent Quality of Life. *Medical Decision Making.* 1997, **17**(3), pp.298-306.
315. Sol Olafsdottir, H., Wikland, M. and Möller, A. Nordic couples' decision-making processes during assisted reproduction treatments. *Sexual & Reproductive Healthcare.* 2013, **4**(2), pp.49-55.

316. Hubbard, G., Illingworth, N., Rowa-Dewar, N., Forbat, L. and Kearney, N. Treatment decision-making in cancer care: the role of the carer. *Journal of Clinical Nursing.* 2010, **19**(13-14), pp.2023-2031.
317. Couper, M.P., Singer, E., Levin, C.A., Fowler, F.J., Fagerlin, A. and Zikmund-Fisher, B.J. Use of the Internet and Ratings of Information Sources for Medical Decisions: Results from the DECISIONS Survey. *Medical Decision Making.* 2010, **30**(5 suppl), pp.106S-114S.
318. Hernandez, B.E. To Bear or Not to Bear: Reproductive Freedom as an International Human Right. *Brooklyn Journal of International Law.* 1991, **17**(2), pp.309-358.
319. Elwyn, G., Hutchings, H., Edwards, A., Rapport, F., Wensing, M., Cheung, W.Y. and Grol, R. The OPTION scale: measuring the extent that clinicians involve patients in decision-making tasks. *Health Expectations.* 2005, **8**(1), pp.34-42.
320. Shenton, A.K. Strategies for ensuring trustworthiness in qualitative research projects. *Education for information.* 2004, **22**(2), pp.63-75.
321. Gotay, C.C. and Muraoka, M.Y. Quality of Life in Long-Term Survivors of Adult-Onset Cancers. *Journal of the National Cancer Institute.* 1998, **90**(9), pp.656-667.
322. Cancer Research UK. *Breast cancer survival statistics.* [Online]. 2014. [Accessed 05/10/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/survival#heading-Zero
323. Cancer Research UK. *Cervical cancer ovarian statistics.* [Online]. 2014. [Accessed 05/10/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer/survival#heading-Zero
324. Cancer Research UK. *Ovarian cancer survival statistics.* [Online]. 2014. [Accessed 05/10/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/ovarian-cancer/survival#heading-Zero

325. Cancer Research UK. *Uterine cancer survival statistics.* [Online]. 2014. [Accessed 05/10/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer/survival#heading-Zero

326. Broadbent, E., Petrie, K.J., Main, J. and Weinman, J. The brief illness perception questionnaire. *Journal of Psychosomatic Research.* 2006, **60**(6), pp.631-637.

327. Watson, D., Clark, L.A. and Tellegen, A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology.* 1988, **54**(6), pp.1063-1070.

328. Brzozowski, P.W.D.B.C.L.A. *Skala uczuc pozytywnych i negatywnych SUPIN : polska adaptacja skali PANAS Davida Watsona i Lee Ann Clark : podrecznik.* Warszawa: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego, 2010.

329. Weiss, D.S. and Marmar, C.R. The impact of event scale-revised. *Assessing psychological trauma and PTSD.* 2004, **2**, pp.168-189.

330. Juczyński, Z. and Ogińska-Bulik, N. Pomiar zaburzeń po stresie traumatycznym-polska wersja Zrewidowanej Skali Wpływu Zdarzeń. *Psychiatria.* 2009, **6**(1), pp.15-14.

331. Ghazali, N., Cadwallader, E., Lowe, D., Humphris, G., Ozakinci, G. and Rogers, S.N. Fear of recurrence among head and neck cancer survivors: longitudinal trends. *Psychooncology.* 2013, **22**(4), pp.807-813.

332. Rogers, S., Scott, B., Lowe, D., Ozakinci, G. and Humphris, G. Fear of recurrence following head and neck cancer in the outpatient clinic. *European Archives of Oto-Rhino-Laryngology.* 2010, **267**(12), pp.1943-1949.

333. Avis, N.E., Smith, K.W., McGraw, S., Smith, R.G., Petronis, V.M. and Carver, C.S. Assessing quality of life in adult cancer survivors (QLACS). *Quality of Life Research.* 2005, **14**(4), pp.1007-1023.

334. Davies, N. *Self-Management Programmes for Cancer Survivors: A Structured Review of Outcome Measures.* [Online]. 2009. [Accessed 19/8/2013]. Available from: http://www.ncsi.org.uk/wp-content/uploads/Outcome-Measures-for-Evaluating-Cancer-Aftercare.pdf

335. Skrzypczak, M., Łaski, P., Czerniak, U. and Kycler, W. Do chronological age and selected socio-demographic factors affect quality of life in females with breast cancer? *Anthropological Review.* 2009, **72**(1), pp.31-44.
336. Funk, J.L. and Rogge, R.D. Testing the ruler with item response theory: increasing precision of measurement for relationship satisfaction with the Couples Satisfaction Index. *Journal of Family Psychology.* 2007, **21**(4), pp.572-583.
337. Coscarelli, A. and Heinrich, R. Cancer rehabilitation evaluation system manual. *Santa Monica, California: CARES Consultants.* 1988.
338. *IBM SPSS Statistics for Windows.* Armonk, NY, 2012.
339. Schafer, J.L. Multiple imputation: a primer. *Statistical Methods in Medical Research.* 1999, **8**(1), pp.3-15.
340. Dong, Y. and Peng, C.-Y.J. Principled missing data methods for researchers. *SpringerPlus.* 2013, **14;2**(1), p.222.
341. Roth, P.L., Switzer, F.S. and Switzer, D.M. Missing Data in Multiple Item Scales: A Monte Carlo Analysis of Missing Data Techniques. *Organizational Research Methods.* 1999, **2**(3), pp.211-232.
342. Shrive, F.M., Stuart, H., Quan, H. and Ghali, W.A. Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. *BMC Medical Research Methodology.* 2006, **13;6**, p.57.
343. Bono, C., Ried, L.D., Kimberlin, C. and Vogel, B. Missing data on the Center for Epidemiologic Studies Depression Scale: a comparison of 4 imputation techniques. *Research in Social and Administrative Pharmacy.* 2007, **3**(1), pp.1-27.
344. Downey, R.G. and King, C. Missing data in Likert ratings: A comparison of replacement methods. *The Journal of General Psychology.* 1998, **125**(2), pp.175-191.
345. Fairclough, D.L. and Cella, D.F. Functional Assessment of Cancer Therapy (FACT-G): Non-Response to Individual Questions. *Quality of Life Research.* 1996, **5**(3), pp.321-329.
346. Ashley, L., Smith, A.B., Jones, H., Velikova, G. and Wright, P. Traditional and Rasch psychometric analyses of the Quality of Life in Adult Cancer Survivors

(QLACS) questionnaire in shorter-term cancer survivors 15 months post-diagnosis. *Journal of Psychosomatic Research.* 2014, **77**(4), pp.322-329.

347. Office for National Statistics. *Annual Survey of Hours and Earnings, 2014 Provisional Results.* [Online]. 2014. [Accessed 19/10/2015]. Available from: http://www.ons.gov.uk/ons/dcp171778_385428.pdf

348. Główny Urząd Statystyczny. *Podstawowe dane.* [Online]. 2014. [Accessed 19/10/2015]. Available from: http://stat.gov.pl/podstawowe-dane/

349. Hayes, A.F. *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach.* New York: The Guilford Press, 2013.

350. Green, S.B. How many subjects does it take to do a regression analysis. *Multivariate Behavioral Research.* 1991, **26**(3), pp.499-510.

351. Field, A.P. *Discovering statistics using SPSS : (and sex and drugs and rock 'n' roll).* Los Angeles [i.e. Thousand Oaks, Calif.]; London: SAGE Publications, 2009.

352. Tabachnick, B.G. and Fidell, L.S. *Using multivariate statistics.* New York: Harper Collins College Publishers, 1996.

353. Howitt, D. and Cramer, D. *Introduction to statistics in psychology: with SPSS.* Harlow: Pearson Education Limited, 2014.

354. Watson, D. and Pennebaker, J.W. Health complaints, stress, and distress: Exploring the central role of negative affectivity. *Psychological Review.* 1989, **96**(2), pp.234-254.

355. Crist, J.V. and Grunfeld, E.A. Factors reported to influence fear of recurrence in cancer patients: a systematic review. *Psychooncology.* 2013, **22**(5), pp.978-986.

356. Mishel, M.H., Hostetter, T., King, B. and Graham, V. Predictors of psychosocial adjustment in patients newly diagnosed with gynecological cancer. *Cancer Nursing.* 1984, **7**(4), pp.291-300.

357. Shapiro, S.L., Lopez, A.M., Schwartz, G.E., Bootzin, R., Figueredo, A.J., Braden, C.J. and Kurker, S.F. Quality of life and breast cancer: relationship to psychosocial variables. *Journal of Clinical Psychology.* 2001, **57**(4), pp.501-519.

358. Landmark, B.T. and Wahl, A. Living with newly diagnosed breast cancer: a qualitative study of 10 women with newly diagnosed breast cancer. *Journal of Advanced Nursing.* 2002, **40**(1), pp.112-121.

359. Mols, F., Vingerhoets, A.J.J.M., Coebergh, J.W. and van de Poll-Franse, L.V. Quality of life among long-term breast cancer survivors: A systematic review. *European Journal of Cancer.* 2005, **41**(17), pp.2613-2619.

360. Cancer Research UK. *Cancer incidence in adults aged 25-49.* [Online]. 2015. [Accessed 25/11/2015]. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Five

361. Kaptein, A.A., Schoones, J.W., Fischer, M.J., Thong, M.S.Y., Kroep, J.R. and van der Hoeven, K.J.M. Illness Perceptions in Women with Breast Cancer—a Systematic Literature Review. *Current Breast Cancer Reports.* 2015, **7**(3), pp.117-126.

362. Liefbroer, A.C. and Billari, F.C. Bringing norms back in: a theoretical and empirical discussion of their importance for understanding demographic behaviour. *Population, Space and Place.* 2010, **16**(4), pp.287-305.

363. Baumeister, R.F. and Tice, D.M. Point-counterpoints: Anxiety and social exclusion. *Journal of Social and Clinical Psychology.* 1990, **9**(2), pp.165-195.

364. Leary, M.R. Responses to social exclusion: Social anxiety, jealousy, loneliness, depression, and low self-esteem. *Journal of Social and Clinical Psychology.* 1990, **9**(2), pp.221-229.

365. Horne, R. and Weinman, J. Self-regulation and Self-management in Asthma: Exploring The Role of Illness Perceptions and Treatment Beliefs in Explaining Non-adherence to Preventer Medication. *Psychology & Health.* 2002, **17**(1), pp.17-32.

366. Ross, S., Walker, A. and MacLeod, M.J. Patient compliance in hypertension: role of illness perceptions and treatment beliefs. *Journal of Human Hypertension.* 2004, **18**(9), pp.607-613.

367. King, J.W., Davies, M.C., Roche, N., Abraham, J.M. and Jones, A.L. Fertility preservation in women undergoing treatment for breast cancer in the UK: a questionnaire study. *The Oncologist.* 2012, **17**(7), pp.910-916.

368. Quinn, G.P., Vadaparampil, S.T., Gwede, C.K., Miree, C., King, L.M., Clayton, H.B., Wilson, C. and Munster, P. Discussion of fertility preservation with newly diagnosed patients: oncologists' views. *Journal of Cancer Survivorship.* 2007, **1**(2), pp.146-155.

369. Humphris, G. and Ozakinci, G. The AFTER intervention: A structured psychological approach to reduce fears of recurrence in patients with head and neck cancer. *British Journal of Health Psychology.* 2008, **13**(2), pp.223-230.

370. Butow, P.N., Bell, M.L., Smith, A.B., Fardell, J.E., Thewes, B., Turner, J., Gilchrist, J., Beith, J., Girgis, A. and Sharpe, L. Conquer fear: protocol of a randomised controlled trial of a psychological intervention to reduce fear of cancer recurrence. *BMC Cancer.* 2013, **13**, p.201.

371. Weiss, D.S. and Marmar, C.R. The Impact of Event Scale-Revised. In: Wilson, J.P.K.T.M. ed. *Assessing psychological trauma and PTSD: A Practitioner's Handbbok.* New York: Guilford Press, 1997, pp.399-411.

Appendix 1 – Systematic review of quantitative literature (1990-2012)

Manuscript Journal of Cancer Survivorship
The final publication is available at Springer via http://dx.doi.org/10.1007/s11764-014-0388-9

Fertility and parenthood issues in young female cancer patients – a systematic review

Aleksandra Sobota[a1] and Gozde Ozakinci[a]

[a]School of Medicine, University of St Andrews, St Andrews, UK

University of St Andrews

School of Medicine

Biological and Medical Sciences Building

North Haugh

St Andrews, Fife

KY16 9TF

Scotland, UK

Email addresses and telephone numbers:

Aleksandra Sobota: as297@st-andrews.ac.uk

Gozde Ozakinci: go10@st-andrews.ac.uk, ++(44) 1334 463 521

Funding:
Aleksandra Sobota's PhD is funded by the Danuta Richardson Medical Scholarship. This systematic review has not received any additional funding.

Conflict of interest:
The authors declare that they have no conflict of interest.

The final publication is available at Springer via http://dx.doi.org/10.1007/s11764-014-0388-9

[1] Corresponding author: Aleksandra Sobota. Email: as297@st-andrews.ac.uk

Manuscript Journal of Cancer Survivorship
The final publication is available at Springer via http://dx.doi.org/10.1007/s11764-014-0388-9

Abstract

Purpose: For young women who were diagnosed with cancer prior to having children, reproductive potential might affect quality of life (QoL). This systematic review looks at fertility issues in young female cancer patients, focusing on their influence on psychological well-being, specific fertility-related interventions and reproductive decisions.

Methods: Thirteen medical and social science databases were searched for relevant articles up to December 2012, according to PRISMA guidelines. Twenty-six articles meeting the eligibility criteria were included in the review, along with 5 additional papers that missed the inclusion criteria narrowly. Narrative synthesis was used to analyse the studies.

Results: Depression, anxiety, and QoL seemed to be related to the perceptions of reproductive issues rather than to the fertility status based on the type of treatment received. Fertility-related interventions improved patients' QoL, decisional regret, and decisional conflict. Finally, cancer influenced women's reproductive decisions. Pursuing pregnancy was affected mainly by worries about child's and mother's health. Decisions about treatment were influenced by the wish to preserve fertility. The generalisability of these results might be undermined by small sample sizes and homogeneity of participants within and across the studies. Inferences about causality of associations are problematic due to predominantly cross-sectional design.

Implications for cancer survivors: The existing literature gives preliminary insight into the importance of fertility for young women diagnosed with cancer. However, more research is needed in order to offer patients comprehensive care.

Keywords: cancer; fertility; parenthood; women; review; decision

Introduction

The development of screening programmes and progress in cancer treatment have led to significant increase in cancer survival rates [1]. Given the comprehensive cancer treatment regimens involved, improving cancer patients' quality of life is an important challenge for clinicians. Evidence shows that for young women with a diagnosis of cancer, being able to build a family and have children may be an important and cherished life goal determining their quality of life after the end of treatment [2, 3]. The qualitative evidence also suggests that being able to have children gives these women back their sense of normality, reconnects them with peers, and gives them additional motivation to survive the cancer diagnosis and treatment [2-6]. Since the age at first birth tends to increase [7], some women are diagnosed with cancer before they have had enough time to complete their families. Unsurprisingly, many of them step into the survivorship phase that is shadowed by reproductive concerns which can arise due to treatment resulting in sterility or the uncertainty regarding fertility status.

Treatment modalities for the most commonly diagnosed cancers (breast, cervical, and ovarian) but also other, less frequent malignancies are known to influence women's reproductive potential. For instance, the first line treatment for most of gynecological cancers but also other types of cancers located in the lower pelvis is surgery during which, depending on the stage of the disease, part or all of the reproductive organs are removed. This can lead to inability to bear biological children if hysterectomy or bilateral oophorectomy is performed. Total body irradiation (TBI) and pelvic irradiation may result in ovarian failure and damage to the uterine musculature and vascular system. Cranial irradiation can alter the functioning of hypothalamic-pituitary-gonadal axis resulting in reduced serum levels of sex-steroids and hence amenorrhea [8]. The negative effect of systemic chemotherapy (a standard treatment for young women with breast cancer) on reproductive function is widely acknowledged and depends on the age of the patient at drug administration, drug dosage, duration of therapy, and type of medications used [8, 9]. Chemotherapy is known to diminish the ovarian reserve which may result in an early-onset menopause even in women who continue menstruating after having received systemic treatment [10]. Hormonal therapy employed in hormone-positive breast cancer has been shown to increase the risk of amenorrhea in cancer survivors [11]. Moreover tamoxifen, the most commonly prescribed drug is considered to be a teratogen, meaning that pregnancy should be contraindicated during the time of therapy [12, 13]. According to the guidelines, tamoxifen should be continued for five years after diagnosis [14]; therefore, for some patients with an already reduced ovarian reserve due to adjuvant chemotherapy, a window for childbearing would be very short.

In 2006, for the first time, the American Society of Clinical Oncology issued guidelines concerning fertility preservation in young people affected by cancer [15]. These, as well as the reviewed version of the guidelines [16] recommend that all clinicians discuss the possibility that cancer treatment may result in infertility at the earliest opportunity with all the patients. For patients interested in looking into their fertility options, early referral to a fertility specialist is advised. Specific recommendations for procedures available for children, adult males and adult females were added to the reviewed version of the guidelines [16]. However, not all patients can undergo these recommended procedures. Some women might be ineligible for a conservative gynaecologic surgery due to the advanced stage of disease at diagnosis and others might feel overwhelmed having to make a fertility preservation decision in a very short time between cancer diagnosis and the onset of treatment [17].

Additionally, some women may fear cancer recurrence due to fertility preservation [18] or may not have the financial resources to afford it. Finally, some young patients do not recall having had a conversation about the impact of cancer treatment on fertility with their treating physicians [19, 20] which prevents them from making an informed decision about their fertility.

Even though discussing the effects that treatment might have on reproductive potential is a sensitive topic, the evidence shows that young women with cancer want information concerning fertility issues. According to Thewes et al. [13] women with breast cancer considered the provision of fertility-related information to be important at three time points: the time of diagnosis, treatment decision-making, and post-treatment follow-up. In a web-based survey by Partridge et al. [21], 57% of breast cancer patients identified fertility concerns as a major issue at the time of their diagnosis. Qualitative data also indicate that some women are willing to alter the course of their cancer treatment [6] or forgo some part of treatment in order to preserve fertility [22].

Fertility is an important concern for young female cancer patients and several reviews tackling different aspects of this issue have been published over the last few years [23-27]. These articles contribute to our understanding of what fertility and parenthood mean to cancer patients [24] and how its meaning can change over cancer trajectory [23]. They also examine knowledge [25] and information needs of patients [27] and when it is appropriate to discuss fertility [25]. The majority, however, [23, 24, 26, 27], only concentrate on breast cancer patients and although breast cancer is the most frequently diagnosed cancer in younger women, other cancers also occur in this group of patients and their treatment can equally affect patients' fertility. One paper that describes how fertility issues are related to the quality of life [26] is not specific to cancer population and

includes women with all types of non-communicable health conditions (e. g. cystic fibrosis, diabetes, epilepsy, PCOS). Although these different diseases can all affect fertility, the psychological burden might be different for a life-threatening disease such as cancer as compared to the other conditions included in the review. Finally, Goncalves et al. [24] discuss reproductive decisions in breast cancer patients only, focusing on survivors' attitudes and decisions towards pregnancy as well as risks and benefits of becoming a parent after cancer. Yet, this review did not include fertility preservation which constitutes one of the reproductive decisions that patients with cancer increasingly face.

Therefore, in this review we will address the gaps still present in the literature. First of all, we will delineate a relationship between fertility issues and psychological well-being of reproductive age women diagnosed with cancer while making a distinction between their objective fertility status and their subjective perception of reproductive concerns (Objective 1). We will also address the impact of fertility-specific interventions on young female cancer patients' psychological well-being (Objective 2). Finally, we will summarise the evidence on how cancer may affect reproductive decisions in young women with cancer, extending the definition of reproductive decisions beyond pregnancy post-cancer to treatment-related decisions that may affect fertility and also fertility preservation (Objective 3). This review will concentrate on all types of cancer diagnosed in women the treatment of which can potentially affect fertility.

For the purpose of this review, several terms needed clarification. Cancer treatment-related fertility issues were defined as both objective (e.g., surgery involving reproductive organs or chemotherapy) and subjective (e.g., self-assessed problems with conceiving or the reproductive concerns score as commonly measured by the Reproductive Concerns Scale [28]) as indicators of reproductive problems. Fertility-related interventions were operationalised as any type of intervention to promote fertility-related knowledge post-cancer diagnosis or provide psychosocial assistance (e.g., counselling by oncologists or fertility specialists, provision of decision aids and online support). Reproductive decisions were conceptualised as any decision that might relate to preserving the possibility of having children after cancer or actual decisions about childbearing post-cancer.

Methods

Search strategy

This systematic review was conducted according to the PRISMA guidelines (see Online Resource 1, Table 1). The search for relevant articles was performed using the following medical and social science search

engines: NCBI (PubMed), OVID (Medline and Embase), Web of Science (Science Citation Index Expanded, Social Sciences Citation Index, Art&Humanities Citation Index, Conference Proceedings Citation Index – Science and Conference Proceedings Citation Index - Social Sciences & Humanities), PROQUEST (PsycArticles, Applied Social Sciences Index & Abstracts) and COCHRANE (Cochrane systematic reviews, Cochrane controlled trials and Cochrane methodological register). All databases were searched up to December 2012 using the keywords presented in Table 2.

Table 1. Search terms

Column 1	Column 2	Column 3	Column 4
'woman'	'cancer OR tumor OR neoplasm OR malignancy'	'fertility OR sterility OR reproduction OR childbearing OR pregnancy'	'psychology OR distress OR depression OR anxiety OR fear OR PTSD OR quality of life OR self-esteem OR sexual OR recurrence OR reproductive decision OR decision making OR intervention OR counseling OR communication'

Inclusion criteria

Population

We included studies in which the study sample, at least in part, consisted of women diagnosed with various types of cancers (excluding childhood cancers and cancer diagnosed in the context of pregnancy) during their reproductive years. Being of reproductive age was defined as: (1) being premenopausal at the time of diagnosis or (2) being between 14 and 50 years of age at the time of diagnosis. The age range was selected based on the mean age at menarche and menopause worldwide [29]. If the study sample included women of all ages, it was eligible to be included only if the results for our target group were presented separately. In the case of studies including both men and women, only those presenting results separately for each gender and also our target age group were deemed eligible for inclusion. Studies that looked at women with various cancer diagnoses including cancers co-occurring with pregnancy or childhood cancers were only included if the results for our target group were presented separately.

Outcomes

Studies were included in the review if they measured the following outcomes for respective questions.

For Objective 1: Anxiety; Depression; Quality of life; Sexual functioning; Worries about future conception/pregnancy

For Objective 2: Anxiety; Depression; Quality of life; Decisional conflict; Decisional regret

For Objective 3: No pre-specified outcomes were selected for this question due to diversity of possible significant outcomes.

Study design

Quantitative experimental, quasi-experimental, and observational studies (cohort and case control studies) were included in the review.

Exclusion criteria

Studies were excluded if cancer diagnosis in the sample co-occurred with pregnancy (any cancer diagnosed in pregnant women or gestational trophoblastic disease); the focus of the study was on childhood cancers; combined results were presented for both genders, for women of all ages or for various cancers including childhood cancers and cancers diagnosed in the context of pregnancy. We also excluded papers that were written in non-English languages; the reviews, book chapters, commentaries, letters, guidelines, case studies and also the articles published before 1990, considering that the medical technology has changed substantially since then and new procedures allowing for the fertility sparing and preservation were established for female cancer patients [30]. Finally, we decided to exclude qualitative studies. We chose to do this since our search produced 44 qualitative articles potentially relevant based on title or abstract (8% of all the articles judged relevant by title) and these articles merit a separate qualitative synthesis, which was outside the scope of this review.

Data collection and analysis

A total number of 8040 articles were identified through the databases search. Automatic and manual de-duplication narrowed the number to 6507 articles. The first reviewer (AS) visually screened all the titles and identified 552 as potentially relevant. These 552 records were then examined by two reviewers as follows:

- The first reviewer extracted and read the abstracts of all the 552 articles; 56 of them were found to be potentially relevant.
- The second reviewer (GO) screened the titles of the 552 articles and singled out 385 that seemed potentially relevant. Subsequently the second reviewer read 385 abstracts and found 126 of them suitable.

Both reviewers subsequently discussed the discrepancies between their choices and after excluding the abstracts that reported on medical outcomes only, did not mention fertility, or concentrated on childhood cancers, 81 articles were retained for full-text assessment. These articles were independently read in full by each reviewer and compared against the established inclusion and exclusion criteria. The first reviewer deemed 40 articles suitable while the second reviewer found 31 articles to match the criteria. The discrepancies were again resolved by discussion. The first reviewer contacted the authors of the publications that needed clarification in order to be included or excluded. We kept 26 articles meeting all the predefined criteria to be included in the review. The decision was also made to retain and separately describe five additional papers that missed one of the criteria (age or type of diagnosis) narrowly (see Online Resource 1, Figure 1). This is because excluding them could have potentially biased the results given that these studies have only slightly deviated from the inclusion criteria. Study by Carter et al. [31] included patients with gestational trophoblastic disease which was one of the exclusion criteria; however, they constituted only 6% of the study sample (5/88) and thus were unlikely to significantly influence the results of the study. Similarly, in the studies that have not met the age criterion, the proportion of participants that were outside the predefined age brackets was minimal (6.4% and 12.8% where it was possible to determine [32, 33]) (for further details see Online Resource 2, Table 6).

In total, 31 papers describing 28 separate studies were included in the review (papers by Letourneau et al. [34] and Letourneau et al. [35]; Peate et al. [36] and Peate et al. [37]; and Carter et al. [38] and Carter et al. [39] referred to the same respective datasets). For details see Tables 3-6 in Online Resource 2.

The following data from the articles were extracted by the first reviewer: authors; date; location of study; study aim; study sample (including cancer type, age at diagnosis, sample size); study design; definitions of fertility; outcomes (constructs and measures); results for outcomes of interest.

Papers were also assessed for their quality using a checklist designed to examine and provide a quality score for quantitative studies employing various study designs [40]. The quality of 10 randomly selected articles was assessed by both reviewers. Where the discrepancies in scores occurred, they were discussed and the inter-rater reliability analysis was performed to determine the consistency between the observers. Kappa scores ranged from 0.44 to 1 representing moderate to substantial inter-rater agreement [41]. Subsequently, the first reviewer rated the quality of the remaining 21 articles. All the quality scores provided in the summary tables (see Tables 3-6 in Online Resource 2) are those assigned by the first reviewer. The narrative synthesis was used to analyse and interpret the data. The heterogeneity of study designs and outcome measures prevented the meta-analytic approach.

Results

For the purpose of this review, the articles were organised according to the specific objective of the review they pertained to and further according to the outcomes they described. Since there were no predefined outcomes related to the third objective, studies falling into this category were classified in the following manner:

- The first group included articles that examined reproductive decisions related to pregnancy after cancer. Within this category, we concentrated on actual attempts to conceive, the desire to have children pre- and post-treatment as well as factors affecting decisions to have children after cancer. These results are summarised in the section titled "Pregnancy-related decisions".
- The second group comprised of the studies that explored decisions related to treatment modalities that could enable future fertility after cancer (fertility-sparing surgery or fertility preservation techniques). These results are summarised in the section titled "Treatment-related decisions".

Impact of cancer treatment-related fertility issues in reproductive age women on their psychological well-being

Worry about pregnancy

Three studies examined worries about pregnancy after cancer. These worries included the ability to become pregnant after treatment for breast cancer [42], the success of conceiving after radical trachelectomy [43], and concerns about conception after radical trachelectomy [38, 43]. In one study, 43.1% of breast cancer patients worried whether they would be able to have a pregnancy after cancer, if they wished that [42]. When asked about the success at conceiving, cervical cancer patients who underwent radical trachelectomy assessed their chance to be between 55% and 60% over a 2-year follow-up post-surgery with no marked change during that time [43]. Concerns about conceiving in cervical cancer patients scheduled for fertility-sparing treatment ranged from 90% before treatment to 100% at six months post-surgery in one study [38] and from 88% at six months post-treatment to 73% at 24 months post-treatment in another study [43].

Depression and anxiety

Four studies looked at the association between fertility issues and depressive symptoms. One study used Hospital Anxiety and Depression Scale to measure depressive symptoms [44] while the remaining three

used the Centre for Epidemiologic Studies-Depression scale [39, 45, 46]. The two studies that defined fertility issues using an objective measure of having undergone either fertility-sparing or radical treatment did not find significant difference in the level of depressive symptoms or anxiety between the two groups of patients (ovarian in Bisseling et al. [44] cervical in Carter et al. [39]). However, the latter study reported that the mean scores for depressive symptoms in both groups of patients, those who underwent radical trachelectomy as well as those treated with radical hysterectomy, were suggestive of depression before the onset of either treatment and remained in a subclinical range after treatment [39]. Another study by Carter et al. [45] examining the group of cervical cancer patients whose fertility was damaged due to treatment, reported that 40% of their sample met the criteria for depression as measured by CES-D. Finally Gorman et al. [46] examined the association between the amount of reproductive concerns and depressive symptoms in breast cancer patients and found a significant association between the two. However, we were not able to ascertain the strength of this relationship.

Quality of life (QoL)

Five studies assessed the relationship between fertility issues and QoL. Two of the studies used the Functional Assessment of Cancer Therapy scale (the Cervical or Trial Outcome Index version) [39, 47], the other two used the Medical Outcomes Scale SF-36 [48, 49], and one used the Medical Outcomes Scale SF-12 [50]. Two studies that operationalised fertility issues in a more objective manner (radical versus fertility-sparing treatment or occurrence of prolonged amenorrhea) did not find significant association between QoL and fertility issues. There was no significant difference in terms of QoL between patients who underwent radical trachelectomy and those who had radical hysterectomy [39]. Neither did prolonged amenorrhea at 12 month post-chemotherapy predict the quality of life in breast cancer patients [47]. The third study that referred to the medical definition of infertility (primary, where a woman did not have any children or secondary, where a woman had children prior to cancer and could not have them after treatment) post-cancer found a significant difference in the Mental Component Summary score (MCS) (SF-12) between women who had the desired children and those who were infertile [50]. Two studies in which fertility issues were defined in a more subjective manner (self-reported inability to have children post-cancer or the level of reproductive concerns as measured by RCS [28]) showed a significant association between QoL and fertility issues. In a study by Mancini et al. [48], cancer patients with various diagnoses who considered themselves infertile had significantly lower both Mental and Physical Component Summary (PCS) scores (SF-36) compared to participants who did not report infertility. Wenzel et al. [49] examined cervical cancer patients and although they found no

differences in MCS and PCS between patients and healthy controls, better MCS scores among patients were significantly associated with fewer reproductive concerns. The latter were also significantly related to better survivor-specific QoL as measured by QoL-CS [49].

Sexual functioning

Four studies reported on the relationship between fertility issues and sexual functioning. To assess sexual functioning, two of the studies used the Female Sexual Functioning Index (FSFI) [39, 50], one study used the Gynecologic Problems Checklist (GCP) as well as the Sexual Activity Questionnaire (SAQ) [49], and lastly one study used a single question assessing sexual functioning [48]. Carter et al. [39] who compared cancer patients who had undergone fertility-sparing surgery for cervical cancer to those who had had radical treatment found no differences between the groups in terms of sexual functioning. However, both groups scored in the range of sexual dysfunction with the scores stable over the 24-month follow-up period. The study by Wenzel et al. [49] where two instruments were used to assess sexual functioning delivered mixed results indicating no difference between infertile cancer patients and controls in sexual functioning as measured by GCP but a significant difference in sexual discomfort as measure by SAQ. In Canada, Schover [50] study, patients with primary or secondary infertility post-cancer scored significantly lower on FSFI than women who had the desired children. In the same study, women who viewed themselves as infertile had lower sexual satisfaction that those who did not. Wenzel et al. [49] also indicated that higher reproductive concerns in survivors were significantly associated with poorer sexual functioning. Finally, Mancini et al. [48] found that patients who self-identified as infertile reported significantly more negative consequences of cancer and its treatment on sexual life that those patients who considered themselves fertile.

Effect of fertility-related interventions delivered prior to cancer treatment on women's psychological well-being

Quality of life (QoL)

Three studies explored the influence of fertility-related interventions for young female cancer survivors on their QoL [34, 51, 52]. Each study used a different QoL measurement tool which makes direct comparisons problematic. Letourneau et al. [34] compared young women diagnosed with various cancers who had been counselled about the possible impact of cancer treatment on their fertility to those who had not been counselled.

Women who remembered being counselled had statistically significantly better physical and psychological health scores as measured by WHOQOL-BREF questionnaire [53] than their non-counselled counterparts. The QoL as measured by Satisfaction With Life Scale (SWLS) [54] did not differ between the groups. Similarly, in the models predicting QoL outcomes, adjusted for age at diagnosis, parity before treatment and cancer site, counselling (as primary predictor) did not reach statistical significance. Letourneau et al. [34] also examined different types of counselling and compared (1) women who had only been counselled by an oncologist to those who had been counselled by both an oncologist and fertility specialist and (2) women who had only been counselled by an oncologist to those who had been counselled by an oncologist and additionally pursued fertility preservation (FP). In the first case, women who had been counselled by both an oncologist and a fertility specialist had significantly better QoL as measured by SWLS and also fared better in the physical health domain of WHOQOL-BREF compared to women who had only been counselled by an oncologist. Counselling by both specialists remained a significant predictor of physical health in a model adjusted as above. A similar pattern was found when comparing women who had been counselled by an oncologist and who decided to pursue FP to those who had only been counselled by an oncologist. In an adjusted model, however, counselling and pursuing FP significantly predicted QoL as measured by SWLS [34].

A study by Meneses et al. [51] studied the effect on an online intervention consisting of educational resources and the possibility to interact with other survivors and the researchers on the QoL of young breast cancer survivors. They noted statistically significant improvements in all the QoL domains (as measured by SF-36 [55]) between baseline and follow-up at six months.

Finally, Reh et al. [52] showed that among young cancer patients with various diagnoses referred to a fertility clinic, social domain of QoL as measured by FACT [56] improved over time in those who had undergone FP procedures, with other QoL scores remaining stable over time.

Decisional regret

Decisional regret was an outcome in two studies [34, 37]. Both used the Decision Regret Scale as a measurement tool [57] and referred to either a "decision to undergo (or not undergo) fertility preservation" [34] or "fertility treatment decisions" [37]. Letourneau et al. [34] found that decisional regret was significantly lower in cancer survivors who had undergone counselling by both an oncologist and a fertility specialist compared to those counselled only by an oncologist. The same pattern was found for women who had been counselled by an oncologist and decided to pursue FP when compared to those who had only been counselled by an oncologist. In

the models adjusted for age at diagnosis, parity before treatment and cancer site, counselling by oncologist and fertility specialist as well as counselling by oncologist and pursuing FP remained significant predictors of decisional regret. Peate et al. [37] studied the effect of a fertility-related decision aid (DA) compared to the usual care in breast cancer patients. They showed that women who received the DA did not significantly differ in decisional regret from women in the usual care at 1-month follow-up. The difference, however, reached significance at 12-month follow-up with women in the DA group having lower decisional regret.

Decisional conflict

Decisional conflict was measured as an outcome in one study using the Decisional Conflict Scale [37]. Young breast cancer survivors who received the DA experienced a greater reduction of the decisional conflict over 12 months than the patients in the usual care. The difference in the scores was not significant at 1-month follow-up but reached statistical significance at 12 months with the scores in the DA group 15.3 units lower on average than the scores in the usual care group.

Depression and anxiety

Peate et al. [37] also included depression and anxiety as outcomes in their study of the effect of the DA in a group of breast cancer patients. They found no significant differences in the change of either anxiety or depression as measured by HADS between the DA group and the usual care group over time.

Impact of cancer diagnosis (from patient's perspective) on reproductive decisions in reproductive age women and the possible psychological factors that might facilitate or hinder these decisions

Pregnancy-related decisions

Three studies looked at attempts to conceive post-cancer. In a study by Carter et al. [43] the number of cervical cancer survivors who had been treated with radical trachelectomy and who were trying to conceive post-treatment increased from 6% at 12-month follow-up to 21% at 24-month follow-up. Among breast-cancer survivors in a study conducted by Gorman et al. [46], 7% reported trying to become pregnant after cancer. Among ovarian cancer patients treated with conservative surgery, 49% attempted to conceive after treatment and out of these, 75% were successful [58].

Eight studies explored the potential impact of cancer on the desire to have children. Huyghe et al. [59] and Gorman et al. [46] asked participants to rate their desire to have children pre- and post-diagnosis. In both studies, the numbers decreased from 43% to 29% and from 48% to 28%, respectively. Braun et al. [60] compared breast cancer survivors to healthy controls and found that the former desired significantly fewer children than the latter. Canada, Schover [50] and Zanagnolo et al. [58] assessed how cancer affected the desire to have children in a mixed cancer group and ovarian cancer patients, respectively. According to Canada, Schover [50] the desire to have children remained unchanged in 68% of patients, 17% reported that cancer decreased their desire to have children whereas 15% described the opposite trend. A similar tendency was reported by Zanagnolo et al. [58] with 78% of patients reporting that cancer had no impact on their desire to have children, and 7% and 5% respectively declaring a decrease and increase in their desire for children.

Mancini et al. [48] and Patel et al. [61] only evaluated the desire to have children post-diagnosis and showed that 26.3% and 45% of participants wanted children after cancer, respectively. Finally, in a study by Atkinson et al. [62], 53.6% of reproductive age melanoma survivors thought that cancer would make them better parents.

Eight studies examined potential factors affecting decisions related to pursuing pregnancy after cancer. A study by Braun et al. [60] showed that reported pros and cons of having children did not differ between breast cancer survivors and healthy controls; however, the remaining literature points to several factors influencing pregnancy-related decisions, specific for cancer survivors. These factors could generally be assigned to four categories: 1) child's health and well-being; 2) fear of cancer recurrence; 3) pregnancy complications; 4) mother's mental well-being.

Child's health and well-being

Across studies, participants were concerned about possible birth defects or malformations due to cancer (3.6% of melanoma survivors in Atkinson et al. [62] and 15% of ovarian cancer patients in Zanagnolo et al. [58]) or its treatment (24% of participants in Zanagnolo et al. [58]), the risk of a child developing cancer (51.7% of melanoma survivors in Atkinson et al. [62]) and prematurely bereaving a child (6.7% of breast cancer survivors in a study by Rippy et al. [63]). Canada, Schover [50] also found that women who felt that cancer had interrupted their childbearing plans were more fearful of the effects that cancer could have on child's health.

Fear of cancer recurrence (FoR)

Fear of cancer recurrence as an explicit category was found to affect survivors' decisions about pregnancy in three studies. It influenced reproductive decisions in 12.9% to 29% of patients ([62-64]. Avis et al. [42] reported that 48.3% of patients who were concerned about their fertility feared that pregnancy could affect the course of their disease. Additionally, Canada, Schover [50] found that women who felt that cancer had interfered with their childbearing plans were more worried that pregnancy could trigger cancer recurrence.

Pregnancy complications

Only Atkinson et al. [62] looked at concerns related to pregnancy complications due to cancer. In their sample of reproductive age melanoma survivors, 11.1% were bothered by the possibility that cancer might cause complications during pregnancy.

Mother's mental well-being

Finally, one study studied how mental health could affect pregnancy rates post-breast cancer [65]. A trend towards better mental health (p=0.08) was reported for women who became mothers after diagnosis and treatment compared to survivors who did not have children after cancer.

Treatment-related decisions

Five studies looked at treatment-related decisions that could impact on survivors' future childbearing. Two studies explored the decisions concerning fertility preservation [35, 36]. Among the three remaining studies each concentrated on a different treatment-related decision such as: the decision to undergo trachelectomy for cervical cancer [38, 39], the decision to undergo chemotherapy for breast cancer [21], and finally one study did not specify the type of treatment received by the participants [64].

Fertility concerns affected the decision about treatment in 29% of breast cancer survivors [21] and in 13% of mixed female cancer group [64]. This was more of a case in women who wanted children, had prior difficulty conceiving, and recalled severe depression prior to diagnosis [21] as well as younger, unmarried women who had no successful pregnancies prior to cancer [64]. Additionally, Partridge et al. [21] analysed the kind of risks and benefits women were willing to accept given that chemotherapy could impair their fertility. Women who were more concerned about their reproductive potential required greater recurrence risk reduction and were less likely to accept higher risk of infertility due to chemotherapy compared to their less concerned counterparts.

Two publications from the same dataset by Carter et al. [38] and Carter et al. [39] examined patients' reasons to undergo radical trachelectomy (RT). The most frequently cited reason was preservation of childbearing (97% of participants in the preliminary report [38] and 55% of participants in the final report [39]), followed by conversations with doctors (41% and 36% in the preliminary [38] and full report [39] respectively), family or future fertility options (41%, [38]), personal factors (28%, [38]) and research (17%, [39]). The full report [39] additionally examined the reasons for undergoing radical hysterectomy (RH) and found that 46% of patients decided upon this type of treatment following doctor's recommendations, 25% because of concerns about survival and another 25% because they felt it was the best or the only available option. A significant difference between the RT and RH groups emerged, showing that 43% of patients in the RH group versus only 7% of patients in the RT group had enough time to complete their families.

Letourneau et al. [35] and Peate et al. [36] concentrated on fertility preservation among cancer survivors. The former study reported several factors associated with pursuing FP procedures, mainly: the age at diagnosis, desire for future children, the number of children at diagnosis, and education level. The latter study found that the intention to undergo FP was related to the importance women attached to fertility information and attitudes towards FP [36]. Additionally, women who had better knowledge about fertility issues related to cancer presented significantly lower decisional conflict concerning FP (less delay in making decision and less uncertainty about the implementation of the choice) than women who had less knowledge about the topic [36].

Additional articles

Among the five articles that has just missed one of the inclusion criteria (age or type of diagnosis), two were related to the first objective of the review [31, 66], whereas 3 were related to the third objective [32, 33, 67]. In general, the results from these studies were in line with the results from the studies that met all the inclusion criteria.

The studies by Gershenson et al. [66] and Carter et al. [31] examined the impact of fertility issues on sexual functioning and depressive symptoms, respectively. Gershenson et al. [66] compared ovarian cancer patients who had undergone fertility sparing surgery to those who had had radical surgery and found that the latter group had a significantly greater sexual discomfort. Carter et al. [31] examined how distress caused by infertility secondary to cancer was associated with depressive symptoms in a sample of gynaecological cancer patients. They found that higher levels of distress were strongly related to depression as measured by CES-D.

Studies related to the third objective of this review all explored pregnancy-related decisions. In a study of a breast cancer population, Ganz et al. [32] found that 7% were attempting to conceive and 17% did manage to get pregnant post-cancer. Similarly, 18% of women reported getting pregnant post-diagnosis in a study of a mixed cancer population [67]. Ganz et al. [32] reported that the desire for children diminished, with 20% of women wanting children pre-diagnosis and only 11% post-diagnosis. However, in a study by Schover et al. [67], 47% of women wanted pregnancy in the future. Sait [33] reported that 44% of the ovarian cancer participants claimed that cancer had not changed their desire to have children. Finally, the factors that could affect the decisions about pregnancy were child's or mother's health. 61% of ovarian cancer patients worried about the possible impact of their disease and treatment on offspring and 15% were anxious about complications or malformations in children [33].Risk of cancer recurrence and worry about pregnancy complications were mentioned by 17% and 13 % of participants respectively in a study by [67].

Discussion

The aim of the current review was to investigate fertility and parenthood issues experienced by young female cancer survivors.

The first objective of this review was to synthesise the evidence for the impact of cancer treatment-related fertility issues in reproductive age women on their psychological well-being. The findings suggest that fertility issues related to cancer treatment can indeed affect women's psychological well-being; however, this depends both on the outcome of interest and also the definitions of fertility issues across the studies.

Worries about pregnancy were present in both breast and cervical cancer survivors [38, 42, 43]. In the group of breast cancer patients this may be due to uncertainty about fertility status after chemotherapy since it is known to diminish fertility. Its effect depends on multiple factors (type of regimen, dose, and age of the patient) [8, 9] and even though methods exist to assess ovarian reserve in patients (and by proxy their fertility potential) these are not systematically used [8]. Therefore, patients cannot be sure about their reproductive potential, unless they get pregnant. Patients with cervical cancer treated with fertility sparing surgery might still worry about future pregnancy since this procedure is known to cause cervical stenosis (the narrowing of the cervical canal), scarring, and changes to the normal anatomy of the cervix which can all lead to infertility [68]. It can also result in pregnancy complications such as pregnancy loss or premature delivery [68, 69].

There was some evidence that depressive symptoms were present among gynaecological cancer patients [39, 45] but they did not seem to differ by treatment modality (fertility sparing versus radical surgery)

[39, 44]. However, self-reported distress or concerns related to fertility issues were associated with more depressive symptoms [31, 46]. A similar pattern emerged from the studies looking at QoL as an outcome. Where fertility issues were conceptualised objectively – as prolonged amenorrhea or radical treatment, they did not correlate with QoL [39, 47]. However, where self-report measures assessing reproductive potential were used, fertility issues were significantly related to QoL [48-50]. Holton et al. [25] systematic review of childbearing concerns and information needs of women with chronic non-communicable health conditions suggests that reproductive issues can influence the quality of life and add to depressive symptoms in this group of women, yet they do not make a distinction between the subjectively and objectively defined fertility issues.

Studies examining sexual functioning delivered mixed results which depended to some extent on the measurement tool used [49]. Yet, similar to the findings on depressive symptoms and QoL, sexual functioning tended to be associated more with self-reported level of fertility concerns [48-50] than objectively defined infertility [39]. Nonetheless, patients, despite the treatment they had received, reported impaired sexual functioning [39].

These results may suggest that depressive mood and QoL of young women who were treated for cancer do not seem to be related to their objective fertility status but rather to the perception they have of their reproductive potential. This is in line with Leventhal's Common Sense Model of Illness [70, 71] which suggests that it is not the objective characteristics of a particular illness but the way individuals conceptualise them that may affect the way they psychologically respond to illness. One of the concepts studied within the context of psycho-oncology, fear of cancer recurrence, showed a similar pattern. According to a recent review by Simard et al. [72], these fears do not seem to be associated with the objective characteristics of the disease such as cancer type, stage or treatment but rather with physical symptoms and various psychological factors.

Since objectively defined fertility status does not seem to be related to psychological well-being as even women who underwent fertility sparing procedures present with psychological issues, fertility-related interventions may play an important role in comprehensive cancer care for young women. The second objective of this review was to look at such interventions and their influence on women's psychological well-being. The scarce evidence from the literature points to beneficial effect of fertility-related interventions. Outcomes specifically related to decision making such as decisional regret and decisional conflict improved when patients were provided with the decision aid or counselled by a fertility specialist [34, 37]. Particularly for decision aids, evidence shows that they reduce decisional conflict related to the feelings of being uninformed or unsure about personal values that may affect the decision [73]. They also stimulate patients to be more active in their

treatment-related decision-making process [73]. Patients may not always be interested in independently deciding upon their treatment [74-76]; however, the literature shows that most of the time they want to be informed about their options [77-79]. This allows individuals to gain control over their life, promotes participation in treatment and increases compliance, reduces anxiety, and also creates realistic expectations about the future [80, 81]. Two systematic reviews targeting breast cancer survivors [26, 27] and one including women with variable chronic non-communicable diseases [25] explored their information needs concerning fertility and found that women wanted information about fertility; however only 34% to 72% across different studies reported having had a conversation about fertility with their physician. Especially women without children and those with a high desire for future children express the importance of fertility-related information since it might be a factor that plays a role in treatment decision-making [27].

Counselling, online support, and finally fertility preservation all seemed to have improved patients' quality of life. Online interventions might be a promising way of delivering support especially to younger cancer survivors. The World Wide Web is a fast growing resource to which particularly younger people turn to in order to find information concerning their health [82, 83]. They also seek peer support via social media [84] or online forums [85]. Likewise, researchers have noticed the benefits of the Internet and a variety of interventions have been designed and delivered online for a range of cancer-related problems [86-90].

Out of all the medical options, fertility preservation treatment not only empowers young women with knowledge conveyed during fertility consultation but also offers a real possibility of having children after the cessation of cancer treatment. As suggested by the American Society of Clinical Oncology [15, 16] as well as National Institute for Health and Care Excellence guidelines [91], all cancer patients in their reproductive years should be counselled concerning the effect of cancer on fertility and where possible, offered FP treatment. This is important since the qualitative evidence shows that patients value childbearing opportunity post-cancer because it gives them the sense of normality, reconnects them with peers and motivates them to look forward to the future [2-6]. Nonetheless, there exist several barriers to discussing fertility with young patients [18, 20, 92] which may in turn affect who gets referred to fertility specialists and undergoes FP.

The third objective of this review was to look at the reproductive decisions in young female cancer survivors. Two studies that looked at predictors of the uptake of FP treatment [34, 37] indicated that several factors exist associated with pursuing FP, including younger age, desire for children, not having children, level of education, and also attitudes towards FP. Whether some of these factors emerged because of the way clinicians selected patients who should be referred to FP or whether effectively younger and childless women

are more likely to pursue FP remains unexplained. Some clinicians may be reluctant to refer their patients to FP treatment which results from their relative lack of knowledge and where to refer patients [20] as well as its relative novelty [93]. Nonetheless, other techniques can be used to spare fertility in cancer patients. Radical trachelectomy for cervical cancer is one of them. This is a choice for patients who were diagnosed with cancer in early stages. As the evidence suggests, young cervical cancer patients report a desire to preserve their fertility as a main reason to undergo this type of treatment [39, 38]. Fertility also seemed to affect decisions concerning chemotherapy for breast cancer with women who wanted to preserve their childbearing potential being less likely to accept chemotherapy [21].

Surviving cancer diagnosis, avoiding cancer recurrence but also preserving one's reproductive potential, is challenging. Often these decisions are made under substantial uncertainty regarding the outcome (more radical treatment that could impair fertility does not necessarily prevent recurrence nor guarantee higher odds of survival in carefully selected groups of patients [94]). According to the prospect theory [95], which describes making decisions under risk and uncertainty, the value of an outcome of a decision is not absolute. This theory purports that in the editing stage of the decision-making process one sets a reference value and the potential outcomes are coded as losses or gains relative to the reference point. Subsequently, in the evaluation phase, the probability of each possible outcome is assessed and these probabilities are weighed against the values. The decision is finally made based on the outcomes' final utilities conceptualised as subjective values. Treadwell, Lenert [96] who applied the prospect theory to health values explain that changes in health states are relative to an individual baseline level of health. If this reference level, even in the context of cancer involves intact reproductive health and the subjective value attached to it is high, then a decision to undergo fertility sparing treatment might be a reasonable one. Similar reasoning might be applied to decisions about pregnancy after cancer treatment. If pregnancy and expanding one's family is highly valued, the decision to conceive might be made despite factors that appear in the literature such as worries about child's and mother's health or fear of cancer recurrence [42, 50, 58, 62-64]. As mentioned earlier, pregnancy subsequent to cancer might be related to cancer survivors' well-being. Adams et al. [23] in their review of qualitative literature focusing on experiences of young breast cancer survivors suggest that being able to achieve a pregnancy after cancer is part of the normalising process which allows women to continue with their everyday lives after diagnosis. In another review exploring attitudes towards childbearing among breast cancer survivors, Goncalves et al. [24] also point to beneficial effects of having children after cancer such as regaining hope about the future, being motivated to stay healthy and alive, and reconnecting with peers. On the other hand, Adams et al. [23], Goncalves et al. [24] ,

and Peate et al. [27] underline that many women change their reproductive decisions and abandon their wish for children because of multiple fears they experience with regard to their own health and the health of future children. Yet, the medical literature suggests that pregnancy after breast does not increase mortality or the risk of cancer recurrence [97-99], nor does it result in foetal malformations [100, 101]. This needs to be brought to patients' attention given that these are the most frequently mentioned factors that might influence decisions about conception post-cancer. As noted earlier, radical trachelectomy may indeed result in perinatal complications, however, with close obstetrical follow-up, a successful pregnancy is possible [69].

On the whole, the results related to the third objective suggest that cancer can have mixed effect on childbearing subsequent to cancer. For the majority of the patients, there was no change in their desire for children; however, the minority that reported the decrease in their desire for children should not be neglected. It is especially important for the latter group that information about risks associated with reproduction post-cancer should be clearly presented in order for them to be able to make informed decisions about their fertility.

Limitations

The above conclusions should be interpreted accounting for both the limitations of the included studies as well as those of the review.

In general, across all the included studies, several weaknesses have been identified. These include small sample sizes, homogeneity of participants within the studies and homogeneity of locations across the studies (with 21 studies having been conducted in the US, 2 in Australia and 1 in each of the following countries: France, Italy, United Kingdom, Israel and Saudi Arabia), predominantly cross sectional design, heterogeneity of outcome measures, and the lack of clear definition of fertility issues. The quality checklist [40] was used to assess the quality of each included study. The overall quality scores ranged from 44.4% to 100% (55.6% to 100% for studies related to objective 1; 68.2% to 90.9% for studies related to objective 2; 44.4% to 100% for studies related to objective 3, and 61.6% to 90.9% for additional articles). The median quality scores for studies pertaining to objectives 1, 2, 3 and for additional studies were 86.4%, 77%, 81.85% and 72.7% respectively. This suggests that on the whole the quality of the included studies was acceptable; however, caution should be applied especially when considering the conclusions related to objective 1.

Three studies pertaining to objective 1 that received the lowest scores: 55.6%, 60% and 66.7% [38, 43, 45] all looked at the psychological well-being of cervical cancer patients and presented descriptive statistics based on very small sample sizes (20-33 participants). All of them defined fertility issues as the provision of

fertility sparing or compromising treatment. This might have introduced bias into our findings that when fertility issues are defined in an objective manner, they do not impact on well-being. However, four other studies of acceptable quality (>80%) which also conceptualised fertility in objective terms, continue to support our conclusions.

Two of the above studies [38, 43] and two additional ones [61, 64] that scored 44.4% and 65% respectively, were included in the summary of the results for objective 3. These results were to a certain extent balanced by the remaining 14 studies of satisfactory quality (>70%) that pertained to objective 3.

Although the quality of the studies related to objective 2 was generally good, the small number of studies (n=4) prevents from drawing firm conclusions.

The number of participants ranged from 20 to 1088 (median 71) across studies related to objective 1, from 29 to 1041 (median 106) across studies related to objective 2 and from 20 to 1088 (median 102) across studies related to objective 3. Given the large numbers of predictors and outcomes looked at in most of the studies, there exists a possibility they might have been underpowered to detect significant associations or changes in outcomes. Additionally, the vast majority of the studies did not provide the information about the estimated sample size needed to power the calculations. This might have biased the results of the individual studies and thus the conclusions of this review.

The samples in most of the studies consisted of well-educated, predominantly white women with relatively high income, which is an issue in this type of research in general. Also, the majority of the studies (81.2%, 75%, 72.2% and 80% for objectives 1, 2, 3 and additional studies, respectively) were conducted in the United States. This undermines the generalizability of the conclusions of this review, especially since the problems with fertility and attitudes towards parenting are strongly dependent on socio-cultural norms [102].

The majority of the studies pertaining to objectives 1 and 3 (63.6% and 66.7%, respectively) used cross-sectional design. This allows drawing conclusions about associations between fertility issues and well-being; however, makes the inferences about causality problematic. For objective 2, three studies were interventions while one used the exposure study methodology [34]. The latter had the biggest sample size (n=918) and also looked at many outcomes of interest, which given the overall small number of studies, might have influenced the conclusions.

The heterogeneity of outcome measures made comparing the results of individual studies problematic, since different instruments, even when measuring the same constructs, might have been based on slightly different definitions of these constructs (e.g. the quality of life).

Finally, the definitions of fertility issues differed between the studies. Even within the categories that were adopted for the purpose of this review (see Review objectives), the definitions were not homogenous. Some of the studies made the definition explicit, while others did not provide the definition at all [42]. This means that we cannot be sure if the results included in this review all tapped into the same construct of fertility issues.

Also, this review only looked at the published literature that was searched via electronic databases. This means that due to publication bias, we might have failed to include studies presenting insignificant results. The exclusion of the articles written in non-English languages might have additionally contributed to the omission of relevant papers and thus introduced bias. However, only 4% of all the articles judged as potentially relevant based on their title were published in a language other than English. Finally, we have not looked at how different healthcare systems across the countries where the studies have been conducted, could potentially influence our findings. Treatment-related decisions, especially pursuing FP can effectively be constrained in the countries where FP is not covered by the health insurance. The studies included in this review that examined the decisions about FP did not specifically investigate costs as a barrier to pursuing FP. In the study by Letourneau et al. [35], income was not related to pursuing fertility preservation, however more research explicitly analysing how costs can influence FP-related decisions is needed.

Conclusions

This review highlights the importance of fertility issues in a population of younger cancer survivors. Overall the evidence suggests that:

- Perception of one's own reproductive potential might be more powerful in affecting women's psychological well-being than the objective fertility status.
- Empowering women with knowledge concerning their fertility after cancer seems to have beneficial effects on their QoL and decision-specific outcomes. Offering fertility preservation to young cancer patients is an important part of the comprehensive cancer care.
- Cancer can have mixed effect on reproductive decisions in young female cancer survivors. Factors that affected women's decisions encompassed mostly medical concerns about the offspring's and mother's health. Yet the evidence from the medical research does not seem to warrant such fears.

The above conclusions should, however, be treated with caution due to multiple limitations of the studies included in the review as well as the limitations of the review itself.

Funding

Aleksandra Sobota's PhD is funded by the Danuta Richardson Medical Scholarship. This systematic review has not received any additional funding.

Conflict of interest

Aleksandra Sobota declares that she has no conflict of interest.

Gozde Ozakinci declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

No animal or human studies were carried out by the authors for this article.

References

1. Aziz NM, Rowland JH. Trends and advances in cancer survivorship research: challenge and opportunity. Semin Radiat Oncol. 2003; doi: 10.1016/S1053-4296(03)00024-9

2. Dow KH. Having children after breast cancer. Cancer Pract. 1994;2(6):407-13.

3. Siegel K, Gorey E, Gluhoski V. Pregnancy decision making among women previously treated for breast cancer. J Psychosoc Oncol. 1997; doi:10.1300/j077v15n01_03

4. Siegel K, Gluhoski V, Gorey E. Age-related distress among young women with breast cancer. J Psychosoc Oncol. 1999; doi:10.1300/J077v17n01_01

5. Connell S, Patterson C, Newman B. A qualitative analysis of reproductive issues raised by young Australian women. Health Care Women Int. 2006; doi:10.1080/07399330500377580

6. Yee S, Abrol K, McDonald M, Tonelli M, Liu KE. Addressing Oncofertility Needs: Views of Female Cancer Patients in Fertility Preservation. J Psychosoc Oncol. 2012; doi:10.1080/07347332.2012.664257.

7. Mean age of mothers at first childbirth. In: OECD Family Database. Organisation for Economic Co-operation and Development. 2012. http://www.oecd.org/social/soc/SF2.3%20Mean%20age%20of%20mother%20at%20first%20childbirth%20-%20updated%20240212.pdf. Accessed 3 Mar 2014.

8. Wallace WH, Anderson RA, Irvine DS. Fertility preservation for young patients with cancer: who is at risk and what can be offered? Lancet Oncol. 2005; doi: 10.1016/S1470-2045(05)70092-9

9. Knobf MT. Reproductive and hormonal sequelae of chemotherapy in women. Premature menopause and impaired fertility can result, effects that are especially disturbing to young women. Am J Nurs. 2006;106(3 Suppl):60-5.

10. Duffy C, Allen S. Medical and psychosocial aspects of fertility after cancer. Cancer J. 2009; doi:10.1097/PPO.0b013e3181976602

11. Lee MC, Gray J, Han HS, Plosker S. Fertility and reproductive considerations in premenopausal patients with breast cancer. Cancer Control. 2010;17(3):162-72.

12. Barthelmes L, Gateley CA. Tamoxifen and pregnancy. The Breast. 2004; doi: 10.1016/j.breast.2004.08.007

13. Thewes B, Meiser B, Taylor A, Phillips KA, Pendlebury S, Capp A et al. Fertility- and menopause-related information needs of younger women with a diagnosis of early breast cancer. J Clin Oncol. 2005; doi: 10.1200/JCO.2005.07.773

14. Breast Cancer Treatment (PDQ®). National Cancer Institute. 2013. http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional/page6#Section_95. Accessed 7 Feb 2013

15. Lee SJ, Schover LR, Partridge AH, Patrizio P, Wallace WH, Hagerty K et al. American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients. J Clin Oncol. 2006; doi:10.1200/jco.2006.06.5888

16. Loren AW, Mangu PB, Beck LN, Brennan L, Magdalinski AJ, Partridge AH et al. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013; doi:10.1200/jco.2013.49.2678

17. Klock SC, Zhang JX, Kazer RR. Fertility preservation for female cancer patients: early clinical experience. Fertil Steril. 2010; doi:10.1016/j.fertnstert.2009.03.028

18. Quinn GP, Vadaparampil S, Gwede C, Miree C, King LM, Clayton HB et al. Discussion of fertility preservation with newly diagnosed patients: oncologists' views. J Cancer Surviv. 2007; doi:10.1007/s11764-007-0019-9

19. Duffy C, Allen S, Clark M. Discussions Regarding Reproductive Health for Young Women With Breast Cancer Undergoing Chemotherapy. J Clin Oncol. 2005; doi:10.1200/jco.2005.01.134

20. Quinn GP, Vadaparampil ST, Bell-Ellison BA, Gwede CK, Albrecht TL. Patient–physician communication barriers regarding fertility preservation among newly diagnosed cancer patients. Soc Sci Med. 2008; doi: 10.1016/j.socscimed.2007.09.013

21. Partridge AH, Gelber S, Peppercorn J, Sampson E, Knudsen K, Laufer M et al. Web-based survey of fertility issues in young women with breast cancer. J Clin Oncol. 2004; doi:10.1200/jco.2004.01.159

22. Partridge AH, Ruddy KJ. Fertility and adjuvant treatment in young women with breast cancer. The Breast. 2007; doi: 10.1016/j.breast.2007.07.029

23. Adams E, McCann L, Armes J, Richardson A, Stark D, Watson E et al. The experiences, needs and concerns of younger women with breast cancer: a meta-ethnography. Psychooncology. 2011; doi: 10.1002/pon.1792

24. Goncalves V, Sehovic I, Quinn G. Childbearing attitudes and decisions of young breast cancer survivors: a systematic review. Hum Reprod Update. 2014; doi: 10.1093/humupd/dmt039

25. Holton S, Kirkman M, Rowe H, Fisher J. The childbearing concerns and related information needs and preferences of women of reproductive age with a chronic, noncommunicable health condition: a systematic review. Womens Health Issues. 2012; doi: 10.1016/j.whi.2012.08.001

26. Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. J Natl Cancer Inst. 2012; doi:10.1093/jnci/djr541

27. Peate M, Meiser B, Hickey M, Friedlander M. The fertility-related concerns, needs and preferences of younger women with breast cancer: a systematic review. Breast Cancer Res Treat. 2009; doi: 10.1007/s10549-009-0401-6

28. Wenzel L, Dogan-Ates A, Habbal R, Berkowitz R, Goldstein DP, Bernstein M et al. Defining and measuring reproductive concerns of female cancer survivors. J Natl Cancer Inst Monogr. 2005; doi:10.1093/jncimonographs/lgi017

29. Thomas F, Renaud F, Benefice E, De Meeus T, Guegan J-F. International variability of ages at menarche and menopause: patterns and main determinants. Hum Biol. 2001:271-90.

30. Dargent D, Brun JL, Roy M, Remy I. Pregnancies following radical tracheletcomy for invasive cervical cancer. Gynecol Oncol. 1994; doi: 10.1006/gyno.1994.1020

31. Carter J, Chi DS, Brown CL, Abu-Rustum NR, Sonoda Y, Aghajanian C et al. Cancer-related infertility in survivorship. Int J Gynecol Cancer. 2010; doi:10.1111/IGC.0b013e3181bf7d3f

32. Ganz PA, Greendale GA, Petersen L, Kahn B, Bower JE. Breast cancer in younger women: reproductive and late health effects of. J Clin Oncol. 2003; doi:10.1200/jco.2003.04.196

33. Sait KH. Conservative treatment of ovarian cancer Safety, ovarian function preservation, reproductive ability, and emotional attitude of the patients in Saudi Arabia. Saudi Med J. 2011;32(9):913-8.

34. Letourneau JM, Ebbel EE, Katz PP, Katz A, Ai WZ, Chien AJ et al. Pretreatment fertility counseling and fertility preservation improve quality of life in reproductive age women with cancer. Cancer. 2012; doi:10.1002/cncr.26459

35. Letourneau JM, Smith JF, Ebbel EE, Craig A, Katz PP, Cedars MI et al. Racial, socioeconomic, and demographic disparities in access to fertility preservation in young women diagnosed with cancer. Cancer. 2012; doi:10.1002/cncr.26649

36. Peate M, Meiser B, Friedlander M, Zorbas H, Rovelli S, Sansom-Daly U et al. It's Now or Never: Fertility-Related Knowledge, Decision-Making Preferences, and Treatment Intentions in Young Women With Breast Cancer-An Australian Fertility Decision Aid Collaborative Group Study. J Clin Oncol. 2011;. doi:10.1200/jco.2010.31.2462

37. Peate M, Meiser B, Cheah BC, Saunders C, Butow P, Thewes B et al. Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-stage breast cancer. Br J Cancer. 2012; doi:10.1038/bjc.2012.61

38. Carter J, Sonoda Y, Abu-Rustum NR. Reproductive concerns of women treated with radical trachelectomy for cervical cancer. Gynecol Oncol. 2007; doi:10.1016/j.ygyno.2006.10.059

39. Carter J, Sonoda Y, Baser RE, Raviv L, Chi DS, Barakat RR et al. A 2-year prospective study assessing the emotional, sexual, and quality of life concerns of women undergoing radical trachelectomy versus radical hysterectomy for treatment of early-stage cervical cancer. Gynecol Oncol. 2010; doi:10.1016/j.ygyno.2010.07.016

40. Kmet L, Lee R, Cook L. Standard quality assessment criteria for evaluating primary research papers from a variety of fields. In: HTA Initiative 13. 2004. http://www.ihe.ca/documents/HTA-FR13.pdf. Accessed 7 Feb 2014.

41. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. 2005;37(5):360-3.

42. Avis NE, Crawford S, Manuel J. Psychosocial problems among younger women with breast cancer. Psychooncology. 2004; doi:10.1002/pon.744

43. Carter J, Raviv L, Sonoda Y, Chi DS, Abu-Rustum NR. Recovery Issues of Fertility-Preserving Surgery in Patients With Early-Stage Cervical Cancer and a Model for Survivorship The Physician Checklist. Int J Gynecol Cancer. 2011; doi:10.1097/IGC.0b013e3182017989

44. Bisseling K, Kondalsamy-Chennakesavan S, Bekkers RLM, Janda M, Obermair A. Depression, anxiety and body image after treatment for invasive stage one epithelial ovarian cancer. Aust N Z J Obstet Gynaecol. 2009; doi:10.1111/j.1479-828X.2009.01074.x

45. Carter J, Rowland K, Chi D, Brown C, Abu-Rustum N, Castiel M et al. Gynecologic cancer treatment and the impact of cancer-related infertility. Gynecol Oncol. 2005; doi:10.1016/j.ygyno.2004.12.019

46. Gorman JR, Malcarne VL, Roesch SC, Madlensky L, Pierce JP. Depressive symptoms among young breast cancer survivors: the importance of reproductive concerns. Breast Cancer Res Treat. 2010; doi:10.1007/s10549-010-0768-4

47. Ganz PA, Land SR, Geyer CE, Cecchini RS, Costantino JP, Pajon ER et al. Menstrual History and Quality-of-Life Outcomes in Women With Node-Positive Breast Cancer Treated With Adjuvant Therapy on the NSABP B-30 Trial. J Clin Oncol. 2011; doi:10.1200/jco.2010.29.7689

48. Mancini J, Rey D, Preau M, Malavolti L, Moatti JP. Infertility induced by cancer treatment: inappropriate or no information provided to majority of French survivors of cancer. Fertil Steril. 2008; doi:10.1016/j.fertnstert.2007.08.064

49. Wenzel L, DeAlba I, Habbal R, Kluhsman BC, Fairclough D, Krebs LU et al. Quality of life in long-term cervical cancer survivors. Gynecol Oncol. 2005; doi:10.1016/j.ygyno.2005.01.010

50. Canada AL, Schover LR. The psychosocial impact of interrupted childbearing in long-term female cancer survivors. Psychooncology. 2012; doi:10.1002/pon.1875

51. Meneses K, McNees P, Azuero A, Jukkala A. Evaluation of the Fertility and Cancer Project (FCP) among young breast cancer survivors. Psychooncology. 2010; doi:10.1002/pon.1648

52. Reh AE, Lu L, Weinerman R, Grifo J, Krey L, Noyes N. Treatment outcomes and quality-of-life assessment in a university-based fertility preservation program: Results of a registry of female cancer patients at 2 years. J Assist Reprod Genet. 2011; doi:10.1007/s10815-011-9559-z

53. The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med. 1998;28(03):551-8.

54. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. J Pers Assess. 1985;49(1):71-5.

55. Brazier J-, Harper R, Jones N, O'cathain A, Thomas K, Usherwood T et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. Br Med J. 1992;305(6846):160.

56. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. J Clin Oncol. 1997;15(3):974-86.

57. Brehaut JC, O'Connor AM, Wood TJ, Hack TF, Siminoff L, Gordon E et al. Validation of a decision regret scale. Med Decis Making. 2003; doi: 10.1177/0272989X03256005

58. Zanagnolo V, Sartori E, Trussardi E, Pasinetti B, Maggino T. Preservation of ovarian function, reproductive ability and emotional attitudes in patients with malignant ovarian tumors. Eur J Obstet Gyn R B. 2005; doi:10.1016/j.ejogrb.2005.04.010

59. Huyghe E, Sui D, Odensky E, Schover LR. Needs Assessment Survey to Justify Establishing a Reproductive Health Clinic at a Comprehensive Cancer Center. J Sex Med. 2009; doi:10.1111/j.1743-6109.2008.01005.x

60. Braun M, Hasson-Ohayon I, Perry S, Kaufman B, Uziely B. Motivation for giving birth after breast cancer. Psychooncology. 2005; doi:10.1002/pon.844

61. Patel A, Sreedevi M, Malapati R, Sutaria R, Schoenhage MB, Patel AR et al. Reproductive health assessment for women with cancer: a pilot study. Am J Obstet Gynecol. 2009; doi:10.1016/j.ajog.2009.04.021

62. Atkinson TM, Noce NS, Hay J, Rafferty BT, Brady MS. Illness-Related Distress in Women with Clinically Localized Cutaneous Melanoma. Ann Surg Oncol. 2012; doi:10.1245/s10434-012-2635-5

63. Rippy EE, Karat IF, Kissin MW. Pregnancy after breast cancer: the importance of active counselling and planning. Breast. 2009; doi:10.1016/j.breast.2009.08.003

64. Scanlon M, Blaes A, Geller M, Majhail NS, Lindgren B, Haddad T. Patient Satisfaction with Physician Discussions of Treatment Impact on Fertility. J Cancer. 2012; doi:10.7150/jca.4408

65. Gorman JR, Roesch SC, Parker BA, Madlensky L, Saquib N, Newman VA et al. Physical and mental health correlates of pregnancy following breast cancer. Psychooncology. 2010; doi:10.1002/pon.1614

66. Gershenson DM, Miller AM, Champion VL, Monahan PO, Zhao QQ, Cella D et al. Reproductive and sexual function after platinum-based chemotherapy in long-term ovarian germ cell tumor survivors: A gynecologic oncology group study. J Clin Oncol. 2007; doi:10.1200/jco.2006.08.4590

67. Schover LR, Rybicki LA, Martin BA, Bringelsen KA. Having children after cancer - A pilot survey of survivors' attitudes and experiences. Cancer. 1999; doi:10.1002/(sici)1097-0142(19990815)86:4<697::aid-cncr20>3.0.co;2-j

68. Boss EA, van Golde RJ, Beerendonk CC, Massuger LF. Pregnancy after radical trachelectomy: a real option? Gynecol Oncol. 2005; doi:10.1016/j.ygyno.2005.07.071

69. Jolley JA, Battista L, Wing DA. Management of pregnancy after radical trachelectomy: case reports and systematic review of the literature. Am J Perinatol. 2007; doi: 10.1055/s-2007-986680

70. Leventhal H, Meyer D, Nerenz D. The Common Sense Representation of Illness Danger. In: Rachman S, editor. Contributions to medical psychology. Oxford: Pergamon Pr.; 1980. p. 7-30.

71. Leventhal H, Leventhal EA, Contrada RJ. Self-regulation, health, and behavior: A perceptual-cognitive approach. Psychology & Health. 1998; doi: 10.1080/08870449808407425

72. Simard S, Thewes B, Humphris G, Dixon M, Hayden C, Mireskandari S et al. Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. J Cancer Surviv. 2013; doi:10.1007/s11764-013-0272-z

73. Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2014(1). doi:10.1002/14651858.CD001431.pub4

74. Bruera E, Sweeney C, Calder K, Palmer L, Benisch-Tolley S. Patient Preferences Versus Physician Perceptions of Treatment Decisions in Cancer Care. J Clin Oncol. 2001;19(11):2883-5.

75. Degner LF, Sloan JA. Decision making during serious illness: What role do patients really want to play? J Clin Epidemiol. 1992; doi: 10.1016/0895-4356(92)90110-9

76. Degner LF, Kristjanson LJ, Bowman D, et al. Information needs and decisional preferences in women with breast cancer. JAMA. 1997; doi:10.1001/jama.1997.03540420081039

77. Blanchard CG, Labrecque MS, Ruckdeschel JC, Blanchard EB. Information and decision-making preferences of hospitalized adult cancer patients. Soc Sci Med. 1988; doi: 10.1016/0277-9536(88)90343-7

78. Gaston CM, Mitchell G. Information giving and decision-making in patients with advanced cancer: A systematic review. Soc Sci Med. 2005; doi: 10.1016/j.socscimed.2005.04.015

79. Jenkins V, Fallowfield L, Saul J. Information needs of patients with cancer: results from a large study in UK cancer centres. Br J Cancer. 2001; doi: 10.1054/bjoc.2000.1573

80. Mills ME, Sullivan K. The importance of information giving for patients newly diagnosed with cancer: a review of the literature. J Clin Nurs. 1999; doi: 10.1046/j.1365-2702.1999.00296.x

81. Street Jr RL, Makoul G, Arora NK, Epstein RM. How does communication heal? Pathways linking clinician–patient communication to health outcomes. Patient Educ Couns. 2009; doi: 10.1016/j.pec.2008.11.015

82. Gray NJ, Klein JD, Noyce PR, Sesselberg TS, Cantrill JA. Health information-seeking behaviour in adolescence: the place of the internet. Soc Sci Med. 2005; doi: 10.1016/j.socscimed.2004.08.010

83. Rideout V. Generation Rx.com. What are young people really doing online? Mark Health Serv. 2002;22(1):26-30.

84. Bender JL, Jimenez-Marroquin M-C, Jadad AR. Seeking support on facebook: a content analysis of breast cancer groups. J Med Internet Res. 2011; doi: 10.2196/jmir.1560

85. Davison KP, Pennebaker JW, Dickerson SS. Who talks? The social psychology of illness support groups. Am Psychol. 2000; doi: 10.1037/0003-066X.55.2.205

86. Gustafson DH, Wise M, McTavish F, Taylor JO, Wolberg W, Stewart J et al. Development and pilot evaluation of a computer-based support system for women with breast cancer. J Psychosoc Oncol. 1994; doi: 10.1300/J077V11N04_05

87. Gustafson DH, Hawkins R, Pingree S, McTavish F, Arora NK, Mendenhall J et al. Effect of computer support on younger women with breast cancer. J Gen Intern Med. 2001; doi: 10.1046/j.1525-1497.2001.016007435.x

88. Lieberman MA, Golant M, Giese-Davis J, Winzlenberg A, Benjamin H, Humphreys K et al. Electronic support groups for breast carcinoma. Cancer. 2003; doi: 10.1002/cncr.11145

89. van den Berg SW, Gielissen MF, Ottevanger PB, Prins JB. Rationale of the BREAst cancer e-healTH [BREATH] multicentre randomised controlled trial: an internet-based self-management intervention to foster adjustment after curative breast cancer by decreasing distress and increasing empowerment. BMC Cancer. 2012; doi:10.1186/1471-2407-12-394

90. Winzelberg AJ, Classen C, Alpers GW, Roberts H, Koopman C, Adams RE et al. Evaluation of an internet support group for women with primary breast cancer. Cancer. 2003; doi: 10.1002/cncr.11174

91. Treasure T, Bewley S, Bhattacharya S, Brian K, Child T, Davies M et al. Fertility: Assessment and treatment for people with fertility problems. In: NICE clinical guidelines. National Institute for Health and Care Excellence. 2013. http://publications.nice.org.uk/fertility-cg156/recommendations. Accessed 14 Mar 2014.

92. Quinn GP, Vadaparampil ST, Lee J-H, Jacobsen PB, Bepler G, Lancaster J et al. Physician Referral for Fertility Preservation in Oncology Patients: A National Study of Practice Behaviors. J Clin Oncol. 2009;27(35):5952-7. doi:10.1200/jco.2009.23.0250

93. Peddie VL, Porter MA, Barbour R, Culligan D, MacDonald G, King D et al. Factors affecting decision making about fertility preservation after cancer diagnosis: a qualitative study. BJOG. 2012; doi:10.1111/j.1471-0528.2012.03368.x

94. Dursun P, LeBlanc E, Nogueira MC. Radical vaginal trachelectomy (Dargent's operation): A critical review of the literature. Eur J Surg Oncol. 2007; doi: 10.1016/j.ejso.2006.11.021.

95. Kahneman D, Tversky A. Prospect theory: An analysis of decision under risk. Econometrica. 1979; doi: 10.2307/1914185

96. Treadwell JR, Lenert LA. Health values and prospect theory. Med Decis Making. 1999; doi: 10.1177/0272989X9901900313

97. Blakely LJ, Buzdar AU, Lozada JA, Shullaih SA, Hoy E, Smith TL et al. Effects of pregnancy after treatment for breast carcinoma on survival and risk of recurrence. Cancer. 2004; doi:10.1002/cncr.11929

98. Gelber S, Coates AS, Goldhirsch A, Castiglione-Gertsch M, Marini G, Lindtner J et al. Effect of pregnancy on overall survival after the diagnosis of early-stage breast cancer. J Clin Oncol. 2001;19(6):1671-5.

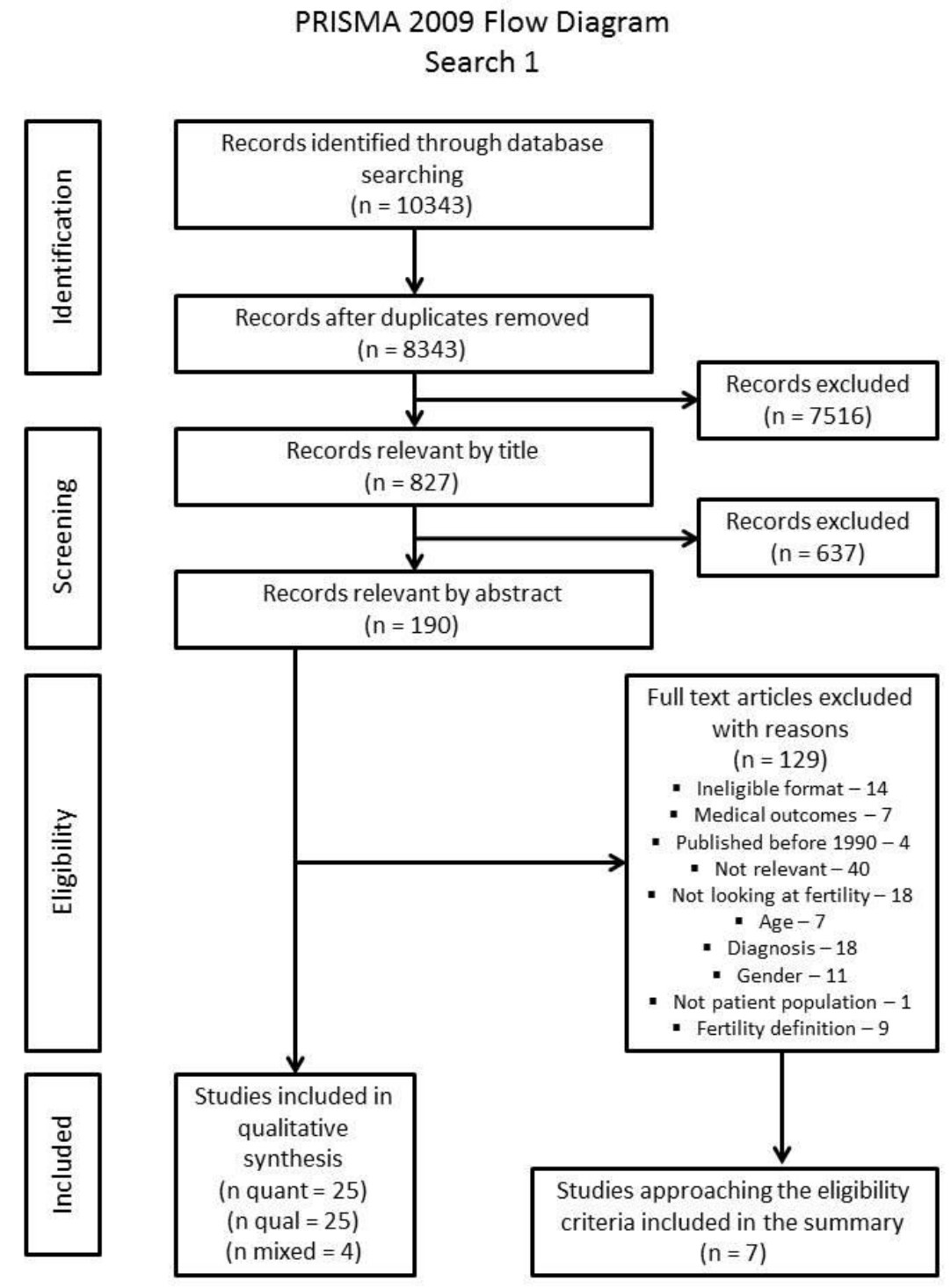
99. Ives A, Saunders C, Bulsara M, Semmens J. Pregnancy after breast cancer: population based study. Br Med J. 2007; doi:10.1136/bmj.39035.667176.55

100. Fosså SD, Magelssen H, Melve K, Jacobsen AB, Langmark F, Skjærven R. Parenthood in Survivors After Adulthood Cancer and Perinatal Health in Their Offspring: A Preliminary Report. J Natl Cancer Inst Monogr. 2005; doi:10.1093/jncimonographs/lgi019

101. Kenney LB, Nicholson HS, Brasseux C, Mills JL, Robison LL, Zeltzer LK et al. Birth defects in offspring of adult survivors of childhood acute lymphoblastic leukemia: A Childrens Cancer Group/National Institutes of Health report. Cancer. 1996; doi:10.1002/(SICI)1097-0142(19960701)78:1<169::AID-CNCR23>3.0.CO;2-X.

102. Hynie M, Burns LH. Cross-Cultural Issues in Infertility Counseling. In: Covington SN, Hammer BL, editors. Infertility Counseling A Comprehensive Handbook for Clinicians. Cambridge: Cambridge University Press; 2006. p. 61-82.

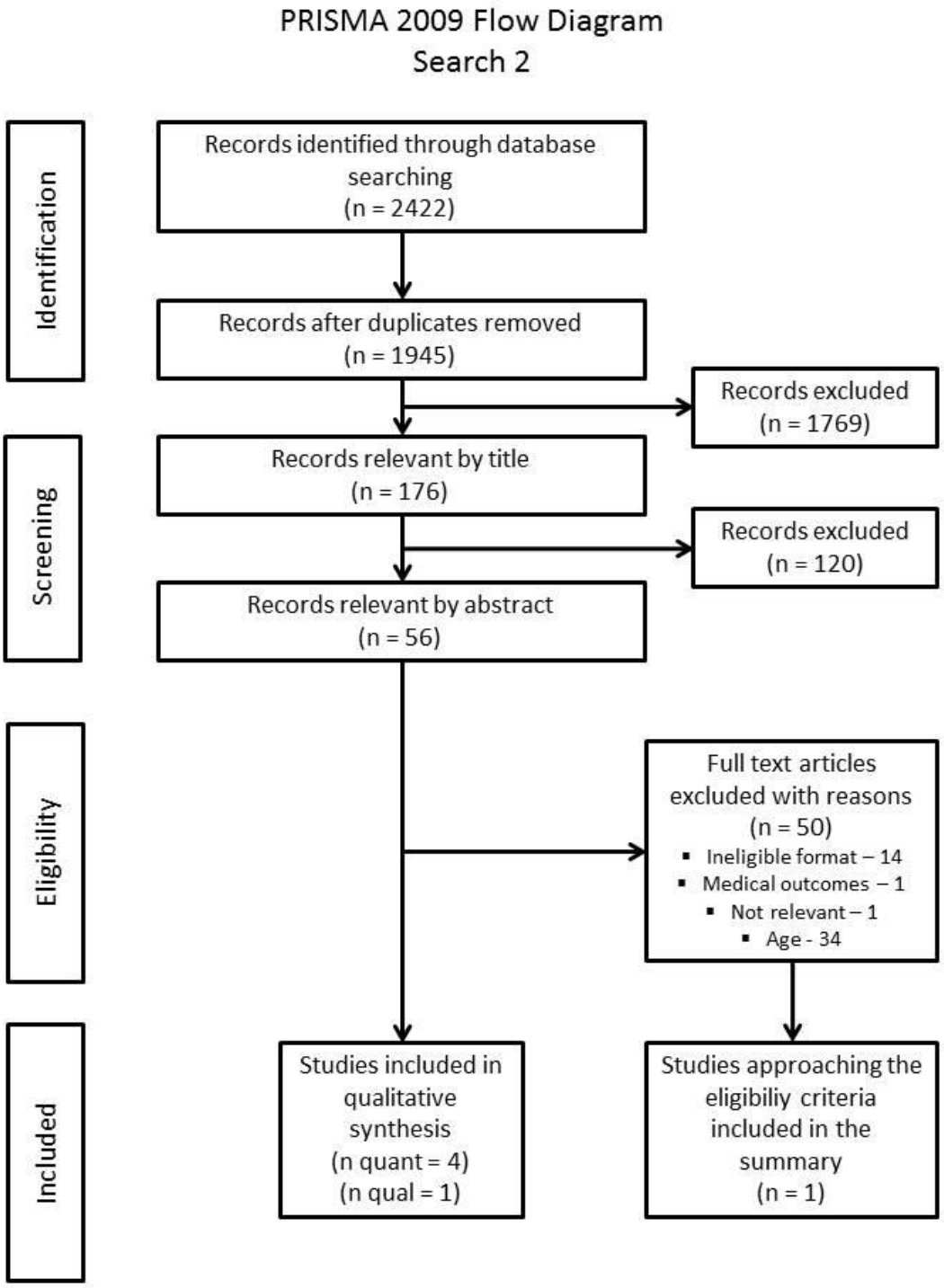
Appendix 2 – PRISMA Flowchart (Search 1)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting Items for *S*ystematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Appendix 3 – PRISMA Flowchart (Search 2)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting Items for *S*ystematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Appendix 4 – Quality assessment checklists ('QualSyst')

Table 1. Quality checklist for quantitative studies

Title: Which patients pursue fertility preservation treatments? A multicenter analysis of the predictors of fertility preservation in women with breast cancer **Authors:** Kim et al. **Year:** 2012	Yes (2)	Partially (1)	No (0)	N/A
1 Question / objective sufficiently described?		x		
2 Study design evident and appropriate?	x			
3 Method of subject/comparison group selection or source of information/input variables described and appropriate?		x		
4 Subject (and comparison group, if applicable) characteristics sufficiently described?	x			
5 If interventional and random allocation was possible, was it described?				x
6 If interventional and blinding of investigators was possible, was it reported?				x
7 If interventional and blinding of subjects was possible, was it reported?				x
8 Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias? means of assessment reported?	x			
9 Sample size appropriate?		x		
10 Analytic methods described/justified and appropriate?	x			
11 Some estimate of variance is reported for the main results?	x			
12 Controlled for confounding?		x		
13 Results reported in sufficient detail?	x			
14 Conclusions supported by the results?	x			
Result: 18/22 = 81.8%				

Table 2. Quality checklist for qualitative studies

Title: Addressing oncofertility needs: views of female cancer patients in fertility preservation **Authors:** Yee et al. **Year:** 2012	Yes (2)	Partially (1)	No (0)
1 Question / objective sufficiently described?	x		
2 Study design evident and appropriate?	x		
3 Context for the study clear?	x		
4 Connection to a theoretical framework / wider body of		x	

knowledge?			
5 Sampling strategy described, relevant and justified?		x	
6 Data collection methods clearly described and systematic?	x		
7 Data analysis clearly described and systematic?		x	
8 Use of verification procedure(s) to establish credibility?			x
9 Conclusions supported by the results?	x		
10 Reflexivity of the account?		x	
Result: 14/20 = 70%			

Appendix 5 – Summary table objective 1

Reference	Location	Definition of fertility issues (inferred)	Cancer diagnoses	Age range at diagnosis	Sample size and % of female 14-50 included	Method	Outcome and measure	Results	Quality assessment
Gorman, J.R. et al. (209)	US	uncertainty about fertility status (high level of fertility-related concerns)	Breast cancer (stage I-III)	26-40	n = 131 (100%)	Cross-sectional quantitative design	Reproductive concerns as measured by RCS	Two groups – high RCS score vs. low RCS score: **being < 35 at diagnosis** (19 (26.0) vs. 14 (24.1); p = 0.8); **irregular periods during or after treatment** (55 (75.3) vs. 40 (69.0); p = 0.42); **treatment-related ovarian damage** (17 (23.3) vs 5 (8.6); p = 0.03); **treatment-decision based on fertility preservation** (12 (16.4) vs. 3 (5.2); p = 0.05); **not preventing pregnancy after diagnosis** (44 (60.3) vs. 25 (43.1); p = 0.05); **wanted children before diagnosis** (48 (65.8) vs. 15 (25.9); p<0.0001); **wanted children after diagnosis** (27 (37.0) vs. 9 (15.0); p<0.01); **nulliparous at diagnosis** (33 (45.2) vs. 9 (15.5); p = 0.0003); **child born after diagnosis** (13 (17.8) vs. 2 (3.5); p = 0.01); **no children** (26 (35.6) vs. 8 (13.8); p = 0.005)	100%
Partridge, A.H. et al. (210)	US	Concern about infertility	Early stage breast cancer	18-40	n = 657 (100%)	Cross-sectional quantitative design	Concern about infertility (measure not specified)	Multivariate analysis – concern about fertility at diagnosis associated with: **wish to have more children** (OR = 120, p<0.0001); **prior number of pregnancies** (OR = 0.78, p = 0.01); **history of prior difficulty conceiving** (OR = 1.86, p = 0.08 for yes and OR = 3.15, p = 0.0001 for not applicable meaning that a women has not tried to conceive previously) controlled for age at diagnosis and stage. Non-significant variables: age at diagnosis, race, education, employment status, financial situation, comorbidity, anxiety of depression as measured on the HADS	81.8%

								before diagnosis, family history of cancer, stage, perceived risk of recurrence, type of surgery, radiation therapy, prior treatment for infertility, prior difficulty conceiving, abortions, miscarriages, stillbirths, prior tubal ligation.	
Gorman, J.R. et al. (178)	US	Reproductive concerns	Mixed diagnoses (childhood cancers included)	infancy-34 years	n = 178 (87%) (results together for childhood and adult cancers)	Cross-sectional quantitative design	Reproductive concerns as measured by RCAC	Mean RCAC scores higher for those women who: **wanted a baby – yes vs. no** (3.34 vs. 2.99; p<0.01**); found biological child very important – yes vs. no** (3.37 vs. 3.13; p<0.05); **were in a partnered relationship – yes vs. no** (3.17 vs. 3.38; p<0.05); **had high school education as compared to college/graduate** (3.42 vs. 3.18; p<0.05); **had a previous miscarriage – yes vs. no** (3.67 vs. 3.22; P<0.01). No significant differences between groups based on age (18-29 vs. 30.35), race (white vs. non-white), Hispanic/Latina ethnicity (yes vs. no), occupation status, previous live births, normal menstruation pattern and history of infertility.	90.9%
Ruddy, K.J. et al. (211)	US	Concern about fertility	Breast cancer (stage 0-IV)	17-40	n = 620 (100%)	Cross-sectional quantitative design	Concern about fertility as measured by a 4-point Likert scale (single question)	Multivariate analysis – concern about fertility at diagnosis associated with: **age <35 at diagnosis** (OR = 0.26; p<0.001); **non-white race** (OR = 0.38; p = 0.003**); reception of chemotherapy** (OR = 1.61; p = 0.03); **not having children** (OR = 0.17; p<0.001). Variables non-significant in multivariate model but significant in univariate model: education, marital status, HADS anxiety, stage, finances, tobacco use, comorbidities, breast surgery, having been pregnant at diagnosis, never having been pregnant, history of miscarriage, stillbirth or infertility.	95.45%

								Variables non-significant in multivariate or univariate model: employment status, history of alcohol use, family history of breast cancer, receipt of endocrine therapy, HADS depression, pregnancy at time of survey, history of abortion, difficulty becoming pregnant, tumour biology (grade, ER, progesterone receptor and HER-2 receptor expression).	
Canada, A.L. and L.R. Schover (208)	US	uncertainty about fertility status (high level of fertility-related concerns); distress related to fertility	Cervical cancer, breast cancer, Hodgkin's lymphoma, NHL	14-41	n = 240 (100%)	Cross-sectional quantitative design	Reproductive concerns as measured by RCS Distress related to fertility as measured by IES	Women with **unfulfilled desire for children** as compared to women who had biological children if desired had higher scores **on IES Intrusion** (5.51 vs. 049, p<0.001); higher scores on **IES Avoidance** (6.52 vs. 0.74; p<0.001); higher scores on **IES Total** (12.03 vs. 1.24; p<0.001); higher scores on **RCS** scale (18.11 vs. 4.99; p<0.001) **Type of relationship to the child** significantly affected the scores on RCS and IES total: biological child only vs. combined biological and social vs. social only vs. childless (RCS: 6.64 vs. 9.6 vs. 14.77 vs. 18.43; p<0.001) and (IES Total: 2.94 vs. 3.96 vs. 4.71 vs. 13.67; p<0.001) **Unfulfilled desire for a child** accounting for a significant variance in IES score ($\Delta R^2 = 0.121$, p<0.001) and in RCS score ($\Delta R^2 = 0.257$, p<0.001).	95.50%

Appendix 6 – Summary table objective 2

Author-title	Location	Definition of fertility issues (inferred)	Cancer diagnoses	Age range at diagnosis	Sample size and % of female 14-50 included	Method	Outcome and measure	Findings	Quality assessment
QUANTITATIVE STUDIES									
Brånvall, E. et al. (218)	Sweden	Not succeeding at having children after cancer	Acute myeloid leukaemia	21-45	n = 22 (100%)	Quantitative design, cross-sectional survey	Depression and anxiety (measure unknown)	Among patients who had attempted to have children and did not succeed, none of the women reported they were psychologically unaffected by this. Five out of six women reported that they were “moderately” or “a lot” distressed by this and one was “a little” distressed by her infertility. The psychological well-being and the acceptance of the life situation, including family-related questions, were overall good. Women who tried to have children after treatment without succeeding (n = 6) showed no clear signs of psychological impairment. They scored well-being and presence of depression or anxiety slightly more favorable than the other women in the study (well-	63.63%

								being mean 5.6 compared to 5.4 where 7 = excellent and 1 = very poor, and depression as well as anxiety 2.0 compared to 2.75 where 7 = all the time and 1 = never).	
Canada, A.L. and L.R. Schover (208)	US	Self-assessed perception of being infertile (one question) Unfulfilled desire for a child	Cervical cancer, breast cancer, Hodgkin's lymphoma, NHL	14-41	n = 240 (100%)	Quantitative design, cross-sectional survey	Quality of life as measured by SF-12 Sexual functioning as measured by FSFI	Women who were unable to have a desired biological child after cancer as compared to those who had biological children if they wanted to reported less sexual satisfaction (10.21 vs. 11.46; p = 0.01) and poorer mental health (MCS/SF-12) (46.93 vs. 50.61; p<0.01). Women who viewed themselves as infertile (compared to their peers) had significantly lower sexual satisfaction (p<0.001), relationship satisfaction (p = 0.002) and confidence about dating (p = 0.052) compared to other women in the study.	95.5%
Eeltink, C.M. et al. (217)	The Netherlands	Self-assessed fertility status	Hodgkin's lymphoma	no age range M = 24(5)	n = 36 (100%)	Quantitative design, cross-sectional survey	Sexual functioning as measured by FSFI	Female survivors older than 30 years of age who perceived themselves as infertile reported the lowest FSFi score (median 21.78, SD 8.7) (p = 0.07), indicating sexual dysfunction.	59.09%
Gorman, J.R.	US	uncertainty	Breast cancer	26-40	n = 131 (100%)	Quantitative design,	Depressive	After adding significant	100%

et al. (209)		about fertility status (high level of fertility-related concerns)	(stage I-III)			cross-sectional survey	symptoms as measured by CES-D	covariates ($p \leq 0.10$) to the model, CES-Dsf was significantly higher in those with a higher RCS score (B = 0.02, p = 0.04), and lower in those with higher scores of physical health (B = -0.002, p<0.001) and those with higher scores of social support (B = -0.01, p<0.0001).	
Mancini, J. et al. (212)	France	Self-assessed perception of being infertile	Various cancers (not specified)	20 -70	n = 1419 (19.9%)	Quantitative design, cross-sectional survey	Quality of life (MOS SF36) Sexual functioning (questions developed for the purpose of the study)	Two years after the diagnosis, women with treatment - induced infertility were more likely than those with preserved fertility to have lower physical (44.3 vs. 48.1; p = 0.001) and mental quality of life (39.9 vs. 42.8; p = 0.31) scores, to report negative consequences of their cancer on their sexual life (p<0.001).	86.4%
Partridge, A.H. et al. (210)	US	Concern about infertility	Early stage breast cancer	18-40	n = 657 (100%)	Quantitative design, cross-sectional survey	Anxiety and depression as measured by the HADS Fear of recurrence as measured by single question	In multivariate analysis […] non-significant variables included […] anxiety or depression as measured by the HADS, […] perceived risk of recurrence.	81.8%
Ruddy, K.J. et al. (211)	US	Concern about fertility	Breast cancer (stage 0-IV)	17-40	n = 620 (100%)	Quantitative design, cross-sectional survey	Anxiety and depression as measured by the HADS	Among variables associated with fertility concern in univariate model but non-significant in multivariate model was anxiety as	95.45%

								measured by the HADS (anxious by HADS vs. not – 1.59; CI 1.09, 2.32; p = 0.02). Depression as measured by the HADS was non-significant in both univariate and multivariate analyses (depressed by HADS vs. not – 1.44; CI 0.8, 2.61; p = 0.23).	
Wenzel, L. et al. (213)	US	Uncertainty about fertility status (high reproductive concerns)	cervical cancer	25-45	n = 51 (100%) controls: n = 50 (Women matched on age and race to cases who have not undergone hysterectomy.)	Quantitative design, case-control survey study	Quality of life (SF -36, QOL - CS) Sexual functioning (GPC, SAQ)	Better mental status was associated with less cancer-specific distress ($P < 0.01$), better social support ($P < 0.0001$), better spiritual well-being ($P < 0.0001$), better sexual functioning ($P < 0.01$), and fewer reproductive concerns ($P < 0.01$). Several important predictors of distress during survivorship emerged: survivor-specific distress was significantly associated with younger age ($P < 0.01$), less social support ($P < 0.001$), more reproductive concerns ($P < 0.001$), worse mental status ($P < 0.0001$), and lower spiritual well-being scores ($P < 0.01$). Reproductive concerns for survivors were associated with poorer QOL ($P < 0.0001$), more cancer-	86.4%

								specific distress ($P < 0.01$), less social support ($P < 0.01$), lower spiritual well-being scores ($P < 0.05$), greater gynecologic pain ($P < 0.0001$), and poorer sexual functioning ($P < 0.05$).	
QUALITATIVE STUDIES									
Avis, N.E. et al. (267)	US	-	breast cancer (stage I-III)	25-50	n = 204	Mixed design, open-ended questions	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility	94.4%
Carter, J. et al. (225)	US	-	cervical cancer, uterine cancer, ovarian cancer	26-46	n = 20 (100%)	Mixed design, open-ended questions	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility	60%
Corney, R.H. and A.J. Swinglehurst (190)	UK	-	Breast cancer	20-41	n = 19 (100%)	Qualitative design, Semi-structured interviews, Thematic analysis	-	Themes: Consequences of cancer related fertility issues – Challenge to relationships	55%
Dryden, A. et al. (229)	Australia	-	Various diagnoses (leukaemia, brain tumour, breast cancer, Hodgkin's lymphoma, Ewing's	no age range at diagnosis, at interviews 18-26	n = 8 (100%)	Qualitative design, In-depth, semi-structured interviews, Foucaultian Discourse Analysis	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility; Challenge to relationships	90%

			sarcoma)					Being different / Comparisons with other women Identity as a social construct – Motherhood central to identity; Threatened femininity; Redefining identity	
Ferrell, B. et al. (180)	US	-	Ovarian cancer	not specified	21806 letters, cards, emails	Qualitative design, content analysis of correspondence sent to *Conversations!: The International Newsletter for Those Fighting Ovarian Cancer*	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility; Challenge to relationships Being different / Comparisons with other women Identity as a social construct – Threatened femininity; Redefining identity	70%
Gorman, J.R. et al. (219)	US	-	Breast cancer (stage I-II)	26-38	n = 20 (100%)	Qualitative design, In-depth semi-structured interviews,	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury	80%

						Thematic analysis			
Gorman, J.R. et al. (177)	US	-	Various diagnoses	0.5-30	n = 22 (77%)	Qualitative design, Focus groups, Thematic analysis	-	Themes: Consequences of cancer related fertility issues – Challenge to relationships	75%
Halliday, L.E. et al. (191)	Australia	-	Haematological malignancies	25-39	n = 12 (100%)	Qualitative design, In-depth interviews, Hermeneutical phenomenological approach, Thematic analysis	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility Being different / Comparisons with other women Identity as a social construct – Motherhood central to identity	85%
Halliday, L.E. et al. (192)	Australia	-	Haematological malignancies	25-39	n = 12 (100%)	Qualitative design In-depth interviews, Hermeneutical phenomenological approach, Thematic analysis	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility; 'It's not all bad' Being different / Comparisons with other women Identity as a social construct – Motherhood central to identity	95%

Hershberger, P.E. et al. (188)	US	-	Various diagnoses (breast, Hodgkin's lymphoma, ovarian, leukaemia, NHL, renal)	19-40	n = 27	Qualitative design, Semi-structured interviews, Grounded theory approach	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury	70%
Keim-Malpass, J. et al. (220)	US	-	Various diagnoses (breast, colorectal, Hodgkin's lymphoma, ovarian cancer, sarcoma, melanoma)	23-39	n = 13 (100%)	Qualitative design, Blog analysis, Phenomenological approach	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility Being different / Comparisons with other women Identity as a social construct – Threatened femininity	85%
Kirkman, M. et al. (194)	Australia	-	Breast cancer	25-41	n = 10 (100%)	Qualitative design, In-depth interviews, Narrative theory, Thematic analysis	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility; Challenge to relationships Identity as a social construct – Motherhood central to identity;	65%

								Redefining identity	
Molassiotis, A. et al. (181)	UK/Hong Kong (Chinese population)	-	Gynaecological cancer	21-64	n = 18 (?)	Qualitative design, Interviews, Phenomenological approach	-	Themes: Consequences of cancer related fertility issues – Challenge to relationships	95%
Perz, J. et al. (179)	Australia	-	Breast cancer	no age range those who responded that cancer affected their fertility	n = 381	Qualitative design, Open-ended questions	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility; Challenge to relationships; 'It's not all bad' Being different / Comparisons with other women Identity as a social construct – Motherhood central to identity; Threatened femininity	65%
Reis, N. et al. (182)	Turkey	-	Gynaecological cancers (vulva, endometrial, cervical, ovarian) stage I-III	28-68	n = 30 (53.3%)	Qualitative design, Semi-structured in-depth interviews	-	Themes: Consequences of cancer related fertility issues – Challenge to relationships Being different/Comparisons with	60%

								other women Identity as a social construct – Threatened femininity	
Schaefer, K.M. et al. (221)	US	-	Ovarian cancer	childbearing years (age not specified)	n = 5 (100%)	Qualitative design, In-depth interviews, Phenomenological approach	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility; Challenge to relationships; 'It's not all bad' Being different / Comparisons with other women Identity as a social construct – Motherhood central to identity; Threatened femininity	80%
Siegel, K. et al. (222)	US	-	Breast cancer	22-35	n = 34 (100%)	Qualitative design, In-depth interviews	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility; Challenge to relationships	60%

								Being different / Comparisons with other women	
Thewes, B. et al. (226)	Australia	-	Breast cancer	26-45	n = 24 (100%)	Qualitative design, Focus groups and individual phone interviews	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility	85%
Tschudin, S. et al. (228)	UK/US	-	Various diagnoses (breast, cervical, uterine, kidney, lymphoma)	m = 36.7(8.3)	n = 80 (100%)	Mixed design, survey with open-ended questions	-	Themes: Consequences of cancer related fertility issues – Grieving the loss of fertility; 'It is not all bad'	75%
Venturini, E. et al. (223)	France	-	Gynaecological cancer (cervical, endometrial, ovarian)	28-79	n = 30 (33.33%) 20 participants menopausal	Qualitative design, Consultation observation, interviews	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury; Grieving the loss of fertility; 'It's not all bad' Identity as a social construct –Threatened femininity	50%
Yee, S. et al. (224)	Canada	-	Various diagnoses (breast, ovarian, NHL, brain, Hodgkin's lymphoma,	24-42	n = 41	Qualitative design, open ended questions	-	Themes: Consequences of cancer related fertility issues – Cancer and infertility – adding insult to injury	70%

			leukaemia)						

Appendix 7 – Summary table for objective 3

Author-title	Location	Cancer diagnoses	Age range at diagnosis	Sample size and % of female 14-50 included	Method	Type of decision	Findings	Quality assessment
QUANTITATIVE STUDIES								
Bastings, L. et al. (183)	The Netherlands	Various diagnoses (including BENIGN disease – nephrotic syndrome 1 patient) (breast cancer, lymphoma, gynaecological cancer, bone or soft tissue tumour, GI tumour)	m = 28.9(5.7)	n = 64 (100%) (33 who received FP)	Quantitative design, Cross-sectional survey	Fertility preservation (ART)	At the free-response section of the questionnaire, patients revealed that their FP decision was mainly dependent on a difficult trade off between their risk of ovarian failure and their wish to start oncological therapy as soon as possible. A significant number of patients indicated that their young age, the recent start of their partner relationship, and/or the short period of time to make a decision complicated their decision-making processes. Patient experience with FCP associated with decisional conflict – less decisional conflict in patients who: had enough time available for counselling (B = -10.59, p<0.0001); had the opportunity to ask all the questions (B = -12.86, p<0.0001); felt supported by counsellor during decision-making (B = -6.51, p = 0.0003); discussed all applicable FP options (B = -7.49, p = 0.0001); had the benefits and disadvantages of different options clearly explained (B = -8.28; p = 0.0005).	85%

							Decisional regret related to the decisional conflict (B = 0.21, 95% CI = 0.15;0.27, p<0.0001, Spearman's rho = 0.74)	
Bell, R.J. et al. (184)	Australia	Breast cancer	m = 58 (12)	n = 1370 (?)	Quantitative design, Longitudinal study	Tamoxifen	Six women discontinued tamoxifen to become pregnant	86.36%
Bramwell, V.H. et al. (234)	France	Breast cancer	29-58 pre- or perimenopausal	n = 672 (100%)	RCT	Tamoxifen	Some of the participant (number not reported) stopped tamoxifen/placebo because of desire for pregnancy.	89.29%
Campos, S.M. et al. (232)	US	Ovarian cancer or borderline tumour (stage I-II)	22-39	n = 16 (100%)	Quantitative design, Cross-sectional survey	Gynaecological surgery (fertility sparing)	Fertility sparing surgery was extremely important to 62.5% of participants, very much important to 25% of participants and somewhat important to 12.5% of participants.	75%
Carter, J. et al. (197)	US	Early-stage cervical cancer	23-40	n = 29 (100%)	Quantitative design, Longitudinal survey	Gynaecological surgery (fertility sparing and radical)	Childbearing was reported to be a primary factor in deciding to undergo trachelectomy (97%, *n* = 28). However, the decision-making process of women with newly diagnosed cervical cancer was also guided by conversations with their doctors (41%, *n* = 12). Reproductive concerns, such as wanting a family or having future fertility options, were also important in their choice of treatment (41%, *n* = 12). Personal initiative was also cited as a factor in treatment selection (28%, *n* = 8). Some of the women indicated that trachelectomy was chosen after they conducted research and/or on their personal belief that this procedure was their best option.	55.6%

Carter, J. et al. (198)	US	Early-stage cervical cancer	20-45	n1 = 71 n2 = 52 (100%)	Quantitative design, Longitudinal survey	Gynaecological surgery (fertility sparing and radical)	Preoperatively, 43women(61%) consented for RT and 28 (39%) for RH. Of the women consented for RT, the majority indicated fertility (98%) and not having enough time to complete childbearing (74%) as factors in the treatment decision-making process. Women undergoing RH demonstrated mixed responses, with approximately half indicating fertility or childbearing as factors in treatment choice. Almost the entire RT sample (n = 42) reported preoperatively a desire for ovarian preservation for future fertility options or menopause prevention, whereas 6 of 28 women planned for RH expressed desire for ovarian removal (bilateral salpingo-oophorectomy [BSO]). A few women consented for RH provided additional insight in their qualitative items, revealing concerns of cancer spread and/or menopause prevention. Seven percent of RT patients reported having had enough time to complete childbearing compared to 43% of RH patients (Pb0.001; Fisher's exact test). Women in the RT group (98% response-rate) reported qualitative themes of fertility (55%, n = 23), doctor discussion/recommendation (36%, n = 15), and research (17%, n = 7) as important factors guiding treatment choice. Among the women consented for RH, 24 (86%) of 28 provided qualitative information. Reasons for choosing this surgical procedure included themes of doctor discussion/recommendation (46%, n =	90.9%

							11), similar to those noted in the RT group; however, additional themes of "concern about survival" (25%, n = 6) and feeling this was the "best option or only choice" (25%, n = 6) were also noted.	
Cluze, C. et al. (195)	France	Breast cancer	<40 (m = 37.7[3.5])	n = 161 (100%)	Cross-sectional quantitative design	Tamoxifen	Early interruption of tamoxifen (between initiation and 16th month after BC diagnosis) – women with less social support (p = 0.03); information about tamoxifen not understandable (p = 0.01) Late interruption of tamoxifen (later than 16 months after BC diagnosis): poor social support (p = 0.04); no longer fearing cancer relapse (p = 0.03); two or fewer treatment modalities (p = 0.04); no opportunity to ask questions at the time of diagnosis (p = 0.007); reporting more than two specific menopausal symptoms (p = 0.01).	95.45%
Güth, U. et al. (235)	Switzerland	Breast cancer	30-80	n = 685 (23.6%)	Cross-sectional quantitative design	Tamoxifen	Reasons for discontinuation of endocrine therapy in the group of patients aged 30-49 (19 patients): Lack of motivation, resistance against drug intake, wish to stop – 28% Desire to get pregnant – 16% Intolerance, general discomfort, malaise – 12% Weight gain – 8%	95.45%

							Hot flushes – 20% Musculoskeletal event (arthralgia, bone pain) – 8% Dermatologic symptoms/hair loss – 4% Alcohol dependency or psychiatric disease – 4%	
Hill, K.A. et al. (237)	Canada	Breast cancer	24-41	n = 27 (100%)	Cross-sectional quantitative study	Fertility preservation (ART)	Fifteen (56%) of the respondents chose to undergo FP. The most common choices were embryo and oocyte cryopreservation. Of the 9 women who opted to freeze embryos, 8 had a male partner whose sperm was used to fertilize their eggs and 1 woman used donor sperm. Of the 6 women who chose to freeze their eggs alone, 2 were married. For those who chose to freeze oocytes, the most common explanation was that they did not feel comfortable creating embryos and/or they would rather wait to fertilize their eggs with a future partner. Women between the ages of 30 and 34 years were more likely to undergo FP than any other age group. Those who were single were far less likely to pursue FP, with only 2 (29%) of 7 women who opted to freeze oocytes. The respondents without children were no more likely to pursue FP than those who had a child before their breast cancer diagnosis, with 56% in each group (5 in the former and 10 in the latter) undergoing FP. Early referral, before surgery and systemic therapy, did not significantly	62.5%

							affect FP uptake. FP delayed systemic treatment for a third of the patients, with an average delay of 3.3 weeks (range, 2-5 weeks). After the consultation, the patients looked to their partners and other family members to provide them with support and assistance in making a decision regarding FP.	
Huiart, L. et al. (196)	France	Breast cancer	<40 (m = 36.9[3.4])	n = 246 (100%)	Longitudinal quantitative design	Tamoxifen	Multivariate analysis: tamoxifen discontinuation increased with low social support (p = 0.003); low material support (p = 0.035); self-reported non adherence (p = 0.001)	95.45%
Huyghe, E. et al. (238)	US	Various diagnoses	>18	n = 253 (34%)	Cross-sectional quantitative design	Fertility preservation (ART)	56 women aged 50 or less – having to pay reduced the estimated service usage	72.7%
Kim, J. et al. (240)	US	Breast cancer (stage I-III)	<42	n = 185 (100%)	Secondary data analysis	Fertility preservation (ART)	Of the 185 patients, 108 patients (58.4%) underwent FPT. In univariate analysis, the FPT group had a lower mean BMI, was wealthier, and had lower cancer stage compared to the group that did not undergo FPT. The rate of administration of NAC was significantly lower in women in the FPT group. Age, parity, BRCA mutation status, history of infertility, family history of breast/ovarian cancers, and hormone receptor status of cancer were not different between women who underwent FPT and those who did not. The likelihood of having insurance coverage or a partner was not different between the two groups.	81.8%
Kim, J. et al. (239)	US	Various diagnoses (breast, haematological,	24.9-36.9	n = 52	Cross-sectional quantitative	Fertility preservation	Decisional conflict scale associations The median DCS score was 29.7 out	81.8%

		gynaecological, colon, skin, brain)			approach	(ART)	of 100 possible points (IQR 18.0–39.1, range 4.7–64.1). Fourteen subjects had scores consistent with high decisional conflict (>37.5), 20 were in the moderate range (25–37.5) and 18 patients had low decisional conflict (<25). Univariate analysis of socio-demographic variables revealed that subjects with annual income less than $20,000 (approximately the US poverty limit in 2011) tended to have lower DCS scores. Age, race, relationship status, parity and level of education were not significantly associated with DCS score. While all patients agreed that they were given opportunities to ask questions during the consultation, the patients who answered 'strongly agree' had significantly lower DCS scores than those who answered 'agree' ($P = 0.001$). DCS scores were significantly lower in patients who received fertility preservation treatment compared with patients who did not ($P < 0.001$). Subjects who reported that cost was strongly influential in their treatment decision had significantly higher DCS scores compared with the patients who did not think that cost was strongly influential ($P < 0.001$). Those who thought that safety of treatment was very influential in decision-making	

							tended to have lower DCS scores than those who did not. There was no association between DCS and knowledge scores (P = –0.11), discussion with anyone about treatment options or the use of additional resources before the fertility preservation consultation. The first values-clarification exercise using a Likert scale revealed that 'desire to have a child after cancer treatment', 'amount of time needed for fertility preservation treatment' and 'cost' were the most influential factors in decision-making (73%, 43% and 41%, respectively). In the second values-clarification exercise, 40% of subjects ranked 'desire for future children' as their most influential factor, followed by 'costs' (13%), 'other' (12%) and the amount of time needed for treatment (8%). Looking at patients' top three choices, 'desire to have a child after my cancer treatment', 'cost' and 'amount of time needed for fertility preservation treatment' were the highest ranking factors in decision-making (65%, 46% and 42%, respectively). Among patients who received treatment, 'desire for future children' (63%), and 'partner's wishes' (11%) were the most commonly reported influential factors. Meanwhile, among those who	

							did not receive treatment, their most influential factors included 'desire for future children' (27%), 'cost' (21%) and 'the amount of time needed for treatment' (12%).	
Letourneau, J.M. et al. (185)	US	Leukaemia, Hodgkin's disease, NHL, breast cancer or gastrointestinal cancer	18-40	n = 918 (100%)	Cross-sectional quantitative design	Fertility preservation (ART)	Of the 918 women who received treatment with potential to impact fertility, those who were aged <35 years at diagnosis were more likely to preserve their fertility than older women (odds ratio [OR], 11.0; 95% confidence interval [CI], 1.5-81.9). Women without children at diagnosis were more likely to take action to preserve their fertility than those with children (OR, 4.6; 95% CI, 1.6-13.5).	77%
Letourneau, J.M. et al. (186)	US	Leukaemia, Hodgkin's disease, NHL, breast or GI cancer	18-40	n = 918 (100%)	Cross-sectional quantitative study	Fertility preservation (ART)	Overall, 4% of women underwent fertility preservation. Age at diagnosis, the desire for future children at diagnosis, parity at diagnosis, and education level were significantly associated with increased odds of pursuing fertility preservation. There was a trend toward decreased access for Latina women versus Caucasian women. No significant differences in access to fertility preservation were noted with regard to: marital status, household income, or population density. After adjustment for age, desire for future children, parity at diagnosis, education level, ethnicity, disease type, disease stage, and treatment	77.3%

							type, several differences persisted. For instance, women older than 35 years at diagnosis were approximately 90% less likely to preserve their fertility than their 18- to 25-year-old counterparts (OR, 0.1; 95% CI, 0.0-1.4); however, this difference did not achieve statistical significance. A trend was seen with regard to pretreatment parity, where women who had already had at least 1 child at diagnosis had 70% lower odds of pursuing fertility preservation than women without children (OR, 0.3; 95% CI, 0.1-1.1); however, this difference also did not achieve statistical significance. Latina women were 80% less likely to preserve fertility than Caucasian women (OR, 0.2; 95% CI, 0.0-1.3), although this difference did not achieve statistical significance. Furthermore, no fertility preservation was noted among the 31 women identifying as African American, despite having no significant differences in childbearing from Caucasian women in our study. A similar pattern was seen among the 29 women who identified with a sexual orientation other than heterosexual, despite having no differences in childbearing desires compared with	

							women identifying as heterosexual.	
Mersereau, J.E. et al. (241)	US	Various diagnoses (Breast, Hodgkin's lymphoma, gynaecological, NHL, leukaemia, other)	median 31; IQR 26-35	n = 208 (?) 85 (41%) underwent FP	Cross-sectional quantitative design	Fertility preservation (ART)	Participants who were not referred to FP consultation had significantly higher DCS scores compared with women who were referred (51.6 [IQR, 37.5-64.1] vs 31.3 [IQR, 18.8-43.8]; *P* < .0001). DCS scores were lower in those who underwent FP treatment (*P* < .0001). Participants who reported lower income, lower level of education completed, and not being in a partnered relationship had higher decisional conflict. Compared with survivors of breast cancer, women reporting other cancers had higher DCS scores. Longer time since diagnosis was also correlated with higher scores (rho = 0.35, *P* < .0001). Subjects who were more than 5 years after cancer were nearly twice as likely to recall high DCS than women in the first year of survivorship. Age, race, parity, and desire for future fertility were not significantly associated with DCS scores. In models of high DCS adjusted only for time since diagnosis, nonreferral was associated with a nearly 2-fold increased likelihood of high DCS (PR, 1.83; *P* < .0001). Undergoing FP treatment was associated with significantly lower likelihood of high DCS (PR, 0.53; *P* < .0001). Reported	95.45%

							cost concerns were also associated with high DCS (PR, 1.23; *P* = .006). In models adjusting for potential confounding factors and time since diagnosis, estimates for each of the FP explanatory variables were attenuated but remained statistically significant. Women who were not referred to FP consultations were significantly more likely to report high decisional conflict (PR, 1.25; *P* = .009). Those who underwent FP treatment were less likely to have high decisional conflict (PR, 0.67; *P* = .001). Finally, women who felt that FP consultation or treatment was cost prohibitive reported more decisional conflict in these adjusted analyses (PR, 1.16; *P* = .01). In all adjusted models, income, partner status, time since diagnosis, and cancer type were no longer significantly associated with high decisional conflict.	
Partridge, A.H. et al. (210)	US	Breast cancer (stage 0 -III)	17-40	n = 657 (100%)	Web -based survey Cross -sectional design	Chemotherapy	Twenty-nine percent of women indicated that concern about fertility impacted on their treatment decisions. Women were asked the minimal decrease in absolute risk of recurrence that they would have been willing to accept from chemotherapy, given that adjuvant chemotherapy might reduce the chances of a future pregnancy and result in other side effects. Women who reported greater concern about	81.8%

							fertility required greater risk reduction from chemotherapy than women who were less concerned about fertility ($P < .05$). Women were also asked about the maximum risk of infertility that they would have accepted from a course of chemotherapy. Women who were more concerned about fertility were much less likely to accept a higher risk of infertility from adjuvant chemotherapy ($P < .0001$), although 57% of women who reported great concern were willing to accept a risk of infertility of ≥ 50%. Women were also asked to what extent they questioned the decisions they made about their breast cancer treatment at the time of the survey. Forty-five percent of all respondents questioned their treatment decisions, although most questioned their decisions only a little. Those who were more concerned were not more likely to question their decision ($P = .28$). However, 33% of the women who were more concerned about fertility reported that such questioning was related to fertility issues, at least to some degree, compared with 8% of the women who were less concerned about fertility at diagnosis.	
Peate, M. et al. (242)	Australia	Early breast cancer (stage I, IIA, IIB, DCIS excluded)	21-40	n = 111 (100%)	Cross sectional quantitative design	Fertility preservation (ART)	Approximately a third (36%) of participants were leaning against using fertility treatments (ie, preferring to “wait and see”), and a similar proportion (31%) were considering IVF. The final ordinal regression model	95.45%

							showed that women who rated fertility information as important were more likely to consider IVF (OR = 2.14; *P* = .004), and women who had negative attitudes toward fertility treatment were less likely to consider IVF (OR = 0.84; *P* < .001). IVF treatment intentions were not associated with being in a committed relationship (OR = 1.20; *P* = .716) or a definite desire for more children (OR = 1.54; *P* = .513) using regression analysis.	
Razzano, A. et al. (243)	Italy	Various diagnoses (breast cancer, haematological cancer, other)	18-40	n = 48 (100%)	Cross-sectional quantitative design	Fertility preservation (ART)	When patients were asked about their main feelings about the FPP (multiple choice answer with the possibility to give more than one reply), 54.2% described it as an ‘‘important part of the cancer therapy’’, 58.3% as an ‘‘open window towards the future’’, 70.8% as ‘‘an option not to be wasted’’. Only 2 patients of the 48 (4.2%) described the FPP as an additional complication of the tricky oncostatic therapy, but interestingly enough they chose to undergo the procedure anyway. The major and more frequent concerns about the FPP were the fear that oocytes or ovarian tissue could be altered during freezing/thawing procedures (37.5%), and the lack of certainty about the real possibility to obtain a future pregnancy (37.5%). A few patients (12.5%) expressed the fear of not surviving, and consequently of never	66.66%

							having the chance to use their cryopreserved material. Only two patients (4.2%) were worried about the risk of worsening cancer prognosis as a consequence of the FPP procedure, or about increasing the risk of cancer recurrence after using the preserved material (e.g. after re-transplantation of ovarian tissue).	
Reh, A.E. et al. (244)	US	Various cancers	16-39	n1 = 29 n2 = 8 (follow up survey with women who underwent FP procedures) (100%)	Longitudinal study (baseline and 1 -year follow -up	Fertility preservation (ART)	52% (15/29) of patients felt having a child was “most important” in their life (scale 1–7; mean 6.1; median 7), and 62% (18/29) were “most concerned” with the impact their cancer treatment would have on fertility (mean 6.1; median 7) Recognizing the limited data on the long-term risks for FP patients, 54% were “unsure” regarding the risk they were willing to undertake to pursue fertility treatment, while 19% were willing to undertake a minimal and 19% a moderate risk. Two patients (8%) indicated they were willing to do “whatever it takes” to conceive a child.	68.2%
Rippy, E.E. et al. (236)	UK	Breast cancer (different stages)	<45	n = 163 (100%)	Cross -sectional quantitative design	Tamoxifen	Six patients cut short their treatment with tamoxifen either to become pregnant or because they thought that they were pregnant.	77.8%
Ruddy, K.J. et al. (211)	US	Breast cancer	17-41	n = 620 (100%)	Prospective study (results from baseline survey)	Various treatments (tamoxifen included)	Concerns about fertility affected treatment decisions a little in 55 (9%), somewhat in 53 (9%), a lot in 52 (8%), and not at all in 456 (74%).	95.45%

							In the 160 women (26%) who reported that concerns about fertility affected their treatment decisions, 90 provided specific details about how their decisions were affected. In the 419 who either reported that concerns about fertility did not affect their treatment decisions or did not respond to this item, 41 still went on to provide specific details about decisions that were affected. Some reported that one treatment decision was affected. Overall, four (1%) chose not to receive chemotherapy, 12 (2%) chose one chemotherapy regimen over another, six (1%) considered not receiving endocrine therapy, 19 (3%) decided not to receive endocrine therapy, and 71 (11%) considered receiving endocrine therapy for < 5 years. Five reported that they underwent mastectomies because of their fertility concerns.	
Scanlon, M. et al. (231)	US	Various diagnoses (breast, gynaecological, haemaological)	Premenopausal at diagnosis	n(baseline) = 104 n(1-year followup) = 53 (100%)	Longitudinal cohort study (follow-up only for some outcomes)	Various treatments (unspecified)	Nineteen (20%) women ranked fertility preservation as important at the time of diagnosis and treatment planning. These women were more likely to be of a younger age and with no previous pregnancies. While fertility preservation was ranked as important 16% of women 40-44 years old, only one woman over the age of 40 was referred to a fertility specialist. Even though none of the women >44	65%

							years old were interested in preserving their own fertility, 12% of these women found it important to discuss the risk of treatment-induced infertility. In addition, the risk of infertility affected treatment choice in 12 (13%) subjects; factors significantly affecting this result were younger age, being unmarried, and having no prior successful pregnancies. After treatment completion, interest in fertility preservation was unchanged in 70% of women who were initially interested in fertility preservation and did not undergo surgically-induced menopause. Marital status and disease-specific cancer care did not affect the importance assigned to fertility preservation over time. Concern about cancer recurrence did affect interest in future pregnancies in 29% of women.	
Senkus, E. et al. (233)	International	Breast cancer (stage I-II)	≤ 35 (from inclusion criteria)	n = 398 (100%)	Cross-sectional quantitative design	Chemotherapy	Acceptance of chemotherapy Thirty-two participants (8%) would refuse chemotherapy, if they knew it could reduce their fertility. Of those, 21 had previously received chemotherapy. By univariate logistic analysis, factors significantly associated with accepting chemotherapy were having children, not wanting children, proposed	95.45%

							chemotherapy, living in Western Europe, and higher disease stage. All these variables remained significant in the final multivariate model. Maximum risk of infertility For the purpose of this analysis, participants refusing chemotherapy were considered to accept 0% risk of infertility. In univariate analysis, a higher accepted infertility risk was related to already having children, not wanting children, proposed chemotherapy, younger age, and living in Western Europe. Tests for interaction identified a significant interaction between the 'wish to have more children' and 'already having children' ($p < 0.0001$). To include this interaction term in the multivariate model, we combined the two explanatory variables into a new categorical variable with four levels: having children: no; wanting children: yes (reference level) having children: no; wanting children: no having children: yes; wanting children: yes having children: yes; wanting	

							children: no We found that women in category '2' would accept a sterility risk 26.6 times higher, than women in category '1'. In contrast, women in category '4' would accept a sterility risk 5.2 times higher, than women in category '1'; women in category '3' would accept a sterility risk only 2.9 times higher, than women in category '1'. Higher chance of cure In the univariate analysis, geographical living area was the only factor significantly predicting the acceptable chance of cure ($p < 0.0001$). Almost all women tested (45 of 51) from South Africa and South America required a >20% increase in the chance of cure in order to accept chemotherapy.	
Treves, R. et al. (245)	France	Various diagnoses (breast cancer, Hodgkin's lymphoma, leukaemia, other)	18-40	n = 85	Cross-sectional quantitative design/open ended questions	Fertility preservation (ART)	By design, at the time of the survey, all patients had their treatment in progress. As expected, most women reported having experienced anxiety after having been informed of the possible negative impact of cancer treatments on their fertility (58.8%), whereas 2.3% felt indifferent. Psychological experience of patients who were offered FP demonstrates that the simple fact of being aware of the opportunity of preserving fertility	59.09%

							immediately restored a significant feeling of hope and generated a feeling of profound relief in a considerable fraction of studied women (67.0 and 48.2%, respectively). It is noteworthy that only 28.2% of women would have wished to have more time to think about the opportunity of FP. In addition, most patients declared that the primary motivation for undergoing FP was to conceive a child and to prevent eventual regret (49.4%). In line with this, the main psychological experiences of FP included the feelings of hope, of ongoing life and of 'life insurance'. Furthermore, among the 85 patients having accepted to undergo FP at our center, 92.9% involved a family member or a significant other in their decision. In addition, 66 (77.6%) reported that such a possibility was instrumental (n = 35) or very instrumental (n = 31) to improving their coping with the burden of cancer treatment. Spontaneous statements such as "FP conveyed the feeling of hope that I needed to struggle against cancer", "the perspective of having a family in the future allowed me to be strong enough to face cancer treatments" or "FP prevented me from giving everything up and represented a positive thinking that was very	

							important to me" were frequent among studied patients.	
Tschudin, S. et al. (228)	UK/US	Various diagnoses (breast, cervical, uterine, kidney, lymphoma)	m = 36.7(8.3)	n = 80 (100%)	Cross-sectional quantitative study	Fertility preservation (ART)	Strength of positive attitudes was significantly greater than that of negative attitudes (t(67)¼13.23, p<0.0001). Willingness to make use of FP techniques, if there were risks involved (e.g., delaying cancer treatment to have stimulation), was 2.32 on a response scale with a maximum score of 5.	75%
QUALITATIVE STUDIES								
Connell, S. et al. (257)	Australia	Breast cancer	29-40	n1 = 35 follow up with 13 women (100%)	Qualitative design, Longitudinal, Interviews three times over 12-18 months	Fertility preservation (ART)	Themes: There are positive and negative consequences to every decision	85%
Corney, R.H. and A.J. Swinglehurst (190)	UK	Breast cancer	20-41	n = 19 (100%)	Qualitative design, In-depth, semi-structured interviews, Framework approach (Braun & Clarke), Thematic analysis	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options The decisions are complex and multifactorial – Moderators: Important people affecting decision-	55%

							making; Barriers: Relationship status, Institutional barriers, Timing There are positive and negative consequences to every decision	
Corney, R. et al. (189)	UK	Breast cancer	27-41	n = 10 (100%)	Qualitative design, In-depth, semi-structured interviews, Framework approach (Braun & Clarke), Thematic analysis	Fertility preservation (ART)	Themes: The decisions are complex and multifactorial – Moderators: Research and evidence; Barriers: Relationship status, Institutional barriers	80%
Crawshaw, M.A. et al. (256)	UK	Various diagnoses (sarcoma, lymphoma, leukaemia, germ cell tumour, CNS tumours)	11(13)-20	n = 38 (21 women; 17 men)	Qualitative design, In-depth interviews, Thematic analysis	Fertility preservation (ART)	Themes: The decisions are complex and multifactorial –Barriers: Timing	70%
Dryden, A. et al. (229)	Australia	Various diagnoses (leukaemia, brain tumour, breast cancer, Hodgkin's lymphoma, Ewing's sarcoma)	no age range at diagnosis, at interviews 18-26	n = 8 (100%)	Qualitative design, In-depth, semi-structured interviews, Foucaultian Discourse Analysis	Various treatments (unspecified)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Being involved vs. feeling excluded The decisions are complex and	90%

							multifactorial – Moderators: Important people affecting decision-making	
Garvelink, M.M. et al. (246)	The Netherlands	Various diagnoses (breast, other)	21-40	n = 34 (100%)	Qualitative design, Semi-structured interviews, Framework approach, Thematic analysis	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options, Being involved vs. feeling excluded The decisions are complex and multifactorial – Moderators: Research and evidence, Important people affecting decision-making; Barriers: Age, Relationship status, Institutional barriers, Cost, Timing, 'Too much to get your head around'; Facilitators There are positive and negative consequences to every decision	75%
Gorman, J.R. et al. (219)	US	Breast cancer (stage I-II)	26-38	n = 20 (100%)	Qualitative design, In-depth semi-structured interviews, Thematic analysis	Various treatments (unspecified)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Options There are positive and negative	80%

							consequences to every decision	
Gorman, J.R. et al. (177)	US	Various diagnoses	0.5-30	n = 22 (77%)	Qualitative design, Focus groups, Thematic analysis	Fertility preservation (ART)	Themes: I need to know… otherwise I can't make a decision… - Information, Options The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Timing	75%
Hershberger, P.E. et al. (187)	US	Various diagnoses (breast, Hodgkin's lymphoma, NHL, ovarian, kidney)	19-40	n = 27 (100%) 13 underwent FP and 14 declined FP	Qualitative design, Semi-structured, in-depth interview, Grounded theory approach	Fertility preservation (ART)	Themes: I need to know… otherwise I can't make a decision… - Information, Options The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Relationship status	80%
Hershberger, P.E. et al. (188)	US	Various diagnoses (breast, Hodgkin's lymphoma, ovarian, leukaemia, NHL, renal)	19-40	n = 27	Qualitative design, Semi-structured interviews, Grounded theory approach	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information The decisions are complex and multifactorial – Moderators: Research and evidence, Important people affecting decision-making; Barriers:	70%

							Relationship status, Cost, Timing, 'Too much to get your head around'	
Kirkman, M. et al. (193)	Australia	Breast cancer	25-41	n = 10 (100%)	Qualitative design, In-depth interviews, Thematic analysis	Various treatments (unspecified)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options, Being involved vs. feeling excluded The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Age, Timing	65%
Kirkman, M. et al. (194)	Australia	Breast cancer	25-41	n = 10 (100%)	Qualitative design, In-depth interviews, Narrative theory, Thematic analysis	Various treatments (unspecified)	Themes: I need to know… otherwise I can't make a decision… - Being involved vs. feeling excluded The decisions are complex and multifactorial – Barriers: Timing	65%
Lee, R.J. et al. (247)	UK	Breast cancer (stage I-III)	23-39	n = 24	Qualitative design, Focus groups, Thematic analysis	Various treatments (unspecified)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options, Being involved vs. feeling	95%

							excluded The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Institutional barriers, Timing, 'Too much to get your head around'	
Lloyd, P.A. et al. (255)	UK	Cervical cancer	29-45	n = 12 (100%)	Qualitative design, In-depth interviews, Descriptive phenomenological framework	Gynaecological surgery (radical trachelectomy)	Themes: The decisions are complex and multifactorial – Moderators: Research and evidence There are positive and negative consequences to every decision	85%
Niemasik, E.E. et al. (249)	US	Various diagnoses (leukaemia, Hodgkin's lymphoma, breast, GI)	m = 31.8(6.7) from inclusion criteria: 18-40	n = 697 (100%)	Qualitative design, survey with open ended questions	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options, Being involved vs. feeling excluded The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Age, Cost, Timing	75%
Pellegrini, I. et al. (250)	Canada	Breast cancer	35-64	n = 34	Qualitative design	Tamoxifen	Themes: Finding a balance between survival	75%

				(79%)			and fertility (quantity vs. quality of life)	
Ruddy, K.J. et al. (253)	US	Breast cancer (stage I-III)	26-44	n = 36	Qualitative design, Focus-groups, Thematic analysis	Fertility preservation (ART)	Themes: I need to know… otherwise I can't make a decision… - Options The decisions are complex and multifactorial – Moderators: Research and evidence; Barriers: Cost, Timing, 'Too much to get your head around'	70%
Schaefer, K.M. et al. (221)	US	Ovarian cancer	childbearing years (age not specified)	n = 5 (100%)	Qualitative design, In-depth interviews, Phenomenological approach	Gynaecological surgery	Themes: I need to know… otherwise I can't make a decision… - Being involved vs. feeling excluded There are positive and negative consequences to every decision	80%
Snyder, K.A. and A.L. Tate (248)	US	Breast cancer	m = 32.1 <40 (from inclusion criteria)	n = 34 (100%)	Qualitative design, Semi-structured interviews	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Being involved vs. feeling excluded The decisions are complex and multifactorial – Moderators: Research and evidence, Important people affecting decision-making; Barriers: Relationship status, Cost, Timing,	65%

							'Too much to get your head around'; Facilitators	
Wilkes, S. et al. (252)	UK	Various diagnoses	5-32	n = 18 (8 men, 10 women) (72%)	Qualitative design, In-depth, semi-structured interviews, Grounded theory approach	Fertility preservation (ART)	Themes: I need to know… otherwise I can't make a decision… - Information, Options, Being involved vs. feeling excluded The decisions are complex and multifactorial – Barriers: Timing	80%
Wright, C.I. et al. (251)	UK	Not given	12-24	n = 14 (young people) 6 aged 12-15 (4 boys, 2 girls) 8 aged 16-24 (5 men, 3 women) 6 parents young partners	Qualitative design, Observation and semi-structured interviews Thematic analysis	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't make a decision… - Information, Options The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Timing	65%
Yee, S. et al. (224)	Canada	Various diagnoses (breast, ovarian, NHL, brain, Hodgkin's lymphoma, leukaemia)	24-42	n = 41	Qualitative design, survey with open ended questions	Fertility preservation (ART)	Themes: Finding a balance between survival and fertility (quantity vs. quality of life) I need to know… otherwise I can't	70%

							make a decision… - Information, Options, Being involved vs. feeling excluded The decisions are complex and multifactorial – Moderators: Important people affecting decision-making; Barriers: Relationship status, Cost, Timing, 'Too much to get your head around'; Facilitators There are positive and negative consequences to every decision	

Appendix 8 – Interview schedule for the longitudinal study

1st Interview – around diagnosis

General questions

- Could you start by telling me about how your cancer was diagnosed and the treatment process?
- Tell me about your family and friends, and how cancer has impacted on them.

Perceptions of illness

- Tell me how you perceive your disease.
    - Tell me about your symptoms.
    - What do you think might have caused your disease?
    - What do you think the consequences of your disease will be?
    - How long do you feel the disease will last?

Fertility

- Tell me what were your expectations regarding parenthood before and after your cancer diagnosis.
- Tell me what your fertility/ the ability to have kids means to you.
- Tell me about your perceptions of the impact of cancer and cancer treatment on your fertility.

Decision-making

- You are now making / have recently made a decision concerning your cancer treatment. Can you tell me about it?
- Tell me what factors were important to you while making your decision. Can you describe them?
    - What were you thinking about when making your decision? Survival, fertility, present family, future family?
- Tell me how and with who did you negotiate / are you negotiating that decision. How do you feel about that?
    - Your family/partner, your doctor, a nurse
- How do you feel about this/your decision?
- How do you feel about this/your treatment?

Ending question

- Do you have any other insights or comments about what we have just discussed that you think are important for me to know?

2nd Interview – after treatment

Decision-making

- You have recently undergone treatment for you cancer / are still receiving treatment for your cancer. From the perspective you have now, what were the important factors that influenced your decision?
    - Survival, fertility, present family, future family, doctor's advice, information?
- How do you feel about this/your treatment now?
- How do you feel about the decision to undergo this treatment?
- How do you think your family and friends feel about this/your decision?

Perceptions of illness

- From the perspective you have now, tell me how you perceive your disease.
    - Tell me about your symptoms.
    - What do you think might have caused your disease?
    - What do you think the consequences of your disease will be?
    - How long do you feel the disease will last?

Fertility

- Tell me what are your expectations regarding parenthood now. How do you feel about them?
- Tell me what your fertility means to you now. / Tell me about you concerns regarding your fertility now.

Impact on family and friends

- Tell me how cancer impacted on your family and friends.

Ending question

- Do you have any other insights or comments about what we have just discussed that you think are important for me to know?

Appendix 9 – Interview schedule for the cross-sectional study

Interview

General questions

- Could you start by telling me about how your cancer was diagnosed and the treatment process?
- Tell me about your family and friends, and how cancer has impacted on them.

Decision-making

- You have undergone treatment for you cancer. From the perspective you have now, what were the important factors that influenced your treatment decision?
    - Survival, fertility, present family, future family, doctor's advice, information?
- How do you feel about this/your treatment now?
- How do you feel about the decision process to undergo this treatment?
- How do you think your family and friends feel about this/your decision?

Perceptions of illness

- From the perspective you have now, tell me how you perceive your disease.
    - Tell me about your symptoms.
    - What do you think might have caused your disease?
    - What do you think the consequences of your disease will be?
    - How long do you feel the disease will last?

Fertility

- Tell me what are your expectations regarding parenthood. How do you feel about them?
- Tell me what your fertility means to you. / Tell me about you concerns regarding your fertility.

Ending question

- Do you have any other insights or comments about what we have just discussed that you think are important for me to know?

Appendix 10 – Table of charities approached to facilitate recruitment

Charity	Type of charity	Website	Newsletter	Forum	Blog	Social media (Twitter/Facebook)	Mailing list	Survey	Interview	Did not participate
Breakthrough Breast Cancer	Breast cancer	☐	☐	☐	☐	☐	☐	☐	☐	☒
Breast Cancer Care	Breast cancer	☐	☒	☒	☐	☒	☐	☒	☒	☐
Breast Cancer UK	Breast cancer	☐	☐	☐	☐	☒	☐	☒	☒	☐
Coppafeel!	Breast cancer	☐	☐	☐	☐	☐	☒	☒	☒	☐
Young Breast Cancer Network	Breast cancer	☐	☐	☐	☐	☒	☐	☒	☒	☐
Jo's Trust	Cervical cancer	☒	☐	☐	☐	☒	☐	☒	☒	☐
Mercedes Curnow Foundation	Cervical cancer	☐	☐	☐	☐	☒	☐	☒	☐	☐
The Faye Knowles Chapmen Foundation	Cervical cancer	☐	☐	☐	☐	☒	☐	☒	☐	☐
Cancer Support Scotland	General	☐	☐	☐	☐	☐	☐	☐	☐	☒
Macmillan	General	☐	☐	☒	☐	☒	☐	☒	☒	☐
Maggie's online	General	☐	☐	☐	☒	☒	☐	☒	☐	☐
Shine Cancer Support	General (for young people)	☐	☐	☐	☐	☒	☐	☒	☒	☐
Youth Cancer Trust	General (for young people)	☐	☐	☐	☐	☒	☐	☒	☐	☐
Eve Appeal	Gynaecological cancers	☐	☐	☐	☐	☒	☐	☒	☐	☐
Ovacome	Ovarian cancer	☐	☐	☒	☐	☐	☐	☒	☐	☐
Target Ovarian Cancer	Ovarian cancer	☐	☐	☐	☐	☐	☐	☐	☐	☒
The Robin Cancer Trust	Ovarian/testicular tumours	☐	☐	☐	☐	☐	☐	☐	☐	☒
Womb Cancer Support UK	Womb cancer	☐	☐	☐	☐	☒	☐	☒	☒	☐

Appendix 11 – Qualitative study advertisement

Fertility issues in gynaecological and breast cancer

My name is Aleksandra Sobota and I am a 2nd year PhD student in medicine at the University of St Andrews. I would like to invite you to take part in the research project that will help me complete my dissertation.

This project looks at how women make decisions concerning cancer treatment in relation to fertility issues they might have.

We know sometimes it is difficult to share such information so if you don't feel comfortable with it, you don't have to participate. However, knowing your story and how you feel is important to us and might also help other women that are or will be in a situation similar to yours.

In order to be eligible to participate you must have been diagnosed with gynaecological (cervical, ovarian, uterine) or breast cancer at the age 18 to 45 and you have to be within 5 years of finishing treatment (except for tamoxifen for breast cancer) at the time of the study.

If you decide to take part in this study you will be interviewed about your experience of cancer, its treatment and how important fertility is to you and how it might have changed due to cancer.

The information you provide will be anonymous and held confidentially by researcher and supervisor involved in this project.

If you think you might be interested in sharing your story, please contact the Researcher (Aleksandra Sobota) via phone or email and provide your contact details (postal address and telephone number). Providing your contact details will mean that the researcher will send you a research pack where you will find more information about this project and

will call you 2 weeks later in order to discuss the project and answer any questions you might have. You have the right to withdraw from the study at any time.

If you wish to consider taking part please use the following contact details in order to get in touch with us.

Thank you!

Contact details

Researcher:	**Supervisor:**
Aleksandra Sobota, PhD student	Dr. Gozde Ozakinci
University of St Andrews	University of St Andrews
Biological and Medical Sciences Building	Biological and Medical Sciences Building
North Haugh	North Haugh
KY16 9TF	KY16 9TF
St Andrews	St Andrews
Fife	Fife
tel: 01334 464748 (ext 14440)	tel: 01334 463521
E-mail address: as297@st-andrews.ac.uk	E-mail address: go10@st-andrews.ac.uk

Appendix 12 – Ethical approvals

University of St Andrews

University Teaching and Research Ethics Committee
Sub-committee

21st February 2014

Aleksandra Sobota
School of Medicine

Ethics Reference No: *Please quote this ref on all correspondence*	**MD10852**
Project Title:	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
Researchers Name(s):	**Aleksandra Sobota**
Supervisor(s):	**Gozde Ozakinci**

Thank you for submitting your application which was considered by the School of Medicine Ethics Convener on the 21st February 2014. The following documents were reviewed:

1. Ethical Application Form — YES
2. Participant Information Sheet — YES
3. Consent Form — YES
4. Debriefing Form — YES
5. External Permissions — YES
6. Advertisement — YES

The University Teaching and Research Ethics Committee (UTREC) approves this study from an ethical point of view. Please note that where approval is given by a School Ethics Committee that committee is part of UTREC and is delegated to act for UTREC.

Approval is given for three years. Projects, which have not commenced within two years of original approval, must be re-submitted to your School Ethics Committee.

You must inform your School Ethics Committee when the research has been completed. If you are unable to complete your research within the 3 three year validation period, you will be required to write to your School Ethics Committee and to UTREC (where approval was given by UTREC) to request an extension or you will need to re-apply.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the School Ethics Committee, and an Ethical Amendment Form submitted where appropriate.

Approval is given on the understanding that the 'Guidelines for Ethical Research Practice' https://www.st-andrews.ac.uk/utrec/guidelines/ are adhered to.

Yours sincerely

Professor Gerry Humphris
Convenor of the School Ethics Committee

UTREC Convenor, Mansefield, 3 St Mary's Place, St Andrews, KY16 9UY
Email: utrec@st-andrews.ac.uk Tel: 01334 462866
The University of St Andrews is a charity registered in Scotland: No SC013532

University of St Andrews
from first to foremost

600 YEARS
1413 – 2013

Project Title	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
Researchers Name(s)	**Aleksandra Sobota**
Supervisor(s)	**Dr Gozde Ozakinci**
Department/Unit	**School of Medicine**
Ethical Approval Code (Approval allocated to Original Application)	**MD10852**
Original Application Approval Date	**21st February 2014**
Amendment Application Approval	**30th May 2014**

Ethical Amendment 1 Approval

Thank you for submitting your amendment application which was considered by the School of Medicine Ethics Convener on the 30th May 2014. The following documents were reviewed:

1. Ethical Amendment Application Form YES

The University Teaching and Research Ethics Committee (UTREC) approves this study from an ethical point of view. Please note that where approval is given by a School Ethics Committee that committee is part of UTREC and is delegated to act for UTREC.

Approval is given for three years from the original application only. Ethical Amendments do not extend this period but give permission to an amendment to the original approval research proposal only. If you are unable to complete your research within the original 3 three year validation period, you will be required to write to your School Ethics Committee and to UTREC (where approval was given by UTREC) to request an extension or you will need to re-apply. You must inform your School Ethics Committee when the research has been completed.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the School Ethics Committee, and an Ethical Amendment Form submitted where appropriate.

Approval is given on the understanding that the 'Guidelines for Ethical Research Practice' (http://www.st-andrews.ac.uk/media/UTRECguidelines%20Feb%2008.pdf) are adhered to.

Yours sincerely

Dr Morven Shearer
Convenor of the School Ethics Committee

UTREC Convenor, Mansefield, 3 St Mary's Place, St Andrews, KY16 9UY
Email: utrec@st-andrews.ac.uk Tel: 01334 462866
The University of St Andrews is a charity registered in Scotland: No SC013532

University of St Andrews
from first to foremost

600 YEARS
1413 – 2013

Project Title	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
Researchers Name(s)	**Aleksandra Sobota**
Supervisor(s)	**Dr Gozde Ozakinci**
Department/Unit	**School of Medicine**
Ethical Approval Code (Approval allocated to Original Application)	**MD10852**
Original Application Approval Date	**21st February 2014**
Amendment Application Approval	**29th September 2014**

Ethical Amendment 2 Approval

Thank you for submitting your amendment application which was considered by the School of Medicine Ethics Convener on the 29th September 2014. The following documents were reviewed:

1.	Ethical Amendment Application Form	YES
2.	Amended Participant Information Sheet	YES
3.	Amended Consent Form	YES
4.	Amended Debriefing Form	YES
5.	Amended Questionnaire	YES
6.	Amended Advertisement	YES
7.	List of documents listed in the Notice of Amendment to the NHS REC	YES
8.	Outline of Recruitment Strategy via social media	YES

The University Teaching and Research Ethics Committee (UTREC) approves this study from an ethical point of view. Please note that where approval is given by a School Ethics Committee that committee is part of UTREC and is delegated to act for UTREC.

Approval is given for three years from the original application only. Ethical Amendments do not extend this period but give permission to an amendment to the original approval research proposal only. If you are unable to complete your research within the original 3 three year validation period, you will be required to write to your School Ethics Committee and to UTREC (where approval was given by UTREC) to request an extension or you will need to re-apply. You must inform your School Ethics Committee when the research has been completed.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the School Ethics Committee, and an Ethical Amendment Form submitted where appropriate.

University of St Andrews
from first to foremost

600 YEARS
1413 – 2013

Approval is given on the understanding that the 'Guidelines for Ethical Research Practice' (http://www.st-andrews.ac.uk/media/UTRECguidelines%20Feb%2008.pdf) are adhered to.

Yours sincerely

Dr Morven Shearer
Convenor of the School Ethics Committee

UTREC Convenor, Mansefield, 3 St Mary's Place, St Andrews, KY16 9UY
Email: utrec@st-andrews.ac.uk Tel: 01334 462866

University of St Andrews
from first to foremost

600 YEARS
1413 – 2013

Project Title	**Fertility issues and fears of cancer recurrence in young gynaecological and breast cancer patients**
Researchers Name(s)	**Aleksandra Sobota**
Supervisor(s)	**Dr Gozde Ozakinci**
Department/Unit	**School of Medicine**
Ethical Approval Code (Approval allocated to Original Application)	**MD10852**
Original Application Approval Date	**21st February 2014**
Amendment Application Approval	**12th March 2015**

Ethical Amendment 3 Approval

Thank you for submitting your amendment application which was considered by the School of Medicine Ethics Convener on the12th March 2015. The following documents were reviewed:

1. Ethical Amendment Application Form YES

The University Teaching and Research Ethics Committee (UTREC) approves this study from an ethical point of view. Please note that where approval is given by a School Ethics Committee that committee is part of UTREC and is delegated to act for UTREC.

Approval is given for three years from the original application only. Ethical Amendments do not extend this period but give permission to an amendment to the original approval research proposal only. If you are unable to complete your research within the original 3 three year validation period, you will be required to write to your School Ethics Committee and to UTREC (where approval was given by UTREC) to request an extension or you will need to re-apply. You must inform your School Ethics Committee when the research has been completed.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the School Ethics Committee, and an Ethical Amendment Form submitted where appropriate.

Approval is given on the understanding that the 'Guidelines for Ethical Research Practice' (http://www.st-andrews.ac.uk/media/UTRECguidelines%20Feb%2008.pdf) are adhered to.

Yours sincerely

Dr Gordon Cramb
Acting Convenor of the School Ethics Committee

UTREC Convenor, Mansefield, 3 St Mary's Place, St Andrews, KY16 9UY
Email: utrec@st-andrews.ac.uk Tel: 01334 462866
The University of St Andrews is a charity registered in Scotland: No SC013532

University of St Andrews
from first to foremost

600 YEARS
1413 – 2013

Project Title	**Fertility issues and fears of cancer recurrence in young gynaecological and breast cancer patients**
Researchers Name(s)	**Aleksandra Sobota and Dr Douglas Adamson**
Supervisor(s)	**Dr Gozde Ozakinci**
Department/Unit	**School of Medicine**
Ethical Approval Code (Approval allocated to Original Application)	**MD10852**
Original Application Approval Date	**21st February 2014**
Amendment Application Approval	**13th March 2015**

Ethical Amendment 4 Approval

Thank you for submitting your amendment application which was considered by the School of Medicine Ethics Convener on the13th March 2015. The following documents were reviewed:

1. Ethical Amendment Application Form YES
2. Protocol v.3 YES

The University Teaching and Research Ethics Committee (UTREC) approves this study from an ethical point of view. Please note that where approval is given by a School Ethics Committee that committee is part of UTREC and is delegated to act for UTREC.

Approval is given for three years from the original application only. Ethical Amendments do not extend this period but give permission to an amendment to the original approval research proposal only. If you are unable to complete your research within the original 3 three year validation period, you will be required to write to your School Ethics Committee and to UTREC (where approval was given by UTREC) to request an extension or you will need to re-apply. You must inform your School Ethics Committee when the research has been completed.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the School Ethics Committee, and an Ethical Amendment Form submitted where appropriate.

Approval is given on the understanding that the 'Guidelines for Ethical Research Practice' (http://www.st-andrews.ac.uk/media/UTRECguidelines%20Feb%2008.pdf) are adhered to.

Yours sincerely

Dr Gordon Cramb
Acting Convenor of the School Ethics Committee

UTREC Convenor, Mansefield, 3 St Mary's Place, St Andrews, KY16 9UY
Email: utrec@st-andrews.ac.uk Tel: 01334 462866

EoSRES

NHS SCOTLAND
Research Ethics Service

East of Scotland Research Ethics Service (EoSRES) REC 1
Tayside Medical Sciences Centre (TASC)
Residency Block C, Level 3
Ninewells Hospital & Medical School
George Pirie Way
Dundee DD1 9SY

Miss Aleksandra Sobota
PhD student
School of Medicine
University of St Andrews
North Haugh
KY16 9TF

Date: 12 November 2013
Your Ref:
Our Ref: LR/**13/ES/0129**
Enquiries to: Mrs Lorraine Reilly
Direct Line: 01382 383878
Email: eosres.tayside@nhs.net

Dear Miss Sobata

Study title:	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
REC reference:	**13/ES/0129**
Protocol number:	**N/A**
IRAS project ID:	**134567**

Thank you for your letter of 01 November 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a sub-committee of the REC. A list of the sub-committee members is attached.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mrs Lorraine Reilly, lorraine.reilly@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

POSITIVE ABOUT DISABLED PEOPLE

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Advertisement	1	26 September 2013
Evidence of insurance or indemnity		22 June 2013
Evidence of insurance or indemnity		25 June 2013
Evidence of insurance or indemnity		01 August 2013
Interview Schedules/Topic Guides	1	26 September 2013
Investigator CV – Miss Sobata		
Investigator CV – Dr Ozakinci		

Letter of invitation to participant: Qualitative Study	2	01 November 2013
Letter of invitation to participant: Quantitative Study	2	01 November 2013
Other: Opt-in form qualitative study	1	26 September 2013
Other: Qualitative Study Debriefing Form	1	26 September 2013
Other: Quantitative Study Debriefing Form	1	26 September 2013
Other: Debriefing Online Participants	1	26 September 2013
Participant Consent Form: Qualitative Study	2	01 November 2013
Participant Information Sheet: Qualitative Study	2	01 November 2013
Participant Information Sheet: Quantitative Study	2	01 November 2013
Protocol	1	26 September 2013
Questionnaire: Value of Children		
Questionnaire	1	26 September 2013
Questionnaire: Whole questionnaire	1	26 September 2013
REC application		26 September 2013
Referees or other scientific critique report		26 September 2013
Referees or other scientific critique report		26 September 2013
Response to Request for Further Information		01 November 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/ES/0129:	***Please quote this number on all correspondence***

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

Yours sincerely

pp
Dr Lynda Cochrane
Alternate Vice-chair

eosres.tayside@nhs.net

Enclosures:	List of names and professions of members who were present at the meeting and those who submitted written comments "After ethical review – guidance for researchers"
Copy to:	David Stevenson, The University Court of the University of St Andrews NHS Tayside R&D office

East of Scotland Research Ethics Service REC 1

Attendance at Sub-Committee of the REC meeting on 12 November 2013

Also in attendance:

Name	Position (or reason for attending)
Mrs Lorraine Reilly	Senior Co-ordinator

Written comments received from:

Name	Position
Dr Lynda Cochrane	Professional Statistician, Alternate Vice-chair
Dr Gary Lyon	Retired

EoSRES

NHS SCOTLAND
Research Ethics Service

East of Scotland Research Ethics Service (EoSRES) REC 1
Tayside Medical Sciences Centre (TASC)
Residency Block C, Level 3
Ninewells Hospital & Medical School
George Pirie Way
Dundee DD1 9SY

Miss Aleksandra Sobota
PhD student
University of St Andrews
School of Medicine
University of St Andrews
North Haugh
KY16 9TF

Date: 26 August 2014
Your Ref:
Our Ref: LR/13/ES/0129
Enquiries to: Mrs Lorraine Reilly
Direct Line: 01382 383878
Email: eosres.tayside@nhs.net

Dear Miss Sobota

Study title:	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
REC reference:	**13/ES/0129**
Protocol number:	**N/A**
Amendment number:	**AM01 (for REC reference only)**
Amendment date:	**08 August 2014**
IRAS project ID:	**134567**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

There were no ethical issues noted.

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Copies of advertisement materials for research participants [Quantitative Study]	2	28 July 2014
Copies of advertisement materials for research participants [Cross-sectional Qualitative Study]	1.3	28 July 2014
Interview schedules or topic guides for participants [Cross-sectional Qualitative Study]	1	28 July 2014
Letters of invitation to participant [Cross-sectional Qualitative Study]	1.2	28 July 2014
Letters of invitation to participant [Quantitative Study]	3	28 July 2014
Letters of invitation to participant [Qualitative Study]	3.2	28 July 2014

POSITIVE ABOUT DISABLED PEOPLE

Letters of invitation to participant [Qualitative Study]	3.1	28 July 2014
Letters of invitation to participant [Cross-sectional Qualitative Study]	1.1	28 July 2014
Non-validated questionnaire [Whole questionnaire]	2	28 July 2014
Notice of Substantial Amendment (non-CTIMP) [134567/650716/13/285/28181]	AM01	08 August 2014
Other [Cross-sectional Qualitative Study - Opt-in form]	1.1	28 July 2014
Other [Qualitative Study - Opt-in form]	2.1	28 July 2014
Other [Quantitative Study - Screening Chart]	1	28 July 2014
Other [Qualitative Study - Debriefing form]	2	28 July 2014
Other [Cross-sectional Qualitative Study - Opt-in form]	1.2	28 July 2014
Other [Cross-sectional Qualitative Study - Screening Chart]	1	28 July 2014
Other [Qualitative Study - Opt-in form]	2.2	28 July 2014
Other [Quantitative Study - Debriefing form]	2	28 July 2014
Other [Cross-sectional Qualitative Study - Debriefing form]	1	28 July 2014
Other [Quantitative Study - Reminder Letter]	1	28 July 2014
Other [Cross-sectional Qualitative Study - Debriefing form]	1.3	28 July 2014
Other [Cross-sectional Qualitative Study – Letter of Invitation]	1.3	28 July 2014
Other [Quantitative Study - Contact Details Sheet]	1	28 July 2014
Participant consent form [Cross-sectional Qualitative Study]	1.1	28 July 2014
Participant consent form [Cross-sectional Qualitative Study]	1.3	28 July 2014
Participant consent form [Qualitative Study]	3.1	28 July 2014
Participant consent form [Qualitative Study]	3.2	28 July 2014
Participant consent form [Cross-sectional Qualitative Study]	1.2	28 July 2014
Participant information sheet (PIS) [Qualitative Study]	3.1	28 July 2014
Participant information sheet (PIS) [Cross-sectional Qualitative Study]	1.1	28 July 2014
Participant information sheet (PIS) [Cross-sectional Qualitative Study]	1.3	28 July 2014
Participant information sheet (PIS) [Quantitative Study]	3	28 July 2014
Participant information sheet (PIS) [Cross-sectional Qualitative Study]	1.2	28 July 2014
Participant information sheet (PIS) [Qualitative Study]	3.2	28 July 2014
Research protocol or project proposal	2	28 July 2014

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

13/ES/0129:	***Please quote this number on all correspondence***

Yours sincerely

pp
Dr Carol Macmillan
Chair

eosres.tayside@nhs.net

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: NHS Tayside R&D office
David Stevenson, The University Court of the University of St Andrews

East of Scotland Research Ethics Service REC 1

Attendance at Sub-Committee of the REC meeting on 25 August 2014

Committee Members:

Name	Profession	Present	Notes
Dr Carol Macmillan	Consultant Anaesthetist	Yes	Chair
Mr John Macleod	Retired	Yes	

Also in attendance:

Name	Position (or reason for attending)
Mrs Lorraine Reilly	Senior Co-ordinator

Written comments received from:

Name	Position
Dr Carol Macmillan	Consultant Anaesthetist
Mr John Macleod	Retired

NHS SCOTLAND

East of Scotland Research Ethics Service *(EoSRES)* **Research Ethics Service**

TAyside medical Science Centre
Residency Block Level 3
George Pirie Way
Ninewells Hospital and Medical School
Dundee DD1 9SY

Miss Aleksandra Sobota
PhD student
University of St Andrews
School of Medicine
University of St Andrews
North Haugh
KY16 9TF

Date: 18 March 2015
Your Ref:
Our Ref: **DL/13/ES/0129**
Enquiries to: Mrs Diane Leonard
Direct Line: 01382 383871
Email: diane.leonard@nhs.net

Dear Miss Sobota

Study title:	**Fertility issues and fears of cancer recurrence in young gynaecological cancer patients**
REC reference:	**13/ES/0129**
Protocol number:	**N/A**
Amendment number:	**AM02 (For REC Reference Only)**
Amendment date:	**16 March 2015**
IRAS project ID:	**134567**

Thank you for your letter of 16 March 2015, notifying the Committee of the above amendment.

The Committee does not consider this to be a "substantial amendment" as defined in the Standard Operating Procedures for Research Ethics Committees. The amendment does not therefore require an ethical opinion from the Committee and may be implemented immediately, provided that it does not affect the approval for the research given by the R&D office for the relevant NHS care organisation.

Documents received

The documents received were as follows:

Document	Version	Date
Notice of Minor Amendment	AM02	16 March 2015
Other [Approval for Amendment 3]		12 March 2015
Other [Approval for Amendment 4]		13 March 2015
Research protocol or project proposal	3	12 March 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

POSITIVE ABOUT DISABLED PEOPLE

13/ES/0129:	Please quote this number on all correspondence

Yours sincerely

Mrs Diane Leonard
Assistant Co-ordinator

E-mail: eosres.tayside@nhs.net

Copy to: NHS Tayside R&D Office
Mr David Stevenson

Appendix 13 – SHARE letter

«forenames» «surname»
«addr1»
«addr2», «addr3»
«addr4»
«postcode»

Division of Public Health Sciences
Mackenzie Building
Kirsty Semple Way
DUNDEE
DD2 4BF
30 November 2015

Dear «title» «surname» —

Scottish Health Research Register
www.registerforshare.org

CHI «CHI» — Register No «id»

You very kindly joined the Scottish Health Research Register as you were interested in hearing about opportunities to help with medical research.
We are writing to let you know about a research opportunity that has arisen and that might appeal to you. We have described the project in brief detail below.
If this sounds interesting to you, please let us know by returning the tear-off slip in the enclosed stamped addressed envelope. If you are not interested on this occasion please also let us know so we do not contact you again. Alternatively you may phone 01382 383471 or email enquiries@registerforshare.org quoting the reference above. If you tell us that you are interested, then we will pass your details on, and a member of the research team will get in touch with you to explain more about the project. You can change your mind at any stage.

Study title: Fertility issues in gynaecological cancer

This study looks at the causes of distress related to fertility issues that may result from gynaecological cancer and its treatment. It also explores how fertility-related distress may affect life quality. Taking part in the study involves filling in a questionnaire that contains 132 or 133 questions (depending on your relationship status) which we anticipate will take approximately 25 minutes to complete. The information provided in the questionnaire will be anonymous and held confidentially by the research team. The questionnaire can be accessed online or delivered by post, depending on the participant's preference.

Yours sincerely,

Professor Frank Sullivan
NHS Tayside Professor of R&D in General Practice
University of Dundee & NHS Tayside

Professor Brian McKinstry
Professor of Primary Care E-Health
University of Edinburgh and NHS Lothian

SHARE Directors on behalf of the SHARE team

✂_____

Please circle the appropriate answer.

YES I would like to take part / find out more about the study. **NO** I do not wish to take part in the study.

NAME: _____

CONTACT TELEPHONE NUMBER: _____

BEST TIME TO CONTACT: _____

E-MAIL ADDRESS: _____

Signature..... **Date**.....

Appendix 14 – Quantitative study advertisement

Fertility issues in gynaecological and breast cancer

My name is Aleksandra Sobota and I am a 2nd year PhD student at the University of St Andrews. I would like to invite you to take part in the research project that will help me complete my dissertation.

This project looks at how the consequences of gynaecological cancers (mainly fertility issues and fear that cancer might come back) can affect the quality of life of young women who were diagnosed with gynaecological or breast cancer in the past. We know sometimes it is difficult to share such information so if you don't feel comfortable with it, you don't have to participate. However, knowing your story and how you feel is important to us and might also help other women that are or will be in a situation similar to yours.

If you decide to take part in this study you will be asked to fill in a questionnaire. Which one you choose is up to you. The questionnaire contains 132 or 133 questions (depending on your relationship status) that we anticipate will take 40 minutes to complete. The information you provide will be anonymous and held confidentially by researcher and supervisor involved in this project. Before agreeing to participate in this research you will be given a Participant Information Sheet that will further detail my research before consenting to participate.

If you wish to consider taking part please access the information and the questionnaire at: http://www.smartsurvey.co.uk/s/fertility1

If you wish to contact us, feel free to do this.

Contact details

Researcher: **Supervisor:**

Aleksandra Sobota, PhD student

University of St Andrews

Biological and Medical Sciences Building

North Haugh

KY16 9TF

St Andrews

Fife

tel: 01334 464748 (ext 14440)

E-mail address: as297@st-andrews.ac.uk

Dr. Gozde Ozakinci

University of St Andrews

Biological and Medical Sciences Building

North Haugh

KY16 9TF

St Andrews

Fife

tel: 01334 463521

E-mail address: go10@st-andrews.ac.uk

Appendix 15 – Psychometric properties of selected scales

Predictor variables

1. Brief-IPQ (illness perceptions) (326). The psychometric properties of this scale were measured among several patient populations. The test-retest reliability evaluated using a sample of renal patients from outpatient clinics ranged from 0.48 to 0.7 at 3 weeks follow-up and from 0.42 to 0.75 at 6 weeks follow-up (326). Concurrent validity was assessed by correlating the scores of Brief-IPQ with those of Illness Perception Questionnaire-Revised (80) in three groups of patients including renal, diabetes and asthma patients. The equivalent subscales of the two questionnaires appeared to be appropriately correlated (coefficients ranging from 0.32 for treatment control to 0.63 for emotional representation). The psychometric properties of the Polish version of the scale are not yet available (Marlena Kossakowska, personal communication, 11 June 2013).
2. PANAS (dispositional negative affect). The internal consistency of the NA subscale in the original study by Watson, D. et al. (327) when NA was measured as trait amounted to $\alpha = 0.87$. The test-retest reliability over an 8-week period among the group of students was 0.71 suggesting that PANAS is a good measure of trait affect. The Polish version of the subscale presents equally appropriate psychometric properties with internal consistency of $\alpha = 0.88$ measured in a random sample and the test-retest reliability over 4 to 6 weeks in a group of students amounting to 0.89 (328).

Outcome variables

1. IES-R (distress related to reproductive issues) (329, 330). Psychometric properties of the IES-R were initially tested on two populations that experienced a traumatic event (earthquake) and yielded the following results. The internal consistencies of the intrusion, avoidance and hyperarousal subscales were 0.87-0.92, 0.84-0.86, and 0.79-0.9, respectively. The test-retest reliabilities were 0.54-0.94 for the intrusion subscale, 0.51-0.89 for the avoidance subscale and 0.59-0.92 for the hyperarousal subscale (371). For the Polish version of the IES-R the internal consistency of the overall scale measured in a group of fire-fighters was 0.92 and the internal consistencies of the intrusion, avoidance and hyperarousal

subscales were 0.89; 0.85 and 0.78, respectively. The test-retest reliabilities (over 2 weeks) were 0.75 for the overall scale, 0.79 for the intrusion subscale, 0.76 for the avoidance subscale, and 0.68 for the hyperarousal subscale (330).

2. QLACS (QoL). The internal consistency of the scale has been reported to range from 0.72 to 0.95 (334). No psychometric properties are available for the Polish adaptation
3. CSI(4) (relationship satisfaction). The internal consistency of the scale in the original study was $\alpha = 0.94$ (336).
4. CARES (dating experiences). The internal consistency of the dating subscale in the original study was $\alpha = 0.90$ (337).

Psychometric properties were unavailable for the following scales:

1. VOC
2. FCR

Appendix 16 – Study questionnaire (with online version filtering questions)

Filtering questions for the online questionnaire

I was diagnosed with gynaecological cancer (cervical, ovarian, endometrial) or breast cancer at the age of 18 to 45.

a. Yes
b. No

I received chemotherapy as part of my breast cancer treatment.

a. Yes
b. No
c. I was diagnosed with gynaecological cancer

I am currently off treatment (in follow-up) (except for Tamoxifen if you were diagnosed with breast cancer)

a. Yes
b. No

Fertility issues in gynaecological and breast cancer

Participant Questionnaire

Thank you for your help with this research. Please answer all questions as honestly and as fully as possible. By completing and returning the questionnaire you are consenting for the information you give to be used in this research. If you have any questions or want help completing the questionnaire, please contact Aleksandra Sobota on:

01334 464748 (ext 14440) or as297@st-andrews.ac.uk

Please provide the following details:

Your age:

Your nationality:
a. British
b. Other, specify: .....

What best describes your monthly income before tax:
a. Less than £430
b. £431-£1500
c. £1501-£2600
d. £2601-£4300
e. £4301-£8300
f. £8301-£12500
g. More than £12500
h. Prefer not to say

Your current relationship status:
a. I am single
b. I am in a relationship

Your children:
a. I do not have children
b. I have 1 child
c. I have 2 children
d. I have 3 or more children

What is the highest degree or level of school you have completed?
a. GCSE Level education (eg GCSE, O-Levels or Standards)
b. A-Level education (eg A, AS, S-Levels, Highers)
c. Undergraduate education (eg University examinations but not completed degree)
d. Degree or Graduate education (eg BSc, BA)
e. Post-graduate education (eg PhD, MSc, MA)
f. Vocational education (eg NVQ, HNC, HND)

Please provide the following details about your diagnosis:

Type of disease:
a. Cervical cancer
b. Ovarian cancer
c. Uterine cancer
d. Breast cancer
e. Other. Please specify .....

Type of treatment received (please indicate all):
a. Conservative surgery (fertility-sparing or breast conserving surgery)
b. Radical surgery (hysterectomy or mastectomy)
c. Radiotherapy
d. Chemotherapy
e. Hormone therapy

Stage of disease at diagnosis:
a. I
b. II
c. III
d. IV

When were you diagnosed (please indicate the year):

For the following questions, please tick the answer that best corresponds to your views.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. How much did you want to have children at the time of your cancer diagnosis?					
If you had a partner at the time of diagnosis please answer question 2, if not, please go to question 3.					
2. How much do you think your partner wanted to have children at the time of your cancer diagnosis?					
3. At the time of your diagnosis, how much did you believe that treatment you were about to receive was the best option for you?					
4. I regret having undergone the cancer treatment that altered my fertility.					
5. How much do you think the culture you come from disapproves of people who do not have children?					

Positive and Negative Affect Schedule

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. **Indicate to what extent you generally feel this way, that is, how you feel on average.**

Use the following scale to record your answers.

1	*2*	*3*	*4*	*5*
very slightly or not at all	*a little*	*moderately*	*quite a bit*	*extremely*

..... distressed	..... irritable
..... upset	..... ashamed
..... guilty	..... nervous
..... scared	..... jittery
..... hostile	..... afraid

The Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

How much does the illness affect your life?

0	1	2	3	4	5	6	7	8	9	10
No affect at all	…	…	…	…	…	…	…	…	…	Severely affects my life

How long do you think your illness will continue?

0	1	2	3	4	5	6	7	8	9	10
A very short time	…	…	…	…	…	…	…	…	…	Forever

How much control do you feel you have over your illness?

0	1	2	3	4	5	6	7	8	9	10
Absolutely no control	…	…	…	…	…	…	…	…	…	Extreme amount of control

How much do you think your treatment can help your illness?

0	1	2	3	4	5	6	7	8	9	10
Not at all	…	…	…	…	…	…	…	…	…	Extremely helpful

How much do you experience symptoms from your illness?

0	1	2	3	4	5	6	7	8	9	10
No symptoms at all	…	…	…	…	…	…	…	…	…	Many severe symptoms

How concerned are you about your illness?

0	1	2	3	4	5	6	7	8	9	10
Not at all concerned	…	…	…	…	…	…	…	…	…	Extremely concerned

How well do you feel you understand your illness?

0	1	2	3	4	5	6	7	8	9	10
Don't understand at all	…	…	…	…	…	…	…	…	…	Understand very clearly

How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)

0	1	2	3	4	5	6	7	8	9	10
Not at all affected emotionally	…	…	…	…	…	…	…	…	…	Extremely affected emotionally

Please list in rank-order the three most important factors you believe caused <u>your illness.</u> *The most important causes for me:*

1. _____
2. _____
3. _____

Value of children

Here is a list of reasons people may give for wanting to have children in general. Please use this scale as a guide. Think about your experience and tick how important the following reasons for wanting to have children are to you personally.

	Not important at all	Not very important	Moderately important	Important	Very important
Because a child helps around the house.					
Because any new family member makes your family more important.					
Because having children brings your husband and you closer together.					
Because having children gives your husband/you more reason to succeed in his/your work.					
Because having children increases your sense of responsibility and helps you to develop.					
Because having children intensifies contacts and communication with your kin.					
Because it is a joy to have a small baby.					
Because it is fun to have young children around the house.					
Because of the pleasure you get from watching your children grow.					
Because of the special feeling of love that develops between a parent and a child.					
Because parenthood improves your standing and betters your reputation among your kin.					
Because people with children are less likely to be lonely in old age.					
Because raising children helps you to learn about life and yourself.					
Because some of your older relatives feel that you should have more children.					
Because you can make new friends through your children.					
Because you want to share what you have with children.					
Because your life will be continued through your children.					

	Not important at all	Not very important	Moderately important	Important	Very important
To be sure that enough children will survive to adulthood.					
To have a girl/another girl.					
To carry on the family name.					
To have one more person to help your family economically.					
To have someone to love and care for.					
To provide a companion for your child/children.					
To have a boy/another boy.					
When it is a duty to have children according to your belief.					
When your husband wants more children.					
Your children can help you when you're old.					

Fear of recurrence questionnaire

Most people who have had cancer are worried to varying degrees about the possibility of a recurrence of the cancer. By **recurrence** we mean the possibility that cancer will **return** or **progress** in the same place or in another part of your body. For each question, please tick the box for the answer that best reflects how you felt in **THE PAST MONTH**.

	No at all	A little	Sometimes	A lot	All the time
I am afraid my cancer may recur.					
I am worried or anxious about the possibility of cancer recurrence.					
How often have you worried about the possibility of getting cancer again?					
I get strong waves of strong feelings about the cancer coming back.					
I think about the cancer returning when I didn't mean to.					
I examine myself to see if I have any physical signs of cancer.					

For the following question **please circle the number** for the answer that best reflects how you felt **IN THE PAST MONTH.**

To what extent does worrying about getting cancer again spill over or intrude on your thoughts and activities?

0 1 2 3 4 5 6 7 8 9 10
Not at all ... ... A great deal

Impact of Event Scale – Revised

Below is a list of difficulties people sometimes have after stressful life events. Please read each item and indicate how distressing each difficulty has been for you **during the past 7 days** with respect to **fertility issues related to cancer and its treatment**. How much were you distressed or bothered by these difficulties?

	Not at all	A little bit	Moderately	Quite a bit	Extremely
Any reminder brought back feelings about it.					
I had trouble staying asleep.					
Other things kept making me think about it.					
I felt irritable and angry.					
I avoided letting myself get upset when I thought about it or was reminded of it.					
I thought about it when I didn't mean to.					
I felt as if it hadn't happened or wasn't real.					
I stayed away from reminders of it.					
Pictures about it popped into my mind.					
I was jumpy and easily startled.					
I tried not to think about it.					
I was aware that I still had a lot of feelings about it, but I didn't deal with them.					
My feelings about it were kind of numb.					
I found myself acting or feeling like I was back at that time.					
I had trouble falling asleep.					
I had waves of strong feelings about it.					
I tried to remove it from my memory.					
I had trouble concentrating.					
Reminders of it caused me to have physical reactions, such as sweating, trouble breathing, nausea, and pounding heart.					
I had dreams about it.					
I felt watchful and on guard.					
I tried not to talk about it.					

Quality of Life Adult Cancer Survivors Scale

We'd like to ask you about some things that can affect the quality of people's lives. Some of these questions may sound similar but please be sure to answer each one. Below is a scale ranging from never to always. Please indicate how often each of these statements has been true for you in the **past four weeks**. CIRCLE ONE ANSWER FOR EACH QUESTION.

	Never	Seldom	Sometimes	About as often as not	Frequently	Very often	Always
In the past 4 weeks…							
You had the energy to do the things you wanted to do.							
You had difficulty doing activities that require concentrating.							
You were bothered by having short attention span.							
You had trouble remembering things.							
You felt fatigued.							
You felt happy.							
You felt blue or depressed.							
You enjoyed life.							
You worried about little things.							
You were bothered by being unable to function sexually.							
You didn't have energy to do the things you wanted to do.							
You were dissatisfied with your sex life.							
You were bothered by pain that kept you from doing the things you wanted to do							
You felt tired a lot.							
You were reluctant to start new relationships.							
You lacked interest in sex.							
Your mood was disrupted by pain or its treatment.							
You avoided social gatherings.							
You were bothered by mood swings.							
You avoided your friends.							
You had aches or pains.							
You had a positive outlook on life.							
You were bothered by forgetting what you started to do.							
You felt anxious.							
You were reluctant to meet new people.							
You avoided sexual activity.							

Pain or its treatment interfered with your social activities.							
You were content with your life.							

The next set of questions asks specifically about the effects of your cancer or its treatment. Again, for each statement indicate how often each of these statements has been true for you in the past four weeks.

	Never	Seldom	Sometimes	About as often as not	Frequently	Very often	Always
You appreciated life more because of having had cancer.							
You worried that your family members were at risk of getting cancer.							
You realized that having had cancer helps you cope better with problems now.							
You were self-conscious about the way you look because of your cancer or its treatment.							
You worried about whether your family members might have cancer-causing genes.							
You felt unattractive because of your cancer or its treatment.							
You were bothered by hair loss from cancer treatment.							
You felt cancer helped you to recognize what is important in life.							
You felt better able to deal with stress because of having had cancer.							
You worried whether your family members should have genetic tests for cancer.							
You felt people treated you differently because of changes to your appearance due to your cancer or its treatment.							

<u>If you do currently have a partner</u>, please answer the questions under <u>Couples Satisfaction Index.</u>

<u>If you do not currently have a partner</u>, please answer the questions under <u>Cancer Rehabilitation Evaluation System</u>.

Couples Satisfaction Index

Please circle the answer that best corresponds to your views.

Please indicate the degree of happiness, all things considered, of your relationship.

Extremely unhappy	Fairly unhappy	A little unhappy	Happy	Very happy	Extremely happy	Perfect

I have a warm and comfortable relationship with my partner.

Not at all true	A little true	Somewhat true	Mostly true	Almost completely true	Completely true

How rewarding is your relationship with your partner?

Not at all	A little	Somewhat	Mostly	Almost completely	Completely

In general, how satisfied are you with your relationship?

Not at all	A little	Somewhat	Mostly	Almost completely	Completely

Cancer Rehabilitation Evaluation System

Below is a list of problem statements that describe situations and experiences of individuals who have or have had cancer. Read each statement and circle the number/tick the answer that best describes **HOW MUCH EACH STATEMENT APPLIES TO YOU** during the **PAST MONTH, INCLUDING TODAY.**

How much does it apply to you?

	Not at all	**A little**	**A fair amount**	**Much**	**Very much**
I have difficulty initiating contact with potential dates					
I have difficulty meeting potential dates					
I am afraid to go to places that I used to visit to meet dates					
I have difficulty telling a date about the cancer or its treatment					
I am afraid to initiate a sexual relationship with someone					

Thank you very much for taking part

Please seal the questionnaire in the stamped-addressed envelope provided and post back to me.

If you have any more questions or comments you would like to make about the questionnaire or the research in general, please contact me on the details below.

If you would like to receive a copy of the results please contact me with your details

Aleksandra Sobota: 01334 464748 (ext 14440)

or as297@st-andrews.ac.uk

Appendix 17 - Kolmogorov-Smirnov test parameters and significance level for scales and subscales from non-imputed and imputed datasets

	Non-imputed dataset		Imputed dataset	
	KS	***p***	**KS**	***p***
VOC_U	1.96	*<0.01**	2.02	*<0.01**
VOC_S	1.17	*n.s.*	1.21	*n.s.*
VOC_P	1.04	*n.s.*	1.02	*n.s.*
PANAS	1.18	*n.s.*	1.13	*n.s.*
IESR_I	1.48	*≤0.05**	1.44	*≤0.05**
IESR_A	1.01	*n.s.*	0.97	*n.s.*
IESR_H	1.95	*<0.01**	1.96	*<0.01**
FCR	0.99	*n.s.*	0.95	*n.s.*
QLACS_NF	0.80	*n.s.*	0.84	*n.s.*
QLACS_PF	0.88	*n.s.*	1.02	*n.s.*
QLACS_CP	1.24	*n.s.*	1.22	*n.s.*
QLACS_P	1.54	*≤0.05**	1.54	*≤0.05**
QLACS_SP	1.10	*n.s.*	1.10	*n.s.*
QLACS_F	1.25	*n.s.*	1.23	*n.s.*
QLACS_SA	1.57	*≤0.05**	1.60	*≤0.05**
QLACS_B	0.94	*n.s.*	0.95	*n.s.*
QLACS_DF	1.70	*≤0.05**	1.70	*≤0.05**
QLACS_A	1.41	*≤0.05**	1.46	*≤0.05**
QLACS_GT	0.82	*n.s.*	0.79	*n.s.*

Appendix 18 – Regression models with separate illness perceptions entered in the last step

Table 1. Multivariate model predicting total fertility-related distress with consequences (IPQ1) entered in the final block

	B	SE B	β	*p*
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-013	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				

Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-0.99	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (consequences)				
Constant	-8.49	11.70		*n.s.*
Age at diagnosis	-0.22	0.24	-0.07	*n.s.*
Country of origin (Britain vs Poland)	11.33	3.65	0.23	*<0.01*
Type of cancer (gynaecological vs breast)	1.48	4.66	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-6.20	4.05	-0.14	*n.s.*
Recruitment site (other vs online)	-7.62	3.03	-0.18	*≤0.05*
Childbearing status (no vs yes)	-1.73	3.07	-0.04	*n.s.*
Negative affect	0.81	0.16	0.35	*<0.01*
Desire to have children	1.99	1.01	0.15	*n.s.*
Treatment related regret (no vs all others)	7.43	3.04	0.16	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	3.48	2.71	0.08	*n.s.*
Value of children – utilitarian	1.40	2.63	0.05	*n.s.*
Value of children – social	-0.88	2.97	-0.03	*n.s.*
Value of children – psychological	3.59	2.24	0.13	*n.s.*
Consequences (IPQ1)	1.14	0.55	0.14	*≤0.05*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, $p =$ n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.575$, adjusted $R^2 = 0.529$, $F(1, 127) = 4.29$, $p \leq 0.05$, $\Delta R^2 = 0.014$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.17 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected

visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 2. Multivariate model predicting total fertility-related distress with timeline (IPQ2) entered in the final block

	B	SE B	β	p
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*

Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-0.99	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (timeline)				
Constant	-5.97	11.76		*n.s.*
Age at diagnosis	-0.26	0.25	-0.08	*n.s.*
Country of origin (Britain vs Poland)	10.99	3.76	0.23	*<0.01*
Type of cancer (gynaecological vs breast)	1.21	4.75	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-6.88	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.11	3.04	-0.18	*<0.01*
Childbearing status (no vs yes)	-0.91	3.06	-0.02	*n.s.*
Negative affect	0.89	0.15	0.39	*<0.01*
Desire to have children	2.26	1.01	0.16	*≤0.05*
Treatment related regret (no vs all others)	7.99	3.05	0.17	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	3.76	2.73	0.09	*n.s.*
Value of children – utilitarian	1.73	2.66	0.06	*n.s.*
Value of children – social	-1.0	3.00	-0.03	*n.s.*
Value of children – psychological	3.32	2.25	0.12	*n.s.*
Timeline (IPQ2)	0.49	0.36	0.09	*n.s.*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$

Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$

Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$

Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, $p =$ n.s., $\Delta R^2 = 0.020$

Step 5: $R^2 = 0.567$, adjusted $R^2 = 0.520$, $F(1, 127) = 1.85$, $p =$ n.s., $\Delta R^2 = 0.006$

The assumptions of the model have been tested and acheved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.27 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 3. Multivariate model predicting total fertility-related distress with identity (IPQ5) entered in the final block

	B	SE B	β	*p*
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*

Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.01	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-1.0	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (consequences)				
Constant	-8.01	11.60		*n.s.*
Age at diagnosis	-0.22	0.24	-0.07	*n.s.*
Country of origin (Britain vs Poland)	11.56	3.61	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	4.69	0.003	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.63	4.05	-0.13	*n.s.*
Recruitment site (other vs online)	-7.45	3.01	-0.17	*≤0.05*
Childbearing status (no vs yes)	-2.89	3.13	-0.07	*n.s.*
Negative affect	0.85	0.15	0.37	*<0.01*
Desire to have children	1.98	1.01	0.14	*n.s.*
Treatment related regret (no vs all others)	7.93	3.00	0.17	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.56	2.69	0.08	*n.s.*
Value of children – utilitarian	1.61	2.61	0.06	*n.s.*
Value of children – social	-1.68	2.97	-0.06	*n.s.*
Value of children – psychological	4.05	2.24	0.15	*n.s.*
Identity (IPQ5)	1.20	0.49	0.16	*≤0.05*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, p = n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.581$, adjusted $R^2 = 0.535$, $F(1, 127) = 6.04$, $p \leq 0.05$, $\Delta R^2 = 0.020$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.18 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 4. Multivariate model predicting total fertility-related distress with illness concern (IPQ6) entered in the final block

	B	SE B	β	*p*
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.153	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*

Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-1.00	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (consequences)				
Constant	-14.83	11.64		*n.s.*
Age at diagnosis	-0.18	0.24	-0.06	*n.s.*
Country of origin (Britain vs Poland)	13.29	3.54	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	0.91	4.54	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.79	3.94	-0.13	*n.s.*
Recruitment site (other vs online)	-5.67	3.04	-0.13	*n.s.*
Childbearing status (no vs yes)	-2.02	2.98	-0.05	*n.s.*
Negative affect	0.72	0.16	0.32	*<0.01*
Desire to have children	2.20	0.98	0.16	*≤0.05*
Treatment related regret (no vs all others)	8.63	2.94	0.19	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.84	2.63	0.09	*n.s.*
Value of children – utilitarian	1.21	2.56	0.04	*n.s.*
Value of children – social	-1.54	2.90	-0.05	*n.s.*
Value of children – psychological	4.22	2.19	0.15	*n.s.*
Illness concern (IPQ6)	1.63	0.49	0.23	*<0.01*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, $p =$ n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.597$, adjusted $R^2 = 0.552$, $F(1, 127) = 11.26$, $p < 0.01$, $\Delta R^2 = 0.036$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.29 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 5. Multivariate model predicting total fertility-related distress with illness coherence (IPQ7) entered in the final block

	B	SE B	β	*p*
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.153	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.04	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*

Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-1.00	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (consequences)				
Constant	1.24	12.82		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	11.37	3.70	0.23	*<0.01*
Type of cancer (gynaecological vs breast)	2.29	4.69	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.68	4.07	-0.17	*n.s.*
Recruitment site (other vs online)	-8.43	3.04	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.70	3.06	-0.02	*n.s.*
Negative affect	0.92	0.15	0.40	*<0.01*
Desire to have children	2.61	1.03	0.19	*≤0.05*
Treatment related regret (no vs all others)	7.66	3.07	0.17	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	3.08	2.78	0.07	*n.s.*
Value of children – utilitarian	1.05	2.67	0.04	*n.s.*
Value of children – social	-0.87	3.00	-0.03	*n.s.*
Value of children – psychological	3.24	2.25	0.12	*n.s.*
Coherence (IPQ7)	-0.80	0.55	-0.10	*n.s.*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, $p =$ n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.568$, adjusted $R^2 = 0.521$, $F(1, 127) = 2.14$, $p =$ n.s., $\Delta R^2 = 0.007$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.29 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 6. Multivariate model predicting total fertility-related distress with illness emotional representation (IPQ8) entered in the final block

	B	SE B	β	*p*
Step 1 – control variables				
Constant	25.49	10.37		*≤0.05*
Age at diagnosis	-0.45	0.25	-0.14	*n.s.*
Country of origin (Britain vs Poland)	12.45	3.67	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	3.14	5.01	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-9.62	4.16	-0.22	*≤0.05*
Recruitment site (other vs online)	-10.42	3.20	-0.24	*<0.01*
Childbearing status (no vs yes)	-3.24	2.90	-0.08	*n.s.*
Negative affect	1.06	0.153	0.46	*<0.01*
Step 2 – desire to have children				
Constant	3.61	11.71		*n.s.*
Age at diagnosis	-0.17	0.25	-0.05	*n.s.*
Country of origin (Britain vs Poland)	13.28	3.53	0.27	*<0.01*
Type of cancer (gynaecological vs breast)	2.32	4.82	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-8.18	4.01	-0.18	*≤0.05*
Recruitment site (other vs online)	-9.27	3.09	-0.21	*<0.01*
Childbearing status (no vs yes)	-0.48	2.89	-0.01	*n.s.*
Negative affect	1.06	0.15	0.46	*<0.01*
Desire to have children	3.43	0.97	0.25	*<0.01*
Step 3 – treatment-related regret				
Constant	-0.41	11.49		*n.s.*
Age at diagnosis	-0.14	0.24	-0.044	*n.s.*
Country of origin (Britain vs Poland)	13.82	3.44	0.28	*<0.01*
Type of cancer (gynaecological vs breast)	1.45	4.70	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.76	4.00	-0.13	*n.s.*
Recruitment site (other vs online)	-8.18	3.03	-0.19	*<0.01*
Childbearing status (no vs yes)	0.63	2.84	0.02	*n.s.*
Negative affect	1.03	0.14	0.45	*<0.01*
Desire to have children	2.97	0.96	0.22	*<0.01*
Treatment related regret (no vs all others)	8.65	3.00	0.19	*<0.01*
Step 4 – culture-related variables				
Constant	-6.25	11.80		*n.s.*
Age at diagnosis	-0.22	0.25	-0.07	*n.s.*
Country of origin (Britain vs Poland)	12.21	3.67	0.25	*<0.01*

Type of cancer (gynaecological vs breast)	2.21	4.71	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-7.26	4.07	-0.16	*n.s.*
Recruitment site (other vs online)	-8.31	3.05	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.80	3.07	-0.02	*n.s.*
Negative affect	0.94	0.15	0.41	*<0.01*
Desire to have children	2.30	1.02	0.17	*≤0.05*
Treatment related regret (no vs all others)	8.27	3.05	0.18	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.85	2.74	0.09	*n.s.*
Value of children – utilitarian	1.50	2.66	0.05	*n.s.*
Value of children – social	-1.00	3.01	-0.03	*n.s.*
Value of children – psychological	3.28	2.26	0.12	*n.s.*
Step 5 – illness perceptions (consequences)				
Constant	-18.42	11.83		*n.s.*
Age at diagnosis	-0.08	0.24	-0.02	*n.s.*
Country of origin (Britain vs Poland)	14.48	3.57	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.93	4.52	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-5.25	3.95	-0.12	*n.s.*
Recruitment site (other vs online)	-6.36	2.97	-0.15	*≤0.05*
Childbearing status (no vs yes)	-2.71	2.99	-0.06	*n.s.*
Negative affect	0.64	0.17	0.28	*<0.01*
Desire to have children	1.99	0.98	0.15	*≤0.05*
Treatment related regret (no vs all others)	7.89	2.93	0.17	*<0.01*
Cultural disapproval of childlessness (no vs all others)	3.67	2.62	0.08	*n.s.*
Value of children – utilitarian	0.77	2.56	0.03	*n.s.*
Value of children – social	-1.80	2.90	-0.06	*n.s.*
Value of children – psychological	4.54	2.20	0.16	*≤0.05*
Emotional representation (IPQ8)	2.07	0.59	0.26	*<0.01*

Note. Step 1: $R^2 = 0.466$, adjusted $R^2 = 0.438$, $F(7, 134) = 16.69$, $p < 0.01$
Step 2: $R^2 = 0.512$, adjusted $R^2 = 0.482$, $F(1, 133) = 12.55$, $p < 0.01$, $\Delta R^2 = 0.046$
Step 3: $R^2 = 0.541$, adjusted $R^2 = 0.509$, $F(1, 132) = 8.31$, $p < 0.01$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.561$, adjusted $R^2 = 0.516$, $F(4, 128) = 1.48$, $p =$ n.s., $\Delta R^2 = 0.020$
Step 5: $R^2 = 0.600$, adjusted $R^2 = 0.556$, $F(1, 127) = 12.363$, $p < 0.01$, $\Delta R^2 = 0.039$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.22 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Appendix 19 – Separate models for IES-R subscales (avoidance, intrusion, hyperarousal)

The same analytical steps as described in Chapter 5, section 5.3.3 were repeated for separate subscales of the Impact of Event Scale – Revised. These are presented here under the appropriate headings.

Avoidance subscale

Univariate analyses including the hypothesised predictors and avoidance subscale as outcome were first performed. These results are presented in Tables 1 and 2.

Table 1. Univariate associations between categorical variables and the outcome (avoidance) (t-Test, ANOVA)

Variables		Mean (SD)	Mean difference	95% CI		*p*
				Lower bound	Upper bound	
Education level						
	less than university (n = 61)	1.38 (1.04)	-0.02	-0.34	0.30	*n.s.*
	at least some university (n = 95)	1.40 (0.95)				
Income						
	below average (n = 98)	1.47 (1.01)				*n.s.*
	above average (n = 41)	1.22 (0.85)				
	prefer not to say (n = 16)	1.34 (1.11)				
Country of origin						
	Britain (n = 116)	1.27 (0.95)	-0.43	-0.78	-0.09	*≤0.05*
	Poland (n = 40)	1.71 (1.01)				
Relationship status						
	partnered	1.37	-0.10	-0.45	0.26	*n.s.*

	(n = 118)	(1.01)				
	single (n = 40)	1.47 (0.91)				
Type of cancer						
	gynaecological (n = 125)	1.52 (0.96)	0.58	0.21	0.94	*<0.01*
	breast (n = 34)	0.94 (0.93)				
Stage of cancer						
	stage 1 (n = 67)	1.40 (0.93)	-0.08	-0.39	0.24	*n.s.*
	other stages (n = 78)	1.48 (0.96)				
Type of treatment						
	sterile (n = 97)	1.62 (0.99)	0.58	0.28	0.88	*<0.01*
	uncertain (n = 62)	1.04 (0.86)				
Recruitment site						
	others (n = 83)	1.53 (0.86)	-0.28	-0.028	0.58	*n.s.*
	online (n = 76)	1.25 (1.07)				
Childbearing status						
	no (n = 79)	1.57 (0.87)	0.34	0.04	0.65	*≤0.05*
	yes (n = 79)	1.23 (1.05)				
Treatment related regret						
	no (n = 104)	1.17 (0.92)	-0.71	-1.01	-0.41	*<0.01*
	all others (n = 53)	1.88 (0.91)				
Cultural disapproval of childlessness						
	no (n = 62)	1.23 (1.01)	-0.32	-0.63	-0.01	*≤0.05*

	all others (n = 94)	1.54 (0.92)				

Table 2. Univariate associations between the continuous predictors and the outcome (avoidance) (Spearman correlations)

Variables	Correlation coefficient
Fertility-related distress (IESR avoidance)	1
Age at diagnosis	-0.20*
Time since diagnosis	-0.05
Negative affect	0.46**
Desire to have children	0.40**
Partner's desire to have children	0.37**
Value of children – utilitarian	0.35**
Value of children – social	0.20*
Value of children – psychological	0.24**
IPQ1 – consequences	0.43**
IPQ2 – timeline	0.21**
IPQ3 – personal control	-0.10
IPQ4 – treatment control	-0.10
IPQ5 – identity	0.24**
IPQ6 – illness concern	0.27**
IPQ7 – coherence	-0.16*
IPQ8 – emotional representation	0.37**
IPQ total	0.40**

Note. *$p \leq 0.05$; **$p < 0.01$

Overall, 20 predictors were significantly associated with the avoidance aspect of fertility-related distress. As opposed to the total scale, the recruitment site was not significantly associated with avoidance.

Predictors significantly ($p \leq 0.05$) associated with the avoidance aspect of fertility-related distress, excluding partner's desire to have children (for reasons see section 5.3.3) were entered into the five-block regression model. In the first model total score of the illness perception questionnaire was entered as a single predictor in the last block. In the subsequent models it was exchanged for the particular illness perceptions (consequences, timeline, identity, illness concern, coherence and emotional representation) (for details see section 5.3.3). The first model is presented in Table 3.

Table 3. Multivariate model predicting the avoidance aspect of fertility-related distress

	B	SE B	β	*p*
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*

Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.59	0.59		*n.s.*
Age at diagnosis	-0.01	0.01	-0.04	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.17	0.20	*≤0.05*
Type of cancer (gynaecological vs breast)	-0.01	0.24	-0.004	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.21	-0.13	*n.s.*
Childbearing status (no vs yes)	-0.19	0.16	-0.10	*n.s.*
Negative affect	0.03	0.01	0.27	*<0.01*
Desire to have children	0.09	0.14	0.16	*n.s.*
Treatment related regret (no vs all others)	0.35	0.15	0.17	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.09	0.14	0.05	*n.s.*
Value of children – utilitarian	0.01	0.13	0.01	*n.s.*
Value of children – social	-0.12	0.15	-0.09	*n.s.*
Value of children – psychological	0.24	0.12	0.19	*≤0.05*
Brief-IPQ total	0.01	0.01	0.20	*≤0.05*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p < 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, p = n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.459$, adjusted $R^2 = 0.405$, $F(1, 130) = 6.31$, $p < 0.05$, $\Delta R^2 = 0.026$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.09 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

The regression model suggests that the control variables contributed significantly to the model ($F(6, 137) = 11.43$, $p < 0.01$) explaining 30.5% of the variance in the avoidance aspect of fertility-related distress. Introduction of desire to have children in step 2 explained an additional 5.1% of the variance and the change in R^2 proved to be significant ($F(1, 136) = 11.23$, $p < 0.01$). Similarly, addition of treatment-related regret further increased the explained variance by 2.9% with the change being statistically

significant ($F(1, 132) = 6.63$, $p < 0.05$). The next step including culture-related variables, although produced a statistically significant overall model ($F(12, 131) = 8.32$, $p < 0.01$), did not significantly contribute to the explained variability of the avoidance aspect of fertility-related distress ($F(4, 131) = 1.09$, p = n.s.). Finally, the introduction the illness perception score explained an additional 2.6% of the variance with the change again being statistically significant ($F(1, 130) = 6.31$, $p \leq 0.05$). The ultimate model explained 40.5% of the variability in the avoidance component of fertility-related distress and five predictors including the country of origin, negative affect, treatment-related regret, psychological value of children, and total illness perception score remained individually significant. In this model, as opposed to the model predicting total fertility-related distress, neither recruitment site nor desire to have children predicted the outcome while psychological value of children proved to be a significant predictor of the avoidance component of distress.

Additional models to investigate which illness perceptions in particular contributed to the avoidance component of the fertility-related distress revealed that when all the other predictors were held constant, the consequences, identity, and illness concern significantly explained the variability in the avoidance component of the fertility-related distress in three separate models (see Tables 4-9). Neither of the significant models including illness perceptions separately, however, attained a better fit to the data than the model including the overall illness perception.

Table 4. Multivariate model predicting the avoidance aspect of fertility-related distress with consequences (IPQ1) entered in the final block

	B	**SE B**	**β**	***p***
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*

Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*
Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.50	0.60		*n.s.*
Age at diagnosis	-0.01	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.41	0.18	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.04	0.24	0.02	*n.s.*
Type of treatment (sterile vs uncertain	-0.27	0.21	-0.13	*n.s.*

fertility)				
Childbearing status (no vs yes)	-0.19	0.16	-0.09	*n.s.*
Negative affect	0.03	0.01	0.30	*<0.01*
Desire to have children	0.09	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.35	0.16	0.17	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.11	0.14	0.06	*n.s.*
Value of children – utilitarian	0.01	0.13	0.01	*n.s.*
Value of children – social	-0.09	0.15	-0.06	*n.s.*
Value of children – psychological	0.23	0.12	0.18	*n.s.*
Consequences (IPQ1)	0.06	0.03	0.17	*≤0.05*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, p = n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.453$, adjusted $R^2 = 0.398$, $F(1, 130) = 4.84$, $p \leq 0.05$, $\Delta R^2 = 0.020$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.08 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 5. Multivariate model predicting the avoidance aspect of fertility-related distress with timeline (IPQ2) entered in the final block

	B	**SE B**	**β**	**p**
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*

Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*
Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.38	0.60		*n.s.*
Age at diagnosis	-0.01	0.01	-0.04	*n.s.*
Country of origin (Britain vs Poland)	0.39	0.18	0.17	*n.s.*
Type of cancer (gynaecological vs breast)	0.04	0.24	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.30	0.21	-0.15	*n.s.*
Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.35	*<0.01*
Desire to have children	0.10	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.39	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.06	*n.s.*

Value of children – utilitarian	0.02	0.14	0.02	*n.s.*
Value of children – social	-0.09	0.15	-0.07	*n.s.*
Value of children – psychological	0.21	0.12	0.17	*n.s.*
Timeline (IPQ2)	0.02	0.02	0.08	*n.s.*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, p = n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.438$, adjusted $R^2 = 0.382$, $F(1, 130) = 1.36$, p = n.s., $\Delta R^2 = 0.006$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.11 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 6. Multivariate model predicting the avoidance aspect of fertility-related distress with identity (IPQ5) entered in the final block

	B	**SE B**	**β**	**p**
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain	-0.25	0.20	-0.12	*n.s.*

fertility)				
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*
Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.45	0.60		*n.s.*
Age at diagnosis	-0.01	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.43	0.18	0.19	*≤0.05*
Type of cancer (gynaecological vs breast)	-0.003	0.24	-0.001	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.21	-0.13	*n.s.*
Childbearing status (no vs yes)	-0.22	0.16	-0.11	*n.s.*
Negative affect	0.04	0.01	0.33	*<0.01*
Desire to have children	0.09	0.05	0.15	*n.s.*
Treatment related regret (no vs all others)	0.38	0.15	0.18	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.12	0.14	0.06	*n.s.*
Value of children – utilitarian	0.02	0.13	0.01	*n.s.*
Value of children – social	-0.12	0.15	-0.09	*n.s.*
Value of children – psychological	0.24	0.12	0.19	*≤0.05*
Identity (IPQ5)	0.05	0.03	0.14	*≤0.05*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, p = n.s., $\Delta R^2 = 0.019$

Step 5: $R^2 = 0.449$, adjusted $R^2 = 0.394$, $F(1, 130) = 3.98$, $p \leq 0.05$, $\Delta R^2 = 0.017$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 1.98 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 7. Multivariate model predicting the avoidance aspect of fertility-related distress with illness concern (IPQ6) entered in the final block

	B	SE B	β	p
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*

Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*
Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.64	0.61		*n.s.*
Age at diagnosis	-0.00	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.51	0.18	0.23	*<0.01*
Type of cancer (gynaecological vs breast)	0.05	0.24	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.28	0.21	-0.14	*n.s.*
Childbearing status (no vs yes)	-0.17	0.16	-0.09	*n.s.*
Negative affect	0.03	0.01	0.30	*<0.01*
Desire to have children	0.10	0.05	0.16	*n.s.*
Treatment related regret (no vs all others)	0.40	0.15	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.06	*n.s.*
Value of children – utilitarian	0.01	0.13	0.01	*n.s.*
Value of children – social	-0.11	0.15	-0.08	*n.s.*
Value of children – psychological	0.24	0.12	0.19	*≤0.05*
Illness concern (IPQ6)	0.05	0.03	0.16	*≤0.05*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, $p =$ n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.451$, adjusted $R^2 = 0.396$, $F(1, 130) = 4.45$, $p \leq 0.05$, $\Delta R^2 = 0.019$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.10 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 8. Multivariate model predicting the avoidance aspect of fertility-related distress with coherence (IPQ7) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*

Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	0.05	0.66		*n.s.*
Age at diagnosis	-0.01	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.39	0.18	0.17	*≤0.05*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.34	0.21	-0.17	*n.s.*
Childbearing status (no vs yes)	-0.13	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.36	*<0.01*
Desire to have children	0.12	0.05	0.20	*≤0.05*
Treatment related regret (no vs all others)	0.37	0.16	0.18	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.09	0.14	0.04	*n.s.*
Value of children – utilitarian	-0.02	0.14	-0.01	*n.s.*
Value of children – social	-0.08	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Coherence (IPQ7)	-0.05	0.03	-0.12	*n.s.*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, $p =$ n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.444$, adjusted $R^2 = 0.389$, $F(1, 130) = 2.82$, $p =$ n.s., $\Delta R^2 = 0.012$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.12 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 9. Multivariate model predicting the avoidance aspect of fertility related distress with emotional representation (IPQ8) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.07	0.52		*n.s.*
Age at diagnosis	-0.02	0.01	-0.11	*n.s.*
Country of origin (Britain vs Poland)	0.33	0.17	0.15	*n.s.*
Type of cancer (gynaecological vs breast)	0.09	0.25	0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.43	.21	-0.21	*n.s.*
Childbearing status (no vs yes)	-0.25	0.15	-0.13	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.03	0.59		*≤0.05*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.4	0.16	0.18	*≤0.05*
Type of cancer (gynaecological vs breast)	0.06	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.36	0.20	-0.18	*n.s.*
Childbearing status (no vs yes)	-0.11	-0.15	-0.06	*n.s.*
Negative affect	0.04	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.26	*<0.01*
Step 3				
Constant	-0.14	0.58		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.45	0.16	0.20	*<0.01*
Type of cancer (gynaecological vs breast)	0.03	0.24	0.012	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.25	0.20	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.14	-0.03	*n.s.*
Negative affect	0.043	0.01	0.41	*<0.01*
Desire to have children	0.14	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.15	0.19	*≤0.05*
Step 4				
Constant	-0.39	0.61		*n.s.*
Age at diagnosis	-0.004	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.44	0.18	0.20	*n.s.*
Type of cancer (gynaecological vs breast)	0.08	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.16	*n.s.*

Childbearing status (no vs yes)	-0.14	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.11	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.40	0.16	0.19	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.07	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.21	0.12	0.16	*n.s.*
Step 5				
Constant	-0.73	0.62		*n.s.*
Age at diagnosis	0.00	0.01	-0.001	*n.s.*
Country of origin (Britain vs Poland)	0.53	0.18	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	0.05	0.24	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.21	-0.13	*n.s.*
Childbearing status (no vs yes)	-0.19	0.16	-0.10	*n.s.*
Negative affect	0.03	0.01	0.29	*<0.01*
Desire to have children	0.10	0.05	0.15	*n.s.*
Treatment related regret (no vs all others)	0.38	0.15	0.18	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.13	0.14	0.06	*n.s.*
Value of children – utilitarian	-0.01	0.13	-0.00	*n.s.*
Value of children – social	-0.12	0.15	-0.08	*n.s.*
Value of children – psychological	0.25	0.12	0.19	*≤0.05*
Emotional representation (IPQ8)	0.06	0.03	0.17	*n.s.*

Note. Step 1: $R^2 = 0.334$, adjusted $R^2 = 0.305$, $F(6, 137) = 11.44$, $p < 0.01$
Step 2: $R^2 = 0.385$, adjusted $R^2 = 0.353$, $F(1, 136) = 11.23$, $p < 0.01$, $\Delta R^2 = 0.051$
Step 3: $R^2 = 0.413$, adjusted $R^2 = 0.379$, $F(1, 135) = 6.63$, $p \leq 0.05$, $\Delta R^2 = 0.029$
Step 4: $R^2 = 0.432$, adjusted $R^2 = 0.380$, $F(4, 131) = 1.09$, p = n.s., $\Delta R^2 = 0.019$
Step 5: $R^2 = 0.448$, adjusted $R^2 = 0.393$, $F(1, 130) = 3.80$, p = n.s., $\Delta R^2 = 0.016$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.06 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Intrusion subscale

Univariate analyses including the hypothesised predictors and intrusion subscale as outcome were first performed. These results are presented in Tables 10 and 11.

Table 10. Univariate associations between categorical variables and the outcome (intrusion) (Mann-Whitney U test, Kruskal-Wallis H test)

Variables		Mean rank	Mann-Whitney U	Z	*p*
Education level					
	less than university (n = 64)	73.09	2598	-1.554	*n.s.*
	at least some university (n = 95)	84.65			
Income					
	below average (n = 101)	84.24			*n.s.*
	above average (n = 41)	68.07			
	prefer not to say (n = 16)	78.88			
Country of origin					
	Britain (n = 117)	76.26	2020	-1.50	*n.s.*
	Poland (n = 41)	88.73			
Relationship status					
	partnered (n = 119)	81.19	2238	-0.56	*n.s.*
	single (n = 40)	76.45			
Type of cancer					
	gynaecological (n = 125)	87.06	1367	-3.39	*<0.01*
	breast (n = 35)	57.06			
Stage of cancer					
	stage 1 (n = 68)	71.60	2523	-0.51	*n.s.*
	other stages (n = 78)	75.15			
Type of treatment					
	sterile (n = 97)	89.98	2135	-3.22	*<0.01*

	uncertain (n = 63)	65.90			
Recruitment site					
	others (n = 82)	65.16	2001	-4.09	*<0.01*
	online (n = 78)	95.09			
Childbearing status					
	no (n = 78)	90.42	2268.5	-2.97	*<0.01*
	yes (n = 80)	68.86			
Treatment related regret					
	no (n = 104)	66.83	1489	-4.71	*<0.01*
	all others (n = 53)	102.91			
Cultural disapproval of childlessness					
	no (n = 63)	67.11	2212	-2.60	*<0.01*
	all others (n = 93)	86.22			

Table 11. Univariate associations between the continuous predictors and the outcome (intrusion) (Spearman correlations)

Variables	Correlation coefficient
Fertility-related distress (IESR intrusion)	1
Age at diagnosis	-0.34**
Time since diagnosis	-0.13
Negative affect	0.50**
Desire to have children	0.45**
Partner's desire to have children	0.39**
Value of children – utilitarian	0.19*
Value of children – social	0.17*
Value of children – psychological	0.22**
IPQ1 – consequences	0.45**
IPQ2 – timeline	0.20**
IPQ3 – personal control	-0.16*
IPQ4 – treatment control	-0.08
IPQ5 – identity	0.25**
IPQ6 – illness concern	0.42**
IPQ7 – coherence	-0.12
IPQ8 – emotional representation	0.55**
IPQ total	0.48**

Note. *$p \leq 0.05$; **$p < 0.01$

Overall, 20 predictors were significantly associated with the intrusion aspect of fertility-related distress. As opposed to the total scale, neither the country of origin nor illness coherence were significantly associated with intrusion, whilst personal control was.

Predictors significantly ($p \leq 0.05$) associated with the intrusion aspect of fertility-related distress, excluding partner's desire to have children (for reasons see section 5.3.3) were entered into the five-block regression model. In the first model total score of the illness perception questionnaire was entered as a single predictor in the last block. In the subsequent models it was exchanged for the particular illness perceptions (consequences, timeline, personal control, identity, illness concern, and emotional representation) (for details see section 5.3.3). The first model is presented in Table 12.

Table 12. Multivariate model predicting the intrusion aspect of fertility-related distress with total illness perception score entered in the final block

	B	**SE B**	**β**	***p***
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*

Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	0.05	0.61		*n.s.*
Age at diagnosis	-0.03	0.01	-0.15	*n.s.*
Type of cancer (gynaecological vs breast)	-0.16	0.24	-0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.31	0.21	-0.14	*n.s.*
Recruitment site (other vs online)	-0.25	0.15	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.05	0.16	-0.02	*n.s.*
Negative affect	0.03	0.01	0.27	*<0.01*
Desire to have children	0.12	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.31	0.16	0.13	*n.s.*
Cultural disapproval of childlessness (no vs all others)	0.24	0.14	0.11	*n.s.*
Value of children – utilitarian	0.14	0.13	0.10	*n.s.*
Value of children – social	-0.13	0.15	-0.09	*n.s.*
Value of children – psychological	0.13	0.12	0.09	*n.s.*
IPQ total	0.02	0.01	0.24	*<0.01*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$

Step 2: R^2 = 0.472, adjusted R^2 = 0.445, F(1, 136) = 12.08, $p < 0.01$, ΔR^2 = 0.047
Step 3: R^2 = 0.495, adjusted R^2 = 0.465, F(1, 135) = 6.16, $p \leq 0.05$, ΔR^2 = 0.023
Step 4: R^2 = 0.522, adjusted R^2 = 0.478, F(4, 131) = 1.85, p = n.s., ΔR^2 = 0.027
Step 5: R^2 = 0.557, adjusted R^2 = 0.513, F(1, 130) = 10.34, $p < 0.01$, ΔR^2 = 0.034
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.07 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

The regression model suggests that the control variables contributed significantly to the model (F(6, 137) = 16.90, $p < 0.01$) explaining 40% of the variance in the intrusion aspect of fertility-related distress. Introduction of desire to have children in step 2 explained an additional 4.7% of the variance and the change in R^2 proved to be significant (F(1, 136) = 12.08, $p < 0.01$). Similarly, addition of treatment-related regret further increased the explained variance by 2.3% with the change being statistically significant (F(1, 135) = 6.16, $p \leq 0.05$). Although the next step including culture-related variables produced a statistically significant overall model (F(12, 131) = 11.93, $p <$ 0.01), it did not significantly contribute to the explained variability of the intrusion aspect of the fertility-related distress (F(4, 131) = 1.85, p = n.s.). Finally, the introduction the illness perception score explained an additional 3.4% of the variance with the change again being statistically significant (F(1, 130) = 10.34, $p \leq$ 0.05). The ultimate model explained 51.3% of the variability in the intrusion component of fertility-related distressand three predictors including the negative affect, desire to have children, and total illness perception score remained individually significant. In this model, as opposed to the model predicting total fertility-related distress, country of origin, recruitment site, and treatment-related regret proved not to significantly predict the outcome.

Additional models to investigate which illness perceptions in particular contributed to the intrusion component of fertility-related-distress revealed that when all the other predictors were held constant, the identity, illness concern, and emotional representation significantly explained the variability in the avoidance component of the fertility-related distress in three separate models (see Tables 13-18). Moreover, the model including emotional representation as final predictor achieved a better fit to the data (adjusted R^2 = 51.8%) than the original model including the total illness perception score. This

suggests that the emotional dimension of illness perceptions contributed most to the intrusion aspect of fertility-related distress in survivorship.

Table 13. Multivariate model predicting the intrusion aspect of fertility-related distress with consequences (IPQ1) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*

Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	0.23	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.06	0.24	-0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.15	*n.s.*
Recruitment site (other vs online)	-0.32	0.15	-0.15	*≤0.05*
Childbearing status (no vs yes)	-0.01	0.16	-0.01	*n.s.*
Negative affect	0.04	0.01	0.33	*<0.01*
Desire to have children	0.12	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.32	0.16	0.14	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.27	0.14	0.12	*n.s.*
Value of children – utilitarian	0.15	0.14	0.10	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.11	0.12	0.07	*n.s.*
Consequences (IPQ1)	0.06	0.03	0.14	*n.s.*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1, 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, p = n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.536$, adjusted $R^2 = 0.489$, $F(1, 130) = 3.80$, p = n.s., $\Delta R^2 = 0.014$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.12 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 14. Multivariate model predicting the intrusion aspect of fertility-related distress with timeline (IPQ2) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*0.05*

Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	0.34	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.15	*n.s.*
Type of cancer (gynaecological vs breast)	-0.09	0.24	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.37	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.36	0.15	-0.16	*0.05*
Childbearing status (no vs yes)	0.02	0.16	0.01	*n.s.*
Negative affect	0.04	0.01	0.35	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.34	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.28	0.14	0.12	*n.s.*
Value of children – utilitarian	0.17	0.14	0.12	*n.s.*
Value of children – social	-0.10	0.16	-0.07	*n.s.*
Value of children – psychological	0.10	0.12	0.07	*n.s.*
Timeline (IPQ2)	0.04	0.02	0.13	*n.s.*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1, 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, $p =$ n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.536$, adjusted $R^2 = 0.490$, $F(1, 130) = 3.86$, $p =$ n.s., $\Delta R^2 = 0.014$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.07 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 15. Multivariate model predicting the intrusion aspect of fertility-related distress with personal control (IPQ3) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.23	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*

Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	0.40	0.65		*n.s.*
Age at diagnosis	-0.02	0.01	-0.14	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.40	0.22	-0.18	*n.s.*
Recruitment site (other vs online)	-0.34	0.15	-0.15	*≤0.05*
Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.04	0.01	0.39	*<0.01*
Desire to have children	0.13	0.06	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.10	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Personal control (IPQ3)	-0.01	0.02	-0.02	*n.s.*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1\ 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, p = n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.522$, adjusted $R^2 = 0.475$, $F(1, 130) = 0.07$, p = n.s., $\Delta R^2 = 0.000$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.12 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 16. Multivariate model predicting the intrusion aspect of fertility-related distress with identity (IPQ5) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.36	0.15	-0.16	*≤0.05*

Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.001*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	0.27	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.12	0.25	-0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.21	-0.15	*n.s.*
Recruitment site (other vs online)	-0.32	0.15	-0.14	*≤0.05*
Childbearing status (no vs yes)	-0.06	0.17	-0.03	*n.s.*
Negative affect	0.04	0.01	0.35	*<0.001*
Desire to have children	0.12	0.05	0.17	*≤0.05*
Treatment related regret (no vs all others)	0.34	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.26	0.14	0.12	*n.s.*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.12	0.16	-0.08	*n.s.*
Value of children – psychological	0.12	0.12	0.09	*n.s.*
Identity (IPQ5)	0.05	0.03	0.13	*≤0.05*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1\ 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, p = n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.536$, adjusted $R^2 = 0.490$, $F(1, 130) = 3.96$, $p \leq 0.05$, $\Delta R^2 = 0.014$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.05 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 17. Multivariate model predicting the intrusion aspect of fertility-related distress with illness concern (IPQ6) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.42	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*

Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.01*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	-0.05	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.11	0.24	-0.04	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.34	0.21	-0.15	*n.s.*
Recruitment site (other vs online)	-0.20	0.15	-0.09	*n.s.*
Childbearing status (no vs yes)	-0.02	0.16	-0.01	*n.s.*
Negative affect	0.03	0.01	0.29	*<0.01*
Desire to have children	0.13	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.37	0.16	0.16	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.30	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.15	0.13	0.11	*n.s.*
Value of children – social	-0.12	0.15	-0.07	*n.s.*
Value of children – psychological	0.13	0.12	0.09	*n.s.*
Illness concern (IPQ6)	0.08	0.03	0.22	*<0.01*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1\ 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, p = n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.554$, adjusted $R^2 = 0.510$, $F(1, 130) = 9.33$, $p < 0.01$, $\Delta R^2 = 0.032$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.1 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 18. Multivariate model predicting the intrusion aspect of fertility-related distress with emotional representation (IPQ8) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	1.92	0.54		*<0.01*
Age at diagnosis	-0.04	0.01	-0.21	*<0.01*
Type of cancer (gynaecological vs breast)	0.02	0.26	0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.53	0.22	-0.23	*≤0.05*
Recruitment site (other vs online)	-0.43	0.15	-0.19	*<0.01*
Childbearing status (no vs yes)	-0.13	0.15	-0.06	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Step 2				
Constant	0.81	0.61		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.25	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.46	0.21	-0.20	*≤0.05*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*
Childbearing status (no vs yes)	0.02	0.15	0.01	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.18	0.05	0.25	*<0.01*
Step 3				
Constant	0.63	0.60		*n.s.*
Age at diagnosis	-0.02	0.01	-0.12	*n.s.*
Type of cancer (gynaecological vs breast)	-0.08	0.25	-0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.35	0.21	-0.16	*n.s.*
Recruitment site (other vs online)	-0.29	0.15	-0.13	*≤0.05*
Childbearing status (no vs yes)	0.07	0.15	0.03	*n.s.*
Negative affect	0.05	0.01	0.42	*<0.01*
Desire to have children	0.16	0.05	0.22	*<0.01*
Treatment related regret (no vs all others)	0.39	0.16	0.17	*≤0.05*
Step 4				
Constant	0.35	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.13	*n.s.*
Type of cancer (gynaecological vs breast)	-0.04	0.24	-0.01	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.41	0.21	-0.18	*n.s.*
Recruitment site (other vs online)	-0.35	0.15	-0.16	*≤0.05*

Childbearing status (no vs yes)	0.04	0.16	0.02	*n.s.*
Negative affect	0.05	0.01	0.38	*<0.001*
Desire to have children	0.14	0.05	0.19	*≤0.05*
Treatment related regret (no vs all others)	0.36	0.16	0.15	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.16	0.14	0.11	*n.s.*
Value of children – social	-0.09	0.16	-0.06	*n.s.*
Value of children – psychological	0.09	0.12	0.06	*n.s.*
Step 5				
Constant	-0.23	0.62		*n.s.*
Age at diagnosis	-0.02	0.01	-0.10	*n.s.*
Type of cancer (gynaecological vs breast)	-0.13	0.24	-0.05	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.32	0.21	-0.14	*n.s.*
Childbearing status (no vs yes)	-0.06	0.16	-0.03	*n.s.*
Negative affect	0.03	0.01	0.25	*<0.01*
Desire to have children	0.12	0.05	0.17	*0.05*
Treatment related regret (no vs all others)	0.33	0.15	0.14	*≤0.05*
Cultural disapproval of childlessness (no vs all others)	0.29	0.14	0.13	*≤0.05*
Value of children – utilitarian	0.14	0.13	0.10	*n.s.*
Value of children – social	-0.12	0.15	-0.08	*n.s.*
Value of children – psychological	0.14	0.12	0.10	*n.s.*
Emotional representation (IPQ8)	0.11	0.03	0.26	*<0.01*

Note. Step 1: $R^2 = 0.425$, adjusted $R^2 = 0.400$, $F(6, 137) = 16.90$, $p < 0.01$
Step 2: $R^2 = 0.472$, adjusted $R^2 = 0.445$, $F(1, 136) = 12.08$, $p < 0.01$, $\Delta R^2 = 0.047$
Step 3: $R^2 = 0.495$, adjusted $R^2 = 0.465$, $F(1\ 135) = 6.16$, $p \leq 0.05$, $\Delta R^2 = 0.023$
Step 4: $R^2 = 0.522$, adjusted $R^2 = 0.478$, $F(4, 131) = 1.85$, p = n.s., $\Delta R^2 = 0.027$
Step 5: $R^2 = 0.562$, adjusted $R^2 = 0.518$, $F(1, 130) = 11.73$, $p < 0.01$, $\Delta R^2 = 0.040$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.07 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Hyperarousal subscale

Univariate analyses including the hypothesised predictors and hyperarousal subscale as outcome were first performed. These results are presented in Tables 19 and 20.

Table 19. Univariate associations between categorical variables and the outcome (Mann-Whitney U test, Kruskal-Wallis H test)

Variables		Mean rank	Mann-Whitney U	Z	*p*
Education level					
	less than university (n = 63)	79.84	3014	-0.146	*n.s.*
	at least some university (n = 97)	80.93			
Income					
	below average (n = 101)	84.24			*n.s.*
	above average (n = 41)	68.07			
	prefer not to say (n = 16)	78.88			
Country of origin					
	Britain (n = 118)	73.81	1689	-2.7	*<0.01*
	Poland (n = 40)	96.28			
Relationship status					
	partnered (n = 120)	80.23	2367	-0.129	*n.s.*
	single (n = 40)	81.31			
Type of cancer					
	gynaecological (n = 126)	85.34	1658	-2.26	*≤0.05*
	breast (n = 35)	65.37			
Stage of cancer					
	stage 1 (n = 67)	70.17	2423.5	-1.00	*n.s.*
	other stages (n = 80)	77.21			
Type of treatment					
	sterile (n = 98)	88.67	2335	-2.62	*<0.01*

	uncertain (n = 63)	69.06			
Recruitment site					
	others (n = 84)	70.48	2425	-2.75	*<0.01*
	online (n = 77)	90.63			
Childbearing status					
	no (n = 80)	87.92	2526.5	-2.198	*≤0.05*
	yes (n = 79)	71.98			
Treatment related regret					
	no (n = 105)	70.83	1872.5	-3.52	*<0.01*
	all others (n = 54)	97.82			
Cultural disapproval of childlessness					
	no (n = 63)	71.09	2462.5	-1.89	*n.s.*
	all others (n = 95)	85.08			

Table 20. Univariate associations between the continuous predictors and the outcome (Spearman correlations)

Variables	Correlation coefficient
Fertility-related distress (IESR hyperarousal)	1
Age at diagnosis	-0.22**
Time since diagnosis	-0.10
Negative affect	0.53**
Desire to have children	0.31**
Partner's desire to have children	0.27**
Value of children – utilitarian	0.32**
Value of children – social	0.34**
Value of children – psychological	0.28**
IPQ1 – consequences	0.44**
IPQ2 – timeline	0.23**
IPQ3 – personal control	-0.14
IPQ4 – treatment control	-0.12
IPQ5 – identity	0.33**
IPQ6 – illness concern	0.45**
IPQ7 – coherence	-0.13
IPQ8 – emotional representation	0.56**
IPQ total	0.51**

Note. *$p \leq 0.05$; **$p < 0.01$

Overall, 19 predictors were significantly associated with the hyperarousal aspect of fertility-related distress. As opposed to the total scale, neither the cultural disapproval of childlessness nor illness coherence were associated with hyperarousal.

Predictors significantly ($p \leq 0.05$) associated with the hyperarousal aspect of fertility-related distress, excluding partner's desire to have children (for reasons see section 5.3.3) were entered into the five-block regression model. In the first model the total score of illness perception questionnaire was entered as a single predictor in the last block. In the subsequent models it was exchanged for the particular illness perceptions (consequences, timeline, identity, illness concern, and emotional representation) (for details see section 5.3.3). The first model is presented in Table 21.

Table 21. Multivariate model predicting the hyperarousal aspect of fertility-related distress with total illness perception score entered in the final block

	B	**SE B**	**β**	***p***
Step 1				
Constant	0.18	0.54		*n.s.*
Age at diagnosis	-0.01	0.01	-0.07	*n.s.*
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.15	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*
Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.002	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.01*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.22	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.16	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*

Age at diagnosis	-0.00	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.10	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.00	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*
Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.01	0.48	*<0.01*
Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.15	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				
Constant	-1.22	0.63		*n.s.*
Age at diagnosis	-0.01	0.01	-0.04	*n.s.*
Country of origin (Britain vs Poland)	0.62	0.19	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	0.05	0.25	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.19	0.22	-0.08	*n.s.*
Recruitment site (other vs online)	-0.30	0.17	-0.13	*n.s.*
Childbearing status (no vs yes)	-0.10	0.16	-0.05	*n.s.*
Negative affect	0.04	0.01	0.37	*<0.01*
Desire to have children	0.06	0.05	0.09	*n.s.*
Treatment related regret (no vs all others)	0.15	0.16	0.07	*n.s.*
Value of children – utilitarian	0.04	0.14	0.03	*n.s.*
Value of children – social	0.16	0.16	0.10	*n.s.*
Value of children – psychological	0.08	0.12	0.06	*n.s.*
IPQ total	0.02	0.01	0.22	*<0.01*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 136) = 15.48$, $p < 0.01$
Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 135) = 4.60$, $p \leq 0.05$, $\Delta R^2 = 0.018$
Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1\ 134) = 2.41$, p = n.s., $\Delta R^2 = 0.010$
Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 131) = 2.08$, p = n.s., $\Delta R^2 = 0.024$
Step 5: $R^2 = 0.527$, adjusted $R^2 = 0.480$, $F(1, 130) = 8.81$, $p < 0.01$, $\Delta R^2 = 0.032$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.31 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

The regression model suggests that the control variables contributed significantly to the model ($F(7, 136) = 15.48$, $p < 0.01$) explaining 41.5% of the variance in the hyperarousal component of fertility-related distress. Introduction of desire to have children in step 2 explained an additional 4.6% of the variance and the change in R^2 proved to be significant ($F(1, 135) = 4.60$, $p \leq 0.05$). Although addition of treatment-related regret in step 3 yielded a statistically significant overall model ($F(9, 134) = 13.27$, $p < 0.01$), it did not significantly contribute to the explanation of the variance in the hyperarousal ($F(1, 134) = 2.41$, p = n.s.). Neither did the inclusion of culture-related variables in step 4 produce a significant increase in the explained variability of the hyperarousal component of the fertility-related distress ($F(3, 131) = 2.08$, p = n.s.). Finally, the introduction the illness perception score explained an additional 3.2% of the variance with the change being statistically significant ($F(1, 130) = 8.81$, $p < 0.01$). The ultimate model explained 48% of the variability in the hyperarousal component of fertility-related distress and three predictors including the country of origin, negative affect, and total illness perception score remained individually significant. In this model, as opposed to the model predicting total fertility-related distress, recruitment site, desire to have children, and treatment-related regret proved not to significantly predict the outcome.

Additional models to investigate which illness perceptions in particular contributed to the hyperarousal revealed that when all the other predictors were held constant, the identity, illness concern, and emotional representation significantly explained the variability in the hyperarousal component of the fertility-related distress in three separate models (see Tables 22-26). Moreover, the models including illness concern and emotional representation as a final predictor achieved a better fit to the data (adjusted $R^2 = 50.1\%$ and $R^2 = 50.7\%$, respectively) than the original model including the total illness perception score. This suggests that the emotional dimensions of illness

perceptions contributed most to the hyperarousal aspect of fertility-related distress in survivorship.

Table 22. Multivariate model predicting the hyperarousal aspect of fertility-related distress with consequences (IPQ1) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	0.18	0.54		*n.s.*
Age at diagnosis	-0.01	0.01	-0.07	*n.s.*
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.16	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*
Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.002	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.001*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.21	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.16	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*

Desire to have children	0.10	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*
Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.01	0.48	*<0.01*
Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				
Constant	-1.01	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.63	0.20	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	0.14	0.26	0.05	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.24	0.22	-0.11	*n.s.*
Recruitment site (other vs online)	-0.38	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	-0.06	0.17	-0.03	*n.s.*
Negative affect	0.05	0.01	0.44	*<0.01*
Desire to have children	0.07	0.06	0.09	*n.s.*
Treatment related regret (no vs all others)	0.18	0.17	0.08	*n.s.*
Value of children – utilitarian	0.05	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.05	0.12	0.03	*n.s.*
Consequences (IPQ1)	0.04	0.03	0.09	*n.s.*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 137) = 15.59$, $p < 0.01$
Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 136) = 4.64$, $p \leq 0.05$, $\Delta R^2 = 0.018$
Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1, 135) = 2.43$, p = n.s., $\Delta R^2 = 0.010$
Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 132) = 2.10$, p = n.s., $\Delta R^2 = 0.024$

Step 5: R^2 = 0.501, adjusted R^2 = 0.451, $F(1, 131) = 1.45$, p = n.s., ΔR^2 = 0.006
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.33 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 23. Multivariate model predicting the hyperarousal aspect of fertility-related distress with timeline (IPQ2) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	0.18	0.54		*n.s.*
Age at diagnosis	-0.01	0.01	-0.07	*n.s.*
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.15	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*
Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.002	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.01*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.21	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.15	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.10	0.05	0.14	*n.s.*

Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*
Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.02	0.48	*<0.01*
Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				
Constant	-0.93	0.64		*n.s.*
Age at diagnosis	-0.01	0.01	-0.03	*n.s.*
Country of origin (Britain vs Poland)	0.61	0.20	0.24	*<0.01*
Type of cancer (gynaecological vs breast)	0.12	0.26	0.05	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.26	0.22	-0.11	*n.s.*
Recruitment site (other vs online)	-0.39	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.04	0.17	-0.02	*n.s.*
Negative affect	0.05	0.01	0.46	*<0.01*
Desire to have children	0.07	0.06	0.10	*n.s.*
Treatment related regret (no vs all others)	0.20	0.17	0.08	*n.s.*
Value of children – utilitarian	0.07	0.15	0.05	*n.s.*
Value of children – social	0.19	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Timeline (IPQ2)	0.02	0.02	0.07	*n.s.*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 137) = 15.59$, $p < 0.01$

Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 136) = 4.64$, $p \leq 0.05$, $\Delta R^2 = 0.018$

Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1, 135) = 2.43$, p = n.s., $\Delta R^2 = 0.010$

Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 132) = 2.10$, p = n.s., $\Delta R^2 = 0.024$

Step 5: $R^2 = 0.500$, adjusted $R^2 = 0.450$, $F(1, 131) = 1.14$, p = n.s., $\Delta R^2 = 0.004$

The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.36 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 24. Multivariate model predicting the hyperarousal aspect of fertility-related distress with identity (IPQ5) entered in the final block

	B	SE B	β	*p*
Step 1				
Constant	0.18	0.54		*n.s.*
Age at diagnosis	-0.01	0.01	-0.07	*n.s.*
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.15	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*
Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.002	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.01*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.21	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.15	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.10	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*

Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.01	0.48	*<0.01*
Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				
Constant	-1.05	0.63		*n.s.*
Age at diagnosis	-0.004	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.62	0.19	0.25	*<0.01*
Type of cancer (gynaecological vs breast)	0.04	0.25	0.02	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.18	0.22	-0.08	*n.s.*
Recruitment site (other vs online)	-0.34	0.16	-0.16	*≤0.05*
Childbearing status (no vs yes)	-0.16	0.17	-0.07	*n.s.*
Negative affect	0.05	0.01	0.43	*<0.01*
Desire to have children	0.06	0.05	0.08	*n.s.*
Treatment related regret (no vs all others)	0.19	0.16	0.08	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.15	0.16	0.10	*n.s.*
Value of children – psychological	0.08	0.12	0.06	*n.s.*
Identity (IPQ5)	0.07	0.03	0.19	*<0.01*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 137) = 15.59$, $p < 0.01$
Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 136) = 4.64$, $p \leq 0.05$, $\Delta R^2 = 0.018$
Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1, 135) = 2.43$, p = n.s., $\Delta R^2 = 0.010$
Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 132) = 2.10$, p = n.s., $\Delta R^2 = 0.024$
Step 5: $R^2 = 0.523$, adjusted $R^2 = 0.476$, $F(1, 131) = 7.70$, $p < 0.01$, $\Delta R^2 = 0.028$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.25 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 25. Multivariate model predicting the hyperarousal voidance aspect of fertility-related distress with illness concern (IPQ6) entered in the final block

	B	**SE B**	**β**	***p***
Step 1				
Constant	0.18	0.54		n.s.

Age at diagnosis	-0.01	0.01	-0.07	n.s.
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.15	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*
Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.002	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.01*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.21	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.15	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.10	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*
Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.01	0.48	*<0.01*

Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				
Constant	-1.47	0.63		*≤0.05*
Age at diagnosis	-0.001	0.01	-0.004	*n.s.*
Country of origin (Britain vs Poland)	0.73	0.19	0.29	*<0.01*
Type of cancer (gynaecological vs breast)	0.09	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.18	0.21	-0.08	*n.s.*
Recruitment site (other vs online)	-0.24	0.16	-0.11	*n.s.*
Childbearing status (no vs yes)	-0.11	0.16	-0.05	*n.s.*
Negative affect	0.04	0.01	0.36	*<0.01*
Desire to have children	0.07	0.05	0.10	*n.s.*
Treatment related regret (no vs all others)	0.23	0.16	0.10	*n.s.*
Value of children – utilitarian	0.04	0.14	0.03	*n.s.*
Value of children – social	0.16	0.16	0.10	*n.s.*
Value of children – psychological	0.09	0.12	0.07	*n.s.*
Illness concern (IPQ6)	0.10	0.03	0.27	*<0.01*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 137) = 15.59$, $p < 0.01$
Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 136) = 4.64$, $p \leq 0.05$, $\Delta R^2 = 0.018$
Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1\ 135) = 2.43$, p = n.s., $\Delta R^2 = 0.010$
Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 132) = 2.10$, p = n.s., $\Delta R^2 = 0.024$
Step 5: $R^2 = 0.546$, adjusted $R^2 = 0.501$, $F(1, 131) = 14.61$, $p < 0.01$, $\Delta R^2 = 0.051$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.37 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Table 26. Multivariate model predicting the hyperarousal aspect of fertility-related distress with emotional representation (IPQ8) entered in the final block

	B	**SE B**	**β**	***p***
Step 1				
Constant	0.18	0.54		*n.s.*
Age at diagnosis	-0.01	0.01	-0.07	*n.s.*
Country of origin (Britain vs Poland)	0.76	0.19	0.30	*<0.01*
Type of cancer (gynaecological vs breast)	0.20	0.26	0.08	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.33	0.22	-0.15	*n.s.*
Recruitment site (other vs online)	-0.44	0.17	-0.20	*≤0.05*

Childbearing status (no vs yes)	-0.09	0.15	-0.04	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Step 2				
Constant	-0.53	0.63		*n.s.*
Age at diagnosis	-0.00	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.79	0.19	0.31	*<0.01*
Type of cancer (gynaecological vs breast)	0.18	0.26	0.07	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.29	0.21	-0.13	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.002	0.15	-0.001	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.11	0.05	0.16	*≤0.05*
Step 3				
Constant	-0.65	0.63		*n.s.*
Age at diagnosis	-0.001	0.01	-0.01	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.15	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.22	0.22	-0.10	*n.s.*
Recruitment site (other vs online)	-0.37	0.17	-0.17	*≤0.05*
Childbearing status (no vs yes)	0.03	0.16	0.01	*n.s.*
Negative affect	0.06	0.01	0.51	*<0.01*
Desire to have children	0.10	0.05	0.14	*n.s.*
Treatment related regret (no vs all others)	0.26	0.16	0.11	*n.s.*
Step 4				
Constant	-0.94	0.64		*n.s.*
Age at diagnosis	-0.003	0.01	-0.02	*n.s.*
Country of origin (Britain vs Poland)	0.66	0.20	0.26	*<0.01*
Type of cancer (gynaecological vs breast)	0.16	0.26	0.06	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.27	0.22	-0.12	*n.s.*
Recruitment site (other vs online)	-0.40	0.17	-0.18	*≤0.05*
Childbearing status (no vs yes)	-0.03	0.17	-0.02	*n.s.*
Negative affect	0.06	0.01	0.48	*<0.01*
Desire to have children	0.08	0.06	0.11	*n.s.*
Treatment related regret (no vs all others)	0.21	0.17	0.09	*n.s.*
Value of children – utilitarian	0.06	0.14	0.04	*n.s.*
Value of children – social	0.20	0.16	0.13	*n.s.*
Value of children – psychological	0.04	0.12	0.03	*n.s.*
Step 5				

Constant	-1.70	0.63		*<0.01*
Age at diagnosis	0.02	0.01	0.03	*n.s.*
Country of origin (Britain vs Poland)	0.80	0.19	0.32	*<0.01*
Type of cancer (gynaecological vs breast)	0.09	0.24	0.03	*n.s.*
Type of treatment (sterile vs uncertain fertility)	-0.15	0.21	-0.07	*n.s.*
Recruitment site (other vs online)	-0.28	0.16	-0.12	*n.s.*
Childbearing status (no vs yes)	-0.15	0.16	-0.07	*n.s.*
Negative affect	0.04	0.01	0.32	*<0.01*
Desire to have children	0.06	0.05	0.08	*n.s.*
Treatment related regret (no vs all others)	0.19	0.16	0.08	*n.s.*
Value of children – utilitarian	0.01	0.14	0.01	*n.s.*
Value of children – social	0.14	0.16	0.09	*n.s.*
Value of children – psychological	0.11	0.12	0.08	*n.s.*
Emotional representation (IPQ8)	0.13	0.03	0.32	*<0.01*

Note. Step 1: $R^2 = 0.443$, adjusted $R^2 = 0.415$, $F(7, 137) = 15.59$, $p < 0.01$
Step 2: $R^2 = 0.462$, adjusted $R^2 = 0.430$, $F(1, 136) = 4.64$, $p \leq 0.03$, $\Delta R^2 = 0.018$
Step 3: $R^2 = 0.471$, adjusted $R^2 = 0.436$, $F(1\ 135) = 2.43$, p = n.s., $\Delta R^2 = 0.010$
Step 4: $R^2 = 0.495$, adjusted $R^2 = 0.449$, $F(3, 132) = 2.10$, p = n.s., $\Delta R^2 = 0.024$
Step 5: $R^2 = 0.552$, adjusted $R^2 = 0.507$, $F(1, 131) = 16.54$, $p < 0.01$, $\Delta R^2 = 0.057$
The assumptions of the model have been tested and achieved. Sample size of 164 was deemed adequate to include 14 predictors in the analysis (Green, 1991). Collinearity tolerance statistics and variance inflation factors were within acceptable ranges (>0.1, <10 respectively). The Durbin-Watson statistic for the final model was 2.29 (acceptable range 1-3), suggesting that residuals were independent. The standardised residual P-P and scatter plots were inspected visually and indicated that the assumptions of normality and homoscedasticity were met.

Summary

These models clarify which subscales – avoidance, intrusion, or hyperarousal – were responsible for determining the predictors found to be significant in the model investigating overall fertility-related distress (see Table 27).

The results suggest that all subscales contributed to a strong association between the total illness perception and overall fertility-related distress. In particular, the relationships between identity and overall fertility-related distress as well as between illness concern and overall fertility-related distress were determined by all the subscales, the relationship between emotional representation and overall fertility-related distress relied on its association with intrusion and hyperarousal, and the relationship between the consequences and overall fertility-related distress was predominantly dependent on the contribution of the avoidance subscale.

All subscales also contributed to the association between the overall fertility-related distress and the negative affect. The relationship between the country of origin and overall fertility-related distress was influenced primarily by the avoidance and hyperarousal subscales, and the association between treatment-related regret and overall fertility-related distress was affected by the avoidance subscale. Finally, the intrusion subscale contributed most to the relationship between overall fertility-related distress and desire to have children.

Table 27. Individually significant predictors of the avoidance, intrusion, and hyperarousal subscales and variance explained by the overall models including total illness perceptions

Subscale	Predictors	IPQ predictors	Explained variance (R^2)
Avoidance	country of origin negative affect treatment-related regret psychological value of children total illness perceptions	consequences identity illness concern	40.5%
Intrusion	negative affect desire to have children total illness perceptions	identity illness concern emotional representation	51.3%
Hyperarousal	country of origin negative affect total illness perceptions	identity illness concern emotional representation	48%