Exploring the clinical guideline development process: influences and interactions

Judith Deborah Hughes

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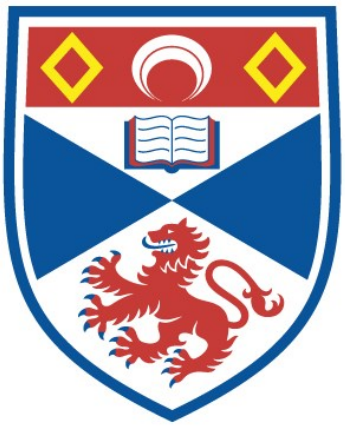
at the
University of St Andrews



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Abstract

Evidence-based clinical guidelines serve as an important support for medical decision-making. To date, research on clinical guidelines has focused mainly on guideline development methodology and the extent of guideline implementation. How guideline groups utilise various forms of evidence and the social processes involved in developing clinical guidelines have not yet been fully explored.

This qualitative study considers the individual, group and external factors that influenced the recommendations made by one guideline development group for the guideline concerning diagnosis and management of macular degeneration within the ophthalmology therapeutic area in the UK. Using direct observation, interviews and document analysis methods, this study explored, over 27-months, how the guideline group proceeded from reviewing the evidence on this condition to drafting guideline recommendations.

This research provides a detailed account of how the guideline group – working within an environment that includes influential external stakeholders – interpreted evidence, interacted and functioned as a group, and made consensus decisions on guideline recommendations. The study reveals that the ready availability (and acceptability) of evidence shapes the extent of reliance on expert opinion. In circumstances of low evidence availability, expert opinion is relied upon and factors such as group composition and dynamics, resource availability and external network challenges appear to be particularly important in the guideline development process and in shaping the guideline recommendations.

The study is the first to provide an account of the guideline development process in the ophthalmology area as well as adding, more generally, to the empirical literature on the clinical guideline development. The findings suggest that clinical and economic evidence does not easily or smoothly translate into strong recommendations. Rather, guideline development involves the interplay of many factors. An additional contribution of this research is the development of an integrative framework to capture and analyse these factors within the guideline development process.

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List of Abbreviations

AGREE	Appraisal of Guidelines for Research and Evaluation
AHRQ	Agency for Healthcare Research and Quality
AMD	Age-related Macular Degeneration
BBC	British Broadcasting Corporation
EBM	Evidence-Based Medicine
EBP	Evidence-Based Practice
GAIN	Guideline Audit and Implementation Network
GDEG	Guideline Development Expert Group
GDG	Guideline Development Group
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IOM	Institute of Medicine
NBHW	National Board of Health and Welfare
NCGC	National Clinical Guideline Centre
NGC	National Guideline Clearinghouse
NHS	National Health Service
NICE	National Institute of Health and Care Excellence
NTT	NICE Technical Team
OCEBM	Oxford Centre for Evidence-Based Medicine
QALY	Quality Adjusted Life Year
RCT	Randomised Controlled Trial
SIGN	Scottish Intercollegiate Guidelines Network
TRIAD	Tracking Roles In and Across Domains

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Chapter 1: Introduction

1.1 Introduction

Clinical guidelines have been an integral part of healthcare practice for many years with standardised methods of development in existence for over three decades (Weisz et al., 2007; Djulbegovich & Guyatt., 2017). As such, there is an extensive body of literature concerning guidelines. This includes their general structure and use, their philosophical and methodological underpinnings and their impact on specific diseases (see for example, Djulbegovich et al., 2009; Goergen et al., 2010; Brennan et al., 2017). In 1990, there were only 73 entries in the PubMed database pertaining to clinical guidelines; by 2012, this had increased to 7,508 (Upshur, 2014). However, the understanding of the guidelines is incomplete with respect to the guideline development process. This process can be divided into a technical part (evidence gathering and appraisal) and a social process (interpretation of the evidence and the forming of guideline recommendations) (Eccles et al., 2012), and it is the latter that is under-represented in the literature. This thesis explores the social processes of guideline development and what influences the activities and outcomes of the core guideline development group. This includes influences from within the group and from the wider environment within which it operates. It does so by studying the development process of one particular guideline being produced by the National Institute of Health and Care Excellence (NICE), the main guideline development agency in the UK which is often considered to be an exemplar of good guideline development (Legido-Quigley et al., 2012).

This introductory chapter firstly discusses the emergence and growth of guidelines in the context of healthcare practice before moving on to address, briefly, what previous research has revealed about guidelines and their use. The need for further research on guidelines is then considered. Following this, the aims of this thesis and its overarching research question are set out, as well as details of the approach taken to this research inquiry. Finally, the way this thesis is structured is outlined.

1.2 The origin and current context of clinical guidelines

Guidelines are seen as a distillation of the most important disease-specific information contained within the medical literature and as a provision of clear evidence-based strategies/recommendations for disease management (Swinglehurst, 2005; Djulbegovic & Guyatt, 2017). They are considered to be a strategy to assist health professionals, overwhelmed by the vast amount of information, in assimilating and applying evidence to their practice (Field & Lohr, 1990; Shekelle et al., 2012). They are also seen as a way to reduce practice variation and improve quality of care by reducing uncertainty concerning the most effective treatments, although some have suggested that the primary motivation for the production of clinical guidelines stemmed from a need for providers to manage increasing healthcare costs (Fowkes & Roberts, 1984; Woolf et al., 1999; Timmermans & Kolker, 2004).

Another reason cited for the initial emergence of guidelines is their potential to defend clinical autonomy. It is argued that groups of physicians produced early guidelines as a way to preserve their self-government (Timmermans & Kolker, 2004). Others feel that guidelines emerged as a method to improve or regulate the quality of medical practice (Weisz et al., 2007). The turn to evidence-based policy, and practice more generally, in the 1990s, also fuelled the growth of guidelines. In the late 1990s in the UK, the new Labour Government sought to make research useable as well as useful (Solesbury, 2001). The enthusiasm in government for evidence-based policy and programmes saw the flowering of organisations such as The Cochrane Collaboration, The Campbell Collaboration, the Social Care Institute for Excellence and NICE. These organisations were tasked with collecting and synthesising evidence for governmental initiatives and practice development.

The guideline movement was enthusiastically driven forward by a variety of organisations. These were state, or other government-sponsored organisations (like NICE in England and Wales and the US Institute of Medicine), who took the lead in developing clinical guidelines. Guidelines were also developed by therapeutic area bodies or professional groups with a vested interest in promulgating their view of treatment pathways (Woolf et al., 1999; Qaseem et al., 2010; Legido-Quigley et al., 2012). As such,

there has been a flowering of guidelines and the volume available is now vast. There are guidelines for every disease from cancer of the skin to diabetes, for many sectors from clinical care to public health and for each point in the patient journey from diagnosis to referral to treatment start and treatment withdrawal (Greenhalgh et al., 2014; Brennan, 2017). The National Guideline Clearinghouse (NGC) is an international database of clinical practice guidelines managed by U.S. Department of Health and Human Services and the Agency for Healthcare Research and Quality (Williams, 2017). As an illustration of the increase in guidelines internationally over a short period of time, the NGC was reported as holding 170 guidelines in one area of mental health, depression, in 2003 (Parry et al., 2003); this had increased to 447 by 2007 (Pilling, 2008).

There are many positive reasons for guidelines. Their advantages were categorised early in their history by Woolf and colleagues (1999) into benefits for healthcare professionals, for patients and for healthcare funders. Benefits cited for healthcare professionals were reduction in practice variation and improvement in the quality of clinical decisions. For patients, there would be an improvement in health outcomes and consistency of care and for healthcare funders, an optimisation of value and efficiency. The development of the guideline "tool" as a resource for clinicians and funders has improved treatment and resource decision-making (Woolf et al., 1999; Djulbegovich & Guyatt, 2017). Furthermore, they have provided an information resource for patients and carers to consult (Pilling, 2008). The current view of guidelines is that they are a healthcare resource to guide medical practice and an important part of the "fabric of service delivery" (Brennan et al., 2017:9).

However, there are certain issues that are said to limit their use and effectiveness. For example, the scientific evidence on which a guideline is based is biased towards systematic reviews and quantitative data (Hammersley, 2005; Djulbegovich & Guyatt, 2017); it is also constrained by study of only narrow populations (Greenhalgh et al., 2014; Horwitz & Singer, 2017). Data included in a guideline is often out of date due to the length of time studies take, or flawed due to data omission, publication lag and publication bias towards quantitative studies (Timmermans & Kolker, 2004; McGauran et al., 2010; Hart et al., 2012; Mangin, 2012). Guidelines are disease-focused rather than patient-

focused (Shaneyfelt, 2012; Upshur, 2014) and often do not recognise co-morbidity as a key factor in designing treatment strategies (Boyd et al., 2005; Shekelle et al., 2012; Hughes et al., 2013; Upshur, 2014). There continues to be claims that guidelines have too much power to dictate practice (McCartney, 2014) resulting in an adherence to rules and suffocation of clinical expertise (Greenhalgh et al., 2014). Further, veering from the guidelines, in primary care for example, can result in penalisation under the pay-for-performance systems in place for General Practitioners (GPs) (McCartney, 2016).

1.3 Current research into clinical guidelines

Research, currently, is concentrated on the methodologies of guideline development and guideline implementation. The methodology of guideline development varies across countries and different health systems. Some countries have centralised development systems but guidelines also continue to be developed locally, using different methodologies, by special interest groups and disease-specific organisations (Legido-Quigley et al., 2012). This has resulted in a mixed picture but efforts have been made to standardise the whole process (Qaseem et al., 2012) and much of the research literature is concerned with these standards. For instance, the Appraisal of Guidelines for Research and Evaluation - AGREE - instrument (AGREE Collaboration, 2003), provides criteria to assess the methodological rigour of guideline development. There are also the US Institute of Medicine standards (IOM, 2011) which set out elements to be included in the development of guidelines, such as, guideline group composition, evidence quality assessment, and a policy on the management of conflicts of interest within guideline groups. Similar elements have been identified by The Guideline International Network standards for guideline development (Qaseem et al., 2012).

Research on the implementation of guidelines reflects increasing concern that guidelines result in little change in individual clinicians' practices (Shaneyfelt & Centor, 2009; Zwolsman et al., 2012; Casey, 2013; Pronovost, 2013). Systematic and realist reviews on the implementation of guidelines suggest that evidence in guidelines does not flow easily into practice (Grimshaw et al., 2004; Gagliardi & Alhabib, 2015; Brennan et al., 2017). The reasons for this include that guideline-supporting evidence focuses on narrowly-defined patient populations and does not account for "real" patients with

multiple conditions (Shekelle et al., 2012; Hughes et al., 2013). There is also the sheer volume of guidelines available which makes them unmanageable in treating patients with many conditions (Allen & Harkins, 2005; Greenhalgh, 2017). Other reasons for the lack of implementaton of guidelines is that they do not reflect the recent emphasis on incorporation of different types of knowledge and on more patient-centred care (Boivin et al., 2009; Boivin et al., 2010; Légaré et al., 2011).

There is a paucity of empirical research on the social processes of guideline development and on the factors that influence the development process (Eccles et al., 2012; Atkins et al., 2013). There are a few studies that focus on elements of the guideline development process. For example, Pagliari and Grimshaw (2002) considered the effect of professional and social status on the level of contribution to group discussion, finding that the highest contribution to discussion was from those with perceived higher status. Similar results were seen from Richter Sundberg and colleagues (2017) in their study of a guideline group in Sweden. Atkins and colleagues (2013) studied three NICE guideline development groups looking at individual interpretation of evidence, on roles played within the group and on social interaction during decision making. They concluded that human judgement plays a key role in guideline development rather than it being based on evidence alone. Influences from the wider environment were not examined in these studies.

1.4 The rationale for further research on guideline development

Guidelines are an integral part of healthcare practice and service provision. They are influential in guiding clinical practice and form part of the evidence on which clinical commissioning decisions are made for populations (Clarke et al., 2013; Brennan et al., 2017). As such, it is important to understand them and their development process as fully as possible, so we can learn how best to incorporate them into healthcare practices.

Guidelines cannot now be isolated from the fabric of the healthcare system. The quandary is how best to ensure they dovetail smoothly with all the other elements of this system and thus, more research concerning their development and use is warranted (Brennan et al., 2017).

There are a number of misgivings about guidelines which have been highlighted above. There is a questioning of their quality, purpose and use. Information on how they are developed may provide some additional answers to these misgivings. Therefore, further research into the development process is warranted, as it will illuminate factors that play into this process.

The guideline development process itself, in terms of what actually happens in guideline development group meetings, is not fully understood. This especially true of the interactions of guideline group participants and the internal and external factors that impact these interactions and relationships. There is a gap in the research literature in this regard and research in this area will contribute to the overall body of guideline literature.

Another reason for conducting this particular research is personal. I have been an ophthalmologist for 30 years, both in clinical practice and within the pharmaceutical industry developing drugs for clinical use. Whilst employed in various pharmaceutical companies, I participated in a number of expert advisory panels that developed clinical guidelines for therapeutic and special-interest groups. Most of the participants of these panels were opinion leaders in their fields. Many of the guideline recommendations appeared to be derived from expert opinion as well as various bodies of evidence. This initially spawned an interest in how opinion leaders were utilised by the pharmaceutical industry (the subject of my Master's dissertation), but also led to a curiosity about how guideline development occurs in more centralised and standardised systems.

1.5 Research aims, task and primary question

This research has three main aims. The first aim is to increase understanding of clinical guidelines by providing a detailed, rich account and analysis of the guideline development process. This aim is directed towards gaining insights into some of the challenges faced when developing guidelines from the perspective of a guideline development group.

The second aim is to contribute to the guideline literature, especially with respect to the social processes of guideline development, identified as a gap in the current guideline

literature. Foci of interest will be how members of the guideline group act and interact in the decision-making process and how evidence is interpreted and used in formulating guideline recommendations.

The third aim of this research is to characterise the major influences on the guideline group, both from within the group and from external sources. This is because the guideline group does not work in isolation; there is a broader set of actors and organisations that play a role in guideline development.

To address these aims, the primary research question is:

"How does a multi-actor group, responsible for developing clinical guidelines within the UK, interact and use evidence?"

In order to fulfil these aims and address the research question, the guideline development process of a particular guideline group (the core research subject) has been followed throughout the development period of the guideline. The guideline topic is an eye disease, macular degeneration, and the guideline encompasses both the diagnosis and management of this condition. The guideline developer is NICE and the research setting is NICE offices in London and Manchester. NICE is the primary developer of clinical guidelines which are used for guiding practice and making commissioning decisions in England and Wales. This, together with its reputation as an exemplar of guideline methodology, makes NICE a fitting choice for guideline development research.

This is a qualitative case study of the guideline development group, using observation of group meetings, semi-structured interviews and document analysis. This research approach is congruent with the multiple perspectives sought and the aim of understanding the guideline process rather than just describing it.

1.6 Organisation of thesis

The main arguments and findings of this thesis are presented within seven further chapters. There are also nine appendices containing additional background information. Chapter 2

critically explores the literature pertaining to clinical guidelines, knowledge and evidence in the clinical environment and influences on the guideline development process. The main debates in each area are examined.

Following on from the literature review, Chapter 3 sets out the multi-perspective framework guiding this inquiry. The chapter describes the framework and discusses how it shaped a series of subsidiary research questions. Further, it links to the development and evolution of the interview protocols seen in Appendices i and ii.

Chapter 4 discusses the philosophical and methodological approach taken in this research, how this aligns with the type of research questions asked and the aims of the research and the methods of data collection and analysis.

Chapter 5 details the NICE clinical guideline process. It also discusses how NICE fits into the wider healthcare policy and practice environment in the UK. This sets the scene for the findings of this research.

The findings chapter, Chapter 6, examines the results that emerged after following the guideline group for 27 months of the guideline development process. It is split into four main parts. The first addresses specific case details. This includes the key timelines for the guideline process and a brief description of macular degeneration, the disease subject of the guideline. The structure of the macular degeneration guideline group is set out and how this changes over the course of the research. It also highlights the group members' motivations to participate and their individual perceptions of guidelines. The second part is about the nature of evidence in the guideline process and how this is interpreted and used. The third part details findings concerning group functioning and key factors affecting this. The fourth part highlights the key external network influences revealed by the study.

Chapter 7 examines the insights gained from the study. It discusses them in relation to the literature, drawing out conceptual and theoretical implications. The final part of the chapter brings together the principal findings in a new integrative framework for

understanding the guideline development process. The elements of the framework are described together with reflections on its development.

The final chapter, Chapter 8, provides an overview of the research. The way it contributes to a wider body of knowledge about guidelines is discussed as well as some practical implications and potential avenues of further research. The study approach taken is reflected upon and there is also a final personal reflection.

1.7 Summary

This introductory chapter has highlighted the importance of guidelines in the healthcare environment. It has pointed to some of the current concerns around guidelines and given a brief review of the guideline literature. The literature focuses on methodologies for guideline development and the implementation of guidelines. There is a paucity of literature that examines the social processes of, and factors influencing, the guideline development group. Exploring these is, not only an opportunity to examine these processes in detail, but it will also contribute to a wider understanding of guideline development.

Chapter 2. Literature Review: Theoretical Perspectives on Clinical Guidelines

2.1 Introduction

Chapter 1 introduced the research subject and the rationale for an inquiry into the guideline development process. This chapter critically reviews the literature in order to provide a theoretical and empirical landscape within which to place guideline development. It provides support for the research aims and questions and establishes an appropriate basis for the conceptual framework discussed in Chapter 3.

The study of clinical guidelines draws on knowledge and understanding from many fields and disciplines: not only health research, but also research on, for example, public policy, sociology, politics, networks, knowledge management and organisation. As such, there is a wide array of potentially relevant literature, so the approach to reviewing the literature has had to be selective and focused. In relation to knowledge and evidence, the focus is on knowledge and knowing in the clinical environment, detailing the concept of evidence-based medicine and other ways of knowing in medicine. Likewise, the approach taken to understanding the wider environment within which guidelines are developed is to draw on the network literatures, especially research on networks in healthcare. This is because the development of guidelines occurs within a complex web of actors, healthcare organisations and processes. Drawing on the networks literature gives insights into that complexity.

The chapter is split into two major parts. First, there is a review of the specific clinical guideline literature and the literature concerning knowledge and evidence in the clinical environment. What has been revealed by research into guidelines is discussed, as well as the issues and concerns about guidelines. Empirical gaps in the literature are identified. This part of the chapter continues by discussing what constitutes evidence, knowledge and ways of knowing in the clinical environment. Here, the creed of evidence-based medicine as an underpinning tenet of guideline development is examined. Other forms of knowledge within healthcare are also discussed since clinical knowledge and decision

making in medicine are about more than just the use of research data. Such knowledge encompasses formal learned knowledge, tacit and experiential knowledge and judgement, values and opinion.

Part 2 of the chapter considers influences on the guideline process. Influences within the process (by individuals and the development group) are separated from those labelled as being external influences on guideline development. Firstly, there is a review of the literature on within-group influences. A guideline group is composed of different individuals coming from various professions and backgrounds. As such, each person will bring with them individual knowledge, ways of knowing, values, assumptions, opinions and experiences. They will have different modes of learning, patterns of thinking, ways of playing roles and developing expertise. Given the vast array of literatures that would be required to elucidate all of these factors for each individual in a multidisciplinary group, the approach is to review within-group influences mainly at the level of the guideline group and not separately for individuals. When appropriate, further reference will be made to individual factors affecting group functioning. The review includes literature relevant to guideline group composition and diversity, roles played within the group, group functioning factors and dynamics, and consensus decision making.

Secondly, within Part 2, there is a review of the external influences on the guideline group. Guideline development occurs within a wide network of people and organisations, all of whom may exert influence on the guideline process. As such, the networks literature offers insights into the characteristics of networks and their effect on decision making. This part of the chapter discusses the turn to networks in public policy and the forms of networks applicable to healthcare. Part 2 concludes by discussing the challenges of working in networks compared with hierarchical structures and looks at a number of perceived future challenges.

2.2 Part 1: The clinical guidelines milieu

2.2.1 Clinical guidelines literature

Guidelines are seen to be important in standardising care and safety for patients in many countries and their use has now been embraced by different state, local and professional healthcare organisations (Woolf et al., 1999; Swinglehurst, 2005; Institute of Medicine, 2011). As such, there is now an extensive guideline literature ranging from the theoretical underpinnings of evidence-based medicine to discussion of guideline impact on specific diseases. As mentioned in Chapter 1, research to date on guidelines has focused predominantly on their methodology and implementation with little focus on the social processes of guideline development (Michie et al., 2007; Eccles et al., 2012; Shekelle et al., 2012; Atkins et al., 2013). Part 2.2.1 discusses the existing literature in these three areas (methodology, implementation and social processes) and, further, highlights the literature pertaining to current concerns with guidelines.

Methodologies of guideline development

Since guidelines emanate from diverse types of organisations and from different health systems in various countries, the methodologies of development and the quality and implementation of guidelines have been variable (Burgers et al., 2003a, 2003b). A recent study examined guidelines across Europe (including Norway and Switzerland), concentrating on five key domains: regulatory basis, development, quality control, implementation and evaluation (Legido-Quigley et al., 2012). What was revealed was widespread inconsistency in the way guidelines are developed, regulated and implemented across the countries studied. This, perhaps, reflects differing political and cultural factors but also points to a lack of standardisation of guideline development. Variability is seen in the quality of guidelines and the methodology of their development. This leads to a suggestion that more resources and research are needed to support a standardisation of guideline terminology as well as further studies to examine the different ways of developing guidelines and how this relates to their quality and implementation (ibid).

Efforts have been made to counter this diversity and improve on the quality of guideline methodologies. For example, the Guidelines International Network, consisting of guideline developers representing 46 countries, proposed minimum standards for a set of key development components. These include composition of the guideline group, assessing conflicts of interest, the methods used, evidence rating and the decision-making process (Qaseem et al., 2012). In 2003, an international group of guideline developers published a 23-item instrument, grouped by six quality domains, to assess the methodological robustness of the guideline process (AGREE Collaboration 2003).
The six domains are summarised in Table 2.1.

Table 2.1: AGREE domains and criteria of high-quality guidelines

1: Scope and Purpose Contain statements about overall objective, the clinical questions and target population.
2: Stakeholder Involvement Provide information about the composition and expertise of the guideline development group. Involve patients in their development.
3: Rigour of Development Provide information on the search strategy, criteria for selecting the evidence and methods used to formulate the recommendations. The recommendations should be explicitly linked to the supporting evidence with discussion about health benefits, side effects and risks.
4: Clarity and Presentation Contain recommendations on patient care and consider different possible options. Summary document and patients' leaflets are provided.
5: Applicability Discuss organisational changes and cost implications of the recommendations. Present review criteria for monitoring the use of guidelines.
6: Editorial Independence Include an explicit statement that the views of the funding body have not influenced the final recommendations. Members of the guideline group have declared possible conflicts of interest.

Adapted from AGREE Collaboration, 2003:22

The AGREE instrument was updated in 2010 adding improved supporting documentation and refining more than half the quality measures (Brouwers et al., 2010; Burls, 2010). It is now utilised routinely where formal guideline development is firmly established, such as in the UK, although in some EU countries its use remains patchy (Legido-Quigley et al., 2012).

In 2011, the US Institute of Medicine (IOM) published a set of standards (in a 290-page document), setting out the "essential elements in the development of trustworthy guidelines" (IOM 2011:9). These involve managing conflicts of interest, guideline group composition, evidence foundations and ratings for strength of recommendations made, measures for external review and the updating process. The IOM standards set high expectations, especially for organisations with more recently established processes. Few guideline organisations met the specifications, especially in areas such as patient representation on guideline committees and processes for public consultation, (Laine et al., 2011).

Formally, NICE appears to have a high level of sophistication in many areas where standards exist (Legido-Quigley et al., 2012). So, for example, evidence gathering and assessment follows a recognised evidence-based medicine quality standard, the process itself is assessed against AGREE standards, there are transparent procedures in place for managing conflicts of interest and how decisions are made, there are multiple opportunities for stakeholder input, and there is a significant effort to involve patients (NICE 2014, updated 2017). Since NICE and its processes are central to this research, the NICE "model" of guideline development is afforded its own chapter (Chapter 5).

Implementation of guidelines

The implementation (or lack of use) of guidelines in practice is also well rehearsed in the literature. A number of systematic and realist reviews have been conducted synthesising the literature on implementation of guidelines and implementation strategies used (Grimshaw et al., 2004; Gagliardi & Alhabib, 2015; Brennan et al.; 2017). The picture that emerges is one that suggests research does not flow smoothly or readily into practice via guidelines. There is lack of compliance with guidance that can lead to patients not

receiving treatments with proven efficacy or receiving care that is sub-optimal (Latosinsky et al., 2007; Llor et al., 2011; Pan et al., 2013; Pronovost 2013; Greenhalgh et al., 2014). For example, Latosinsky and colleagues (2007) reviewed the practice of breast cancer surgeons in Manitoba, Canada, in their compliance with the Canadian Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. There was wide practice variation in the way breast cancer was treated and this did not change after the publication and implementation of the guideline. This suggested little standardisation of care and a failure of guideline implementation (ibid).

Another example of how guidelines are not fully implemented in practice comes from primary care. Guidelines for the treatment of upper respiratory tract infections in children now discourage the first-line use of antibiotics (NICE CG69, 2008, NICE NG84, 2018; AHRQ, 2016). However, in a retrospective, observational study reviewing the prescribing practices in primary care for children with fever, ear or respiratory infections in the Netherlands, Ivanovska and colleagues (2016) found that antibiotics were prescribed in 40% of cases of bronchitis. Further, they revealed a wide variation in adherence to guidelines across different respiratory diagnoses and different general practices.

Evidence on the implementation of guidelines demonstrates little change in individual clinicians' practices (Latosinsky et al., 2007; Shaneyfelt & Centor 2009; Llor et al. 2011; Zwolsman et al., 2012; Casey, 2013; Pronovost, 2013). One recent study examined the implementation of NICE guidelines by National Health Service (NHS) Trusts. The study by Lowson and colleagues (2015) used a cross-sectional survey technique to question policies around managing NICE guidance in 181 acute hospitals across the UK. They found that, while there were processes in place to implement the guidance, resource limitations, lack of clarity of the relevance of the guidance, and poor engagement by clinicians were among the reasons for failure (Lowson et al., 2015). Their results are mirrored by studies of implementation of individual guidelines for specific diseases. For instance, Platt and colleagues (2015) reviewed the implementation of a NICE guideline on the management of urinary tract infection in children in primary and secondary care in England. They found compliance to be poor as a result of the complexity of the

guideline and inadequate information technology resources to support clinical documentation systems.

There is a plethora of literature concerning the barriers to implementation of individual disease-specific guidelines. For example, barriers to the implementation of physical activity guidelines for lung cancer patients included limited staffing and resources, focus on delivery of other medical details, and low motivation and fear of exercise in patients (Granger et al., 2016). Many of the barriers identified for individual guidelines are reflected in a more general summary of guideline implementation barriers (Greenhalgh, 2017). Drawing on the Capability-Motivation-Opportunity-Behaviour framework of Michie and colleagues (2011) and Cabana's (1999) framework of barriers to guideline adherence, Greenhalgh sets out the main barriers. Summarised in Table 2.2, they include lack of time for clinicians to stay up-to-date with guidance, guidelines interfering with perceived clinical autonomy, patients not agreeing with the suggested treatment option, lack of applicability to individual patients, and external barriers such as technology and funding issues.

Table 2.2: Barriers to guideline adherence

1: Lack of Capability
Guideline unavailable or inaccessible
Clinician is unfamiliar with guideline
Volume of information is unmanageable
Clinician has insufficient time to stay informed
2: Lack of Motivation to Use the Guideline
Guideline interferes with clinician autonomy
Guideline does not apply to the patient being treated
Guidelines are too rigid and impractical
Patient rejects the guideline recommendation
3. Organisational/external barriers
Conflict between the guideline and organisational policy
Insufficient resources or competing priorities
Technology challenges
Reimbursement issues

Adapted from Greenhalgh, 2017:42

The barriers are context-specific. So, for example in middle or low-income countries (World Bank, 2015), a lack of appropriate resources can lead to low implementation of guidelines (Stokes et al., 2016; Maaløe et al., 2018). In order to improve implementation of guidelines, some have advocated tailoring guideline implementation strategies to specific contexts (Baker et al., 2001; Wensing et al., 2010). However, evidence suggests that, while tailoring can have a positive effect on guideline uptake, the results are variable and more research is needed to determine the elements of tailoring that have the most effect (Baker et al., 2015).

Whilst there appear to be many barriers to the implementation of guidelines, there are also facilitators. Guideline implementation strategies are commonly seen to bridge the gap between interventions like guidelines and practice (Gagliardi & Alhabib, 2015). Having these in place at the time of guideline publication is now seen to be a feature of a high-quality guideline (IOM 2011). It is suggested that these strategies are more successful when they have multiple components, including education systems, and when they actively involve clinicians throughout the implementation process (Prior et al., 2008). Some authors highlighting barriers to implementation of guidelines, state that facilitators of implementation can be inferred as the converse of barriers (Baateima et al., 2017). Thus, the uptake of guidelines is enhanced by features such as, having a manageable amount of supporting evidence, or having a narrow scope, or being tailored to context, or having appropriate resources available. Further, being developed by a reputable agency or where there is end-user input during the guideline development process, also aids guideline uptake by physicians.

The social processes of guideline development

One area that is under-represented in the guideline literature is research on the social processes of the development of clinical guidelines (Michie et al., 2007; Eccles et al. 2012). There is little understanding of how evidence is interpreted and formed into recommendations by guideline groups or what factors influence group functioning (Atkins et al. 2013).

Bond and Grimshaw (1995) conducted a study of multi-disciplinary guideline development (prior to the standardisation of guideline methodology or the institution of guideline developers such as NICE). This study described the processes of putting together local guidelines for community pharmacy management of dyspepsia. Participants involved three levels of care, community, primary and secondary healthcare and involved a mix of participants from these three levels. There were two gastroenterologists, two primary care physicians, three pharmacists, a facilitator with previous experience of developing guidelines, a research assistant and a group leader (not specified further). Five meetings of the guideline group were observed over two months. An interaction process analysis matrix (Bales, 1950) was used to classify group interactions. The results demonstrated the existence of professional hierarchies in the group. This led to different contributions to discussions with the greatest input from the secondary care clinicians. There were differing perspectives on care and an initial lack of understanding of the role of others, although this understanding increased over the period of development. The authors concluded that guideline developers should be aware that multi-disciplinary guideline development could be problematic due to inherent professional hierarchies.

One study (Pagliari & Grimshaw, 2002) observed a primary care guideline process over several months and considered the influence of social interactions on guideline development. Four, three-hour meetings of a multi-disciplinary guideline group were observed during a 12 month period and their interactions assessed using interaction process analysis. The results revealed that the level of contribution to discussions was strongly associated with professional role and status. There was a marked difference in input to discussions and decision making with the highest level of contribution from the chair of the group, followed by expert hospital consultants. The primary care doctors and allied health professionals were less active in discussions with a nurse and a pharmacist being the least active. Group composition changed frequently with only four (of between 19 and 27) members of the group being present on all four occasions of observation. This limited capturing the interactions of a stable core group over time but the study's findings did substantiate earlier research that group interactions and relations are linked with

social/professional hierarchies that play out within the group (Berger et al., 1972; Ridgeway et al., 1998).

Another more recent study from Sweden, (Richter-Sundberg et al., 2017) looked at the development of guidelines with a disease-prevention focus produced by the National Board of Health and Welfare (NBHW). This was a qualitative, longitudinal study assessing the decision-making process against the NBHW model's criteria of research evidence, curative/preventive effect size, severity of the condition, cost-effectiveness and ethical considerations. The study demonstrated that the guideline group modified the model as they encountered dilemmas, such as low availability of evidence. Also, additional criteria were added to the model: clinical experience and judgement, needs of vulnerable people and potential guideline consequences. A further finding was that group discussions during decision making were influenced by professional status and interpersonal skills. The study focused on factors which were mainly internal to the guideline group and did not investigate external influences. Thus, it is difficult to assess the impacts of external influences on individuals within the group. It was also undertaken within a different healthcare system from the UK with healthcare being tax-payer funded but devolved to county councils. However, the NBHW, the main guideline-producing body, is a state-sponsored body and follows many of standardised procedures for guideline development (Legido-Quigley et al., 2012).

In the UK, there have been two studies undertaken with NICE. The first (Moriera et al., 2006) aimed to review the process of evidence appraisal and discussion within a guideline development group. This was an observational study (with a non-participant observer) of two guideline groups, over 21 meetings, focusing on how the groups organised their discussion of the evidence. The recorded meetings were transcribed and then analysed using grounded theory and frame analysis with the qualitative results complemented by descriptive statistics. Results showed that the groups used four domains of reasoning for discussion: "science", "practice", "politics" and "process". The domains of "science" and "practice" accounted for two-thirds of the groups' discussions. This could be accounted for by the importance ascribed to scientific evidence in the guideline process or the high contribution seen from the hospital specialists and the methodologist. The authors

suggested that these methods of analysis would be useful in further studies to identify the relative proportions and relationships between domains of discussion during the guideline process. There have, however, been no further reported studies using this framework.

One more recent study investigated the internal interactions of three groups developing guidance for clinical, mental and public health with the aim of exploring the translation of evidence into guideline recommendations (Atkins et al., 2013). The study focused on the perception of individuals having the most influence within the group, beliefs about evidence and strategies used in appraising evidence and forming recommendations, and views on the social interactions during the guideline process. Interview data was first analysed using a qualitative thematic analysis method. It then underwent content analysis of the number of utterances of participants. This provided quantitative data to contextualise the themes identified. The study showed that individuals had different conceptualisations of the value of different types of evidence. Also identified was the challenge of managing diverse, multi-disciplinary groups in this context and that good relationships between group members were important for successful group functioning and task outcome. The study concluded that evidence alone did not make recommendations, rather, human judgement plays a key role. Also, for this judgement to have a positive influence, a diverse range of opinions is required, including a louder voice for service users. However, it is this diversity that can cause tensions throughout the guideline process.

Concerns around guidelines

Despite the benefits of guidelines in guiding clinical practice and reducing variation in patient treatment, there appears to be discomfort with many aspects of them. Some of these may help explain why there continues to be poor implementation and compliance with guidelines in both primary and secondary care.

One concern is the volume of guidelines available. For instance, Matthys and colleagues (2007) reviewed guidelines for pharyngitis across national boundaries. Four North American guidelines and six European guidelines were included in their study. An expectation was that their content would be similar. However, the results showed

differences both in treatment recommendations and in the supporting evidence. These were due to differences in selection and interpretation of evidence and this led to inappropriate regional variation in patient management (ibid). Even within the UK, there are multiple versions of guidelines for the same disease which can be consulted by health professionals. For glaucoma, for example, there are at least 4 guidelines published by central guideline developers or professional organisations (European Glaucoma Society, 2014; SIGN, 2015; NICE NG81, 2017; College of Optometrists, 2018).

Another concern is that guidelines have become very detailed with multiple recommendations for single diseases. Revisions of guidelines can lead to increases of over 45% in the number of recommendations published (Tricoci et al., 2009). Guidelines are disease-focused rather than patient-focused (Shaneyfelt, 2012) and, as many patients do not have just one condition, this can lead to many guidelines having to be consulted in the management of a single patient. Allen and Harkins (2005), reviewing the number of guidelines to be consulted for the admission of 18 patients to hospital in a 24-hour period, estimated that physicians would be required to read for 122 hours if they were to digest all the relevant information for these patients.

Guidelines often do not recognise co-morbidity in treatment strategy (Boyd et al., 2005; Shekelle et al., 2012; Hughes et al., 2013; Upshur, 2014). Boyd and colleagues (2005) used an hypothetical patient to illustrate the problem. The patient they devised was a 79-year old woman with diabetes, chronic respiratory disease, high blood pressure, osteoporosis and arthritis. On applying the relevant guidelines to the patient, they discovered that the clinician would have to perform 18 tasks and the patient would have to take 12 different medications per day. Furthermore, a number of recommended medications would interact unfavourably with each other. The conclusion was that, for such a patient with multiple conditions, following the relevant guidelines may have harmful effects. In effect, guidelines foster polypharmacy (Hughes et al., 2013).

Further concerns are around a number of biases identified in guidelines. There is bias towards systematic reviews and quantitative data in the medical evidence on which the guideline is based (Hammersley 2005; Djulbegovich & Guyatt, 2017). The evidence is

restricted by the study of only narrow populations (Greenhalgh et al. 2014; Horwitz & Singer 2017). As patients with increasing age tend to have multiple conditions, there are calls for more individualised care (Greenhalgh et al., 2014; Horwitz & Singer, 2017). This includes access to new types of evidence describing clinical, social and cultural characteristics of individuals, not just of populations.

Some authors have highlighted publication bias in the available evidence (McGauran et al., 2010; Song et al., 2010; Hart et al., 2012). Song and colleagues (2010) reviewed empirical studies from 1998-2008 on publication and related biases for a UK Health Technology Assessment (HTA) report. The results of the review revealed that studies with positive results were more likely to be reported and published. They also tended to be published earlier than studies with negative (or non-significant) results. This reporting and publication bias can, then, skew what evidence is included to support a guideline (Ioannidis & Trikalinos, 2005; Ioannidis, 2005, 2006; McGauran et al., 2010; Hart et al., 2012) since, generally, only published material is considered for the guideline evidence base.

Data included in guidelines is often out of date with more than half of guidelines taking only five years to become less relevant as new evidence appears (Shekelle et al., 2001). The length of time studies take to complete, especially drug intervention studies, is one reason. Another reason is publication lag where the time between a study finishing and its publication can be four-five years or longer (Hopewell et al., 2007a). So-called "trustworthy" guidelines (IOM, 2011; Laine et al., 2011) include mechanisms and timeframes for the updating of guidelines so that new evidence can be taken into account. For example, NICE check regularly whether a guideline needs to be updated. This usually occurs every two years or at least every four years (Hill et al., 2011; NICE 2014, updated 2017).

Intellectual and financial conflicts of interest are common. In 2002, Choudry and colleagues detailed that more than 85% of 192 guideline authors from 44 guidelines had some kind of relationship with the pharmaceutical industry that could indicate a conflict of interest. A more recent survey suggested that, despite the passing of a further decade,

little had changed: Kung and colleagues (2012) screened, at random, 130 guidelines for compliance with 18 of 25 Institute of Medicine standards for guidelines (IOM, 2011) one of which is the declaration of interests of guideline authors. Fewer than 50% of guidelines screened detailed any information on conflicts of interest and, where information was included, for more than 70% of committee chairs, financial conflicts of interest were evident.

The presence of conflicts of interest may negatively influence the guideline process by creating advocacy of, or attachment to, certain treatments which can then prejudice appropriate consideration of all the evidence (Shaneyfelt & Centor, 2009; Guyatt et al., 2010; Gale, 2011; Kung et al., 2012; Shaneyfelt, 2012; Lenzer, 2013). Many guideline development bodies, such as NICE, take steps to exclude those with conflicts of interest from the decision-making process (Steinbrook, 2007; Legido-Quigley et al., 2012; NICE Conflicts of Interest Policy, 2014).

In summary, the guideline literature comprehensively covers certain aspects of guidelines such as methodological issues and implementation. Key points are that methodological rigour is required for guidelines to be considered "trustworthy". Standards to be met in this regard have been published and guideline development organisations are expected to meet these standards. Despite these standards, implementation remains a concern and compliance with guidelines is low. Concerns around guidelines, such as how they do not address co-morbidity in patients and the sheer volume of guidelines to be considered by physicians, may account for this low uptake. There is limited literature on the social processes of guideline development: what actually happens at guideline committee meetings during debate and formation of guideline recommendations, and what influences those interactions. Thus, there appears to be a gap for such empirical work that would augment the existing body of guideline literature.

It is important to understand the evidence, and assumptions underlying the evidence, on which guidelines are based. This is because guideline recommendations, which guide clinical practice and underpin many funding decisions in healthcare, are formulated directly from a body of available evidence. Also, the literature, reviewed above, suggests

that this evidence is an area of concern with respect to its content and use in guidelines. The next section, then, considers the evidence and knowledge underlying guidelines. It reviews conceptualisations of medical evidence and knowledge in the healthcare environment with a focus on evidence-based medicine, since guidelines emerged from this movement.

2.2.2 Knowledge and evidence in the clinical environment

This section teases out what is meant by knowledge and evidence in the clinical environment. It includes notions of formal medical knowledge, such as that provided by scientific research. There is a review of the literature concerning evidence-based medicine, the tenets of which underpin clinical guidelines. It also explores tacit knowledge gained from practical experience, a form of knowledge recognised as an important part of how health professionals think and make decisions (Montgomery, 2006).

Formal evidence in medicine

The technological and scientific aspects of medicine are evolving at a rapid rate. This is alongside changes in strategies of health-service provision, a focus on patient-centred care, frequent organisational re-design, changing resource priorities and political transformations (NHS England, 2014; Costa-Font, 2017; National Audit Office, 2017). Scientific research continues to be privileged as robust evidence on which to base practice despite calls that other types of evidence, such as findings from qualitative studies, have at least complementary value, if not, equal validity (Mol, 2008; Greenhalgh et al., 2014; Shaw et al., 2014). The privileging of scientific research is exemplified by evidence-based medicine (EBM), a framework that has guided clinical practice over the past three decades. The next section elucidates the concept and principles upon which EBM is based before moving on to how the EBM movement categorises evidence, and the benefits and challenges of such a framework.

The concept of EBM

Advocacy for evidence-based medicine began in the early 1990s to provide a stronger empirical basis for clinical practice (Guyatt, 1991; Evidence-based medicine working group, 1992; Djulbegovic & Guyatt, 2017). It arose, also, as a response to what was

termed the "postcode lottery" for healthcare where the geographical location of patients dictated availability of treatments (Butler, 2000). This resulted in inequitable, local and regional variations of care, a situation that could result in a cancer patient living in one area receiving funded treatment while a similar patient, living in a different postcode area with the same disease, did not (Bungay, 2005; Patel et al., 2007).

EBM was originally envisioned as: "[T]he conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett et al., 1996:71). It was argued that the use of the "best" evidence should be integrated with individual clinical expertise thus combining experimental and experiential evidence (Sackett et al., 1996). The original definition of EBM has been refined a number of times in an attempt at clarity. Some definitions are illustrated in Table 2.3 below.

Table 2.3: Examples of EBM definitions

EBM is:
1. "….a method of problem solving which involves identifying the clinical problem, searching the literature, evaluating the research evidence, and deciding on the intervention" (White, 1997:175).
2. "….the integration of our clinical expertise with the best available external evidence and patients' values by translating our need for information into an answerable question and then tracking down the best information with which to answer that question" (Sackett & Straus, 1998:1336).
3. "….identifying more clearly those health care interventions that can be shown to be effective on scientific grounds" (Elkan et al., 2000:1316).
4. "….a continually evolving heuristic structure for optimizing clinical practice" (Djulbegovich et al., 2009:158).
5. "….a useful metaphor for a vision of critically informed individualized care, freed from the constraints of blind obeisance to tradition" (Wyer & Silva, 2009:896).

This multiplicity of definitions has led some to claim that the term "EBM" is meaningless (for example see: French, 2002; Jenicek, 2006; Loughlin, 2009) and for others to suggest that "EBM" should be replaced with the term "research evidence" (Duggal & Menkes, 2011).

The concept was claimed as a new paradigm (Guyatt, 1991), and it was even given the accolade by the New York Times as one of the most influential ideas of the year (Hitt, 2001). In the past few decades, the concept has become embedded in clinical teaching and practice where it is now commonly known as "evidence-based healthcare" although this thesis will continue to refer to "evidence-based medicine" since "EBM" is an accepted and widely-used acronym. Multiple articles, books and tools have been published as guides to the concept and how to "do" EBM is now a standard part of medical education (Guyatt & Rennie, 1993; Montori & Guyatt, 2008; Maggio et al., 2013).

Principles of EBM

Based on a wider discourse around EBM, three recurring principles can be discerned. One principle is that decisions are justified by how much trust can be placed in the evidence. Djulbegovic & Guyatt (2017:416) put it thus: "central to the epistemology of EBM is that what is justifiable or reasonable to believe depends on the trustworthiness of the evidence, and the extent to which we believe that evidence is determined by credible processes". The question of *what* evidence can be trusted continues to be disputed: there are debates around the narrow EBM definitions applied to evidence (discussed in the next section on hierarchies of evidence), the undervaluing of basic science and experience, the applicability of population research to individuals and the effects of multi-morbidity on outcomes (Lambert, 2006; Hughes et al., 2013; Greenhalgh et al., 2014; Guthrie et al., 2017).

Linked to the pursuit of trustworthy evidence, a second underpinning principle of EBM is that summaries of the best available evidence should support clinical decision making. This is in preference to selective studies being used to support particular claims or directions of treatment (Djulbegovich et al., 2009; Djulbegovic & Guyatt, 2017).

Endorsing the idea of cumulative science, the possibly detrimental consequences of selective evidence can be avoided (Chalmers, 2005; 2007).

However, evidence alone does not determine clinical management and the third principle of EBM is that decisions should be made by clinicians in the context of patient preferences and values (Guyatt et al., 2000; Haynes et al., 2002; McCartney et al., 2016). This applies to individual patient preferences for treatments as well as the processes by which patients consider options and make decisions (Montori & Guyatt, 2008). This principle has gained momentum over the past twenty years as medicine has turned towards more patient-centred care. However, some have pointed out that placing patients at the centre of healthcare and incorporating their values and preferences in clinical decision-making is not often borne out in practice (Da Cruz, 2002; Silva & Wyer, 2009; Miles & Mezzich, 2011; Greenhalgh et al., 2014; Miles et al., 2015).

In summary, the set of principles on which EBM is based looks to ensure that clinical decisions are made with high quality evidence of treatment effectiveness for individual patient benefit. Hierarchies of evidence, according to EBM principles and definitions, have been constructed and these are now considered in the next section.

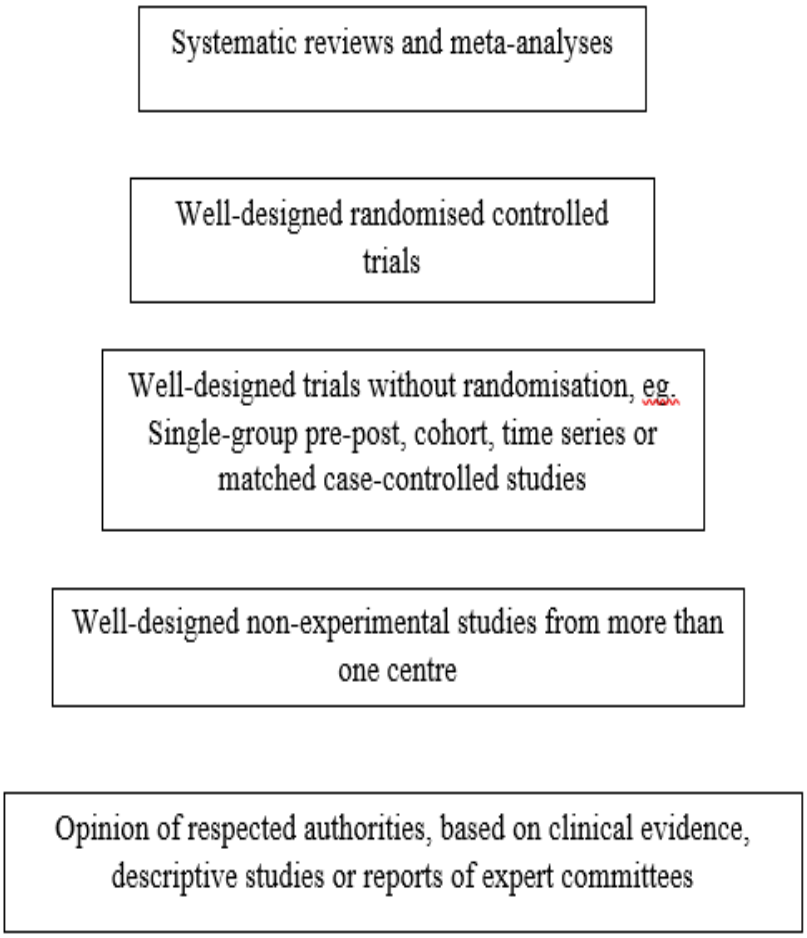
Hierarchies and levels of evidence

In keeping with the first principle of EBM, is the premise that all research evidence is not equal and discerning the relative quality of research studies will aid clinicians in their search for, and application of, the "best" available evidence to their practice. The initial hierarchies of evidence of the effectiveness of treatments provided a classification of evidence according to study design and propensity to introduce bias. (Guyatt et al., 1995; Djulbegovic & Guyatt, 2017).

The hierarchies were first promoted by the Canadian Task Force on the Periodic Health Examination (1979), and then, in many variations, by many others since (Cook, 1992, 1995; Guyatt et al., 1995; Petticrew & Roberts, 2003; Bagshaw & Bellomo, 2008). Two examples of hierarchies are depicted below in Figures 2.1 and 2.2 - the original Canadian

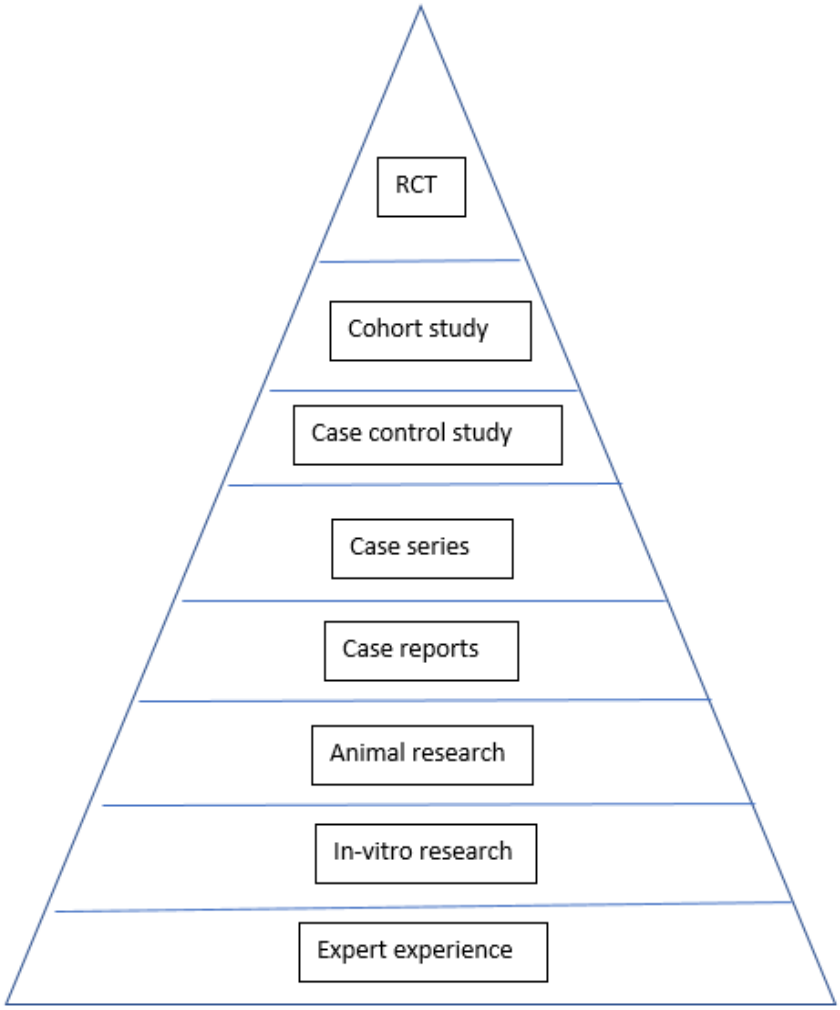
Task Force hierarchy (Figure 2.1) and a later version (Figure 2.2), adapted from Guyatt and colleagues (1995).

Figure 2.1: Canadian Task Force hierarchy of evidence



Source: Canadian Task Force Hierarchy of Evidence, 1979

Fig 2.2: Hierarchy of evidence based on study design



Source: Adapted from Guyatt et al., 1995

Most versions of hierarchies are based on study design, with the "gold-standard" randomised controlled trials (RCTs) at the apex. In some versions, systematic reviews and meta-analyses of RCTs appear at the apex. Further down in the hierarchy are other study designs, such as cohort and case studies, with basic sciences research and expert opinion at the base of the pyramidal structure. In essence, if the evidence being considered is lower down in the hierarchy, the bias introduced is said to increase and thus weaken the justification for using this evidence to influence practice (Greenhalgh et al., 2014; Djulbegovic & Guyatt, 2017).

That these are hierarchies of "evidence" has been refuted: Bluhm (2005) has argued that this is a misnomer. Rather, they should be named a "hierarchies of methodologies" with treatment decisions being based on study methodology, not on the actual efficacy results. While some label systematic reviews and meta-analyses as a study design (Haidich, 2010), others are in accord with Bluhm's (2015) view that having systematic reviews/meta-analyses in the hierarchy is incongruous (Paul & Leibovici, 2014). Further criticism of the inclusion of systematic reviews and meta-analyses in hierarchies is that the effect of context is largely ignored (Axford & Pawson, 2014; Paul & Leibovici, 2014). In addition, synthesising evidence in this way, using only the highest quality studies, can result in the loss of valuable evidence (Feinstein & Horwitz, 1997; Konnerup and Kongsted, 2012). That being said, these methods for aggregating data result in a broad view of the available research according to agreed standards (Chalmers, 1993; Boaz et al., 2002; Higgins & Green, 2011).

Proponents for EBM hierarchies are strong in their advocacy of RCTs as the "gold standard" of study designs (La Caze et al., 2012; Campbell Collaboration, 2017; Cochrane Collaboration, 2017), with some going so far as to suggest that even reading study results from a non-randomised study is not worthwhile (Straus et al., 2005). However, there are objections to the privileging of RCTs, especially for interventions where study sample sizes are small and where there is questionable application to patients outside the closely-controlled study population (Worrall, 2002). Others highlight that RCTs may be less relevant where the intervention is in a population with complicated medical problems or where a particular local context means the evidence is more, or less, applicable (Davies & Nutley, 2000; Shaw et al., 2014).

The detailed statistical arguments for, or against, randomisation and concerns about the accuracy of estimates are not a concern of this thesis so will not be reviewed further. However, it is pertinent to point out that debates about bias within RCTs and the value of RCTs continue, with the subject of RCT superiority remaining contentious (Worrall, 2002, 2007a, 2007b; Rawlins, 2008; La Caze, 2009, 2012; Axford & Pawson, 2014; Paul & Leibovici, 2014).

There have been a number of other criticisms of basing hierarchies on study design. The hierarchies undervalue the study designs further down the pyramid, especially observational studies which investigate interventional effects (Rawlins, 2008; Konnerup and Kongsted, 2012; La Caze et al., 2012). There is little space for qualitative studies, an important omission when an intervention is directed towards a social outcome and where complexity exists (Boaz & Ashby, 2003; Denzin, 2009a). There has been a more recent impetus to include qualitative studies in systematic reviews (Noyes et al., 2010; Shaw et al., 2014) but the balance is still heavily in favour of quantitative research (Pearson, 2004; Pope et al., 2006; Noyes et al., 2010). Hierarchies based on study design also tend to avoid consideration of how studies have been implemented (Stegenga, 2014) or whether interventions should be adopted (Bagshaw & Bellomo, 2008). Interpretation of hierarchies of evidence should be about what evidence is provided by a specific study rather than by the study design *per se* (Guyatt & Rennie, 2008).

Many current evidence hierarchies have mirrored the initial hierarchy promoted by Canadian Task Force on the Periodic Health Examination (1979), for example, the US Agency for Health Care Policy and Research Levels of Evidence (US AHCPR, 1992), Scottish Intercollegiate Guidelines Network Levels of Evidence (Harbour & Miller, 2001) and, more recently, the Oxford Centre for EBM (OCEBM Levels of Evidence Working Group, 2011) levels of evidence. The latter relates levels of evidence to specific clinical practice questions. An example is given in Table 2.4.

Table 2.4: OCEBM levels of evidence

OCEBM Levels of Evidence when the question is 'Does this intervention help?'
Level 1: Systematic review of randomised trials or *n*-of-1 trials
Level 2: Randomised trial or observational study with dramatic effect
Level 3: Non-randomised controlled cohort/follow-up study
Level 4: Case-series, case-control studies, or historically-controlled studies
Level 5: Mechanism-based reasoning

Source: Abstracted from OCEBM Levels of Evidence Working Group, 2011

The details of the levels of evidence in Table 2.4 illustrate that current hierarchies are similar to earlier hierarchies with systematic reviews and RCTs higher up the hierarchy than cohort or case studies. However, the OCEBM Levels of Evidence represent a refinement in that they are presented as a matrix relating to specific clinical questions and they reflect clinical decision making. As well as the question concerning how helpful an intervention is, there are also six other questions for which levels of evidence (based on study design) are set out (see Table 2.5 below). Such evidence matrices can help to tie evidence to specific clinical questions, but they still primarily use study design as the predominant ranking parameter.

Table 2.5: OCEBM clinical questions

1. Does this intervention help?
2. How common is the problem?
3. Is this diagnostic or monitoring test accurate?
4. What will happen if we do not add a therapy?
5. What are the common (treatment) harms?
6. What are the rare (treatment) harms?
7. Is this early detection test worthwhile?

Source: Abstracted from OCEBM Levels of Evidence Working Group, 2011

The limitations and concerns about earlier hierarchies of evidence led to a new approach for grading the quality of evidence: this is the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for evaluation of healthcare interventions, published first in 2004 (Atkins et al., 2004). GRADE is a framework for determining the quality of a body of evidence and the strength of recommendations. It represents an evolution of EBM by highlighting the importance of specifying the question to be answered, the identification of outcomes important to the patient, and acknowledgement of the importance of expert opinion and patient preferences and values (Montori & Guyatt, 2008, Djulbegovic & Guyatt, 2017). It addresses elements related to precision,

consistency (variability of results between studies), applicability, magnitude of effect, publication bias, and dose-response gradients as well as study design. GRADE reduces the undue reliance on RCTs and, in situations where RCTs are inappropriate, such as in cataract surgery (a RCT assessing the implantation of a new ocular lens versus no lens would not be ethical), permits the inclusion of observational studies as high-quality. The improvements of the new approach have led to widespread adoption of the GRADE framework. The GRADE Working Group have stated that, currently, over 100 organisations from 19 countries have endorsed, or are using, GRADE (GRADE Working Group, 2017). This includes guideline bodies such as NICE (NICE, 2014, updated 2017) and the Cochrane Collaboration (Higgins & Green, 2011), a leading systematic review organisation.

Hierarchies of evidence continue to evolve but a recent, detailed examination of their use concluded that, while influential in appraising evidence for clinical decision making, there is wide variation in the interpretation of what they are and how they should be utilised (Blunt, 2015). Similarly, there is variation in how EBM as a whole is perceived and the next section details the main arguments and counterarguments.

Critique of the evidence-based medicine concept

Table 2.6 below summarises the perceived advantages and disadvantages of the EBM framework and provides the basis for the discussion that follows.

Table 2.6: Benefits and criticisms of EBM

Benefits	Limitations and misperceptions
Distils huge volumes of evidence into manageable pieces, eg guidelines	Narrow definitions of evidence in use
Sets standards for evidence	Shortage of coherent, replicable scientific research
Allows robust causal claims to be transformed into effective treatments	Biases in evidence have been identified (such as narrow study populations, data omissions, publication bias)
Encourages development of evidence appraisal skills and critical thinking in clinicians	Difficult to apply evidence to the care of individuals
Endorses clinical expertise and judgement in patient care	Promotes an algorithmic approach to medicine
Allows for patient values and involvement in decision making and care	Incorporation of patient values and preferences is minimal
	Often viewed as a cost cutting tool

Main sources: Greenhalgh et al., 2014; Kelly et al., 2015; Djulbegovich & Guyatt, 2017; Horwitz & Singer, 2017.

One criticism of EBM, well-documented in the literature and mentioned previously in this thesis, concerns the narrow definition of evidence employed. This can lead to studies with small sample sizes which have little power to detect meaningful clinical differences between treatments (Duggal et al., 2011). Furthermore, context is largely ignored and evidence from lower levels of the evidence hierarchy is sidelined (Denzin, 2009a; Konnerup & Kongsted, 2012; Shaw et al., 2014). The narrowness of the study populations in RCTs, the gold standards of evidence in the EBM framework, is a particular concern (Worrall, 2002, 2007a, 2007b; Greenhalgh, 2012; Axford & Pawson, 2014). This is because the exclusion of many study participants, for example, due to age, gender and pre-existing conditions, means that the results of such studies do not mirror real-world populations of patients. As Ioannidis (2017:11) puts it: [medical research] "is interested in averages and ignores the wide variability in individual risks and responsiveness". Thus,

the studies are not applicable to the majority of patients outside of the study boundaries (Heneghan et al., 2017). However, advocates of RCTs point out that the randomisation methodology employed avoids confounding factors, such as allocation and selection bias, affecting the results and means a more robust causal claim can be made (La Caze et al., 2012). Further support for RCTs lies in their role supporting marketing applications for drugs. In these studies, one drug is usually compared with another in order that superiority claims may be made. RCTs are beneficial in this context as they account for confounding variables and it is easier to discern true superiority if these are controlled (Stang, 2011). As such, they are key to marketing authorisations for many drugs that have transformed or improved patients' lives (Horwitz & Singer, 2017). Highly active anti-retroviral treatment for human immunodeficiency virus disease is an example of the positive effects of using RCTs for licensing purposes.

Most evidence within the practice of EBM, especially for drug interventions, is provided by the undertaking of comparative clinical trials. Running clinical trials is an expensive business and many of the larger RCTs are now funded by the pharmaceutical industry (Perlis et al., 2005; Every-Palmer & Howick, 2014). This biases results according to the particular interests of the companies who are perceived as serving their own agendas. A recent study found that 96.5% of comparative trials with non-inferiority designs sponsored by the pharmaceutical industry give results favouring the sponsor (Flacco et al., 2015). This leads to consideration of conflicts of interest in producing research evidence, an issue that has been concerning the medical profession for two decades or more. (Neuman et al., 2011; Eccles et al., 2012). The areas of concern have been the use of industry ghost writers for publications, relationships of clinicians with the pharmaceutical industry and the payment of large sums of money to opinion leaders to "advise" companies on their products and clinical programmes (Moynihan, 2008; Ross et al., 2008; Okike et al., 2009; Chimonas et al., 2011). There is also the issue of publication bias in evidence, highlighted previously with respect to guidelines. Not only are commercially-funded studies ghost-written for study investigators but, even where studies are non-industry sponsored, positive results are more likely to be published than negative results thus skewing any research syntheses carried out (Song et al., 2010; Goldacre, 2016).

One positive aspect of the EBM framework is that standards for the quality of research evidence have been developed, for example, methods of randomisation in clinical studies and techniques and tools for systematic review and meta-analyses. The initiatives to develop these standards have contributed to an improvement in the quality of research and permitted challenge to previously unsubstantiated therapeutic claims (Upshur, 2005). The design, conduct and reporting of research studies have been improved and this has reduced the previously variable nature of research results, provided more of an empirical grounding for treatment decisions and, thus, made care more consistent (Djulbegovic & Guyatt, 2017).

The standards of EBM have also led to the development of skills in gathering and appraising evidence on which to base treatment choices (Straus et al., 2005). There is now a vast amount of information that health professionals may consult including learned articles, health-resource databases, structured templates and internet-based tools (Simera et al., 2010). The EBM framework has enabled the amalgamation and presentation of this data, for example, as guidelines, systematic reviews and meta-analyses. This has facilitated the search for evidence and saves time for clinical practitioners, although, now too, the amalgamated evidence is becoming unmanageable (Greenhalgh et al., 2014). Richardson (2017) has suggested that the broad embrace of EBM and the vast amounts of information available means that it is now difficult to defend making clinical decisions that are not, at least in part, based on current research evidence.

A concern about the EBM concept is what has been termed an over emphasis on "cookbook" medicine meaning a reliance on formulaic rules (Timmermans & Mauck, 2005). This, then, can give rise to diminishing use of clinical judgement and expertise and, as long as two decades ago, it was suggested that the interpretive element of understanding evidence is lost in EBM practice (Upshur, 1999). Despite the original intent of EBM to involve a combination of the best research evidence with experiential expertise, recent authors continue to echo this observation (Greenhalgh et al., 2014; Ioannidis, 2016; Djulbegovic & Guyatt, 2017).

EBM, in theory, does incorporate patient values and preferences (Post & Guyatt, 2014; Kelly et al., 2015), despite some views to the contrary. Linked with the perceived decline in clinical expertise, which mirrors views of the death of expertise in society in general (Nichols, 2017), is the view that EBM has turned medicine away from patient-centred care (Greenhalgh et al., 2014; Miles & Mezzich, 2011; Miles et al., 2015). Greenhalgh and colleagues (2015) discuss what they see as six "biases" against patients and carers in EBM. These are the low status afforded to patient experience in hierarchies of evidence, the lack of patient input to research, a tendency to view the use of decision tools as equating to patient-centred consulting, an emphasis on the clinical consultation, a focus on patients who seek out care (versus those who do not, or cannot), and suppression of the patient voice. They conclude that to reverse the trend away from patient-centred care, the practice of EBM should include more patient involvement in research, an increased acknowledgement and use of patient anecdote and steps to balance the power dynamics in consultations which tend to muzzle patient opinions.

Another view is that the EBM framework and patient-centred care have developed in parallel without exchange and interaction (Miles & Mezzich, 2011). However, Post and Guyatt (2014), while agreeing that more dialogue between the two movements would be beneficial, suggest that Miles and Mezzich (2011) have ignored the principles of EBM with regard to inclusion of patient values and preferences. Furthermore, Post and Guyatt (2014) suggest that EBM is a good starting point for encouraging more patient-centred care. From Horwitz and Singer (2017) is a suggestion of a possible way forward that brings patient-centred care closer to EBM practices. They recognise the success of EBM in building evidence bases of population research but, like other authors discussed above, they see EBM as failing individual patients. They propose what they term "medicine-based evidence", where individual profiles of patients are built using various kinds of evidence: all study types (not just RCTs) and other socio-behavioural information. Referring to a database of similar patients and how they reacted to various treatment options will allow a physician to tailor clinical management to patients more individually.

Indeed, what Greenhalgh and colleagues (2014) describe as "real" evidence-based medicine puts patients at the heart of treatment decisions and encourages more

individualised medical practice. This is not at odds with the original intent of Sackett and colleagues (1992), although perhaps EBM's focus has drifted away from the humanistic dimension of medicine in the rush to characterise and package research evidence (Miles et al., 2015). Greenhalgh and colleagues (2014) suggest more could be done to deliver "real" EBM, such as improving clinical trial reporting requirements, revamping medical training to sharpen clinical judgement and shared decision-making skills and expanding the research agenda to include more experiential and behavioural studies.

Knowledge in medicine incorporates more than just empirical data and the next section characterises some of the other forms of knowledge and modes of knowledge production that play into medical practice.

Other forms of knowledge in medicine

What constitutes knowledge is complex and a lack of consensus remains such that attempts to create universally agreed abstract classifications of knowledge continue to be unsuccessful (Tsoukas & Vladirimou, 2001; Swan et al., 2016). Differing and contested ontological and epistemological assumptions underlie this confused landscape and there is a profusion of different perspectives on what knowledge is and how it is used (Orr et al., 2016). Knowledge has been conceptualised in many different ways using different metaphors and models although many of these can be aligned with Aristotelian forms: *episteme* or formal knowledge, *techne* or skills/craft-based knowledge and *phronesis* or practical wisdom (Greenhalgh & Weiringa, 2011). There are also different conceptualisations of "ways of knowing". For example, Brechin and Sidell (2000) consider ways of knowing in three domains: empirical, derived from objective measurement, which aligns with Aristotelian episteme, theoretical knowledge achieved by conceptual reasoning, and experiential knowledge or craft/practice-based knowledge. Ryle (1949) separated knowing *that* (a cognitive form of knowing involving accumulating relevant facts) from knowing *how* (an embodied form of knowing suggesting the acquisition of skills by doing) and inseparable from the "knower". Thus, knowledge and ways of knowing are understood and used differently in different, or even in the same, contexts. Knowledge is a "tricky concept" (Tsoukas & Vladimirou, 2001:975).

Much medical knowledge is based on scientific research which leads some to the supposition that such knowledge is invariant, universal and replicable (Montgomery, 2006). Yet replicable research, as outlined by the evidence-based medicine framework, is only one part of knowledge in healthcare (Malterud, 2001; Gabbay & le May, 2011; Ferlie et al., 2012a). Formal scientific research does provide much of the information required to assess an individual patient's signs and symptoms and prescribe a treatment, but as Malterud (1995:183) reflects: this "fails to represent medical knowledge adequately". A considerable part of medical knowledge-in-practice is contingent interpretation based on human interaction, judgement and experience (Malterud, 2001; 2006).

Tacit and experiential knowledge

Described as "we know more than we can tell" (Polanyi, 1966), or "know-how" (Ryle, 1949), tacit knowledge is a dimension of knowing that is non-codified (or non-propositional), is acquired by experience and is difficult to communicate. However, some later authors believe that tacit knowledge, can, in part, be articulated (Nonaka & Toyama, 2002). Further, in the creation of knowledge, there is an interplay between explicit and tacit knowledge where social interaction plays a critical role (Nonaka & Takeuchi, 1995; Nonaka & Toyama, 2003). So tacit knowledge is not separate from explicit knowledge; rather it is more of a continuum (Jasimuddin et al., 2005) and can be complementary (Nonaka & Takeuchi, 1995; Smith et al., 2003). Different terminology, reflecting its adoption by different disciplines, has been applied to tacit knowledge: skills, professional craft knowledge, intuition, procedural knowledge, implicit knowledge, experiential knowledge, to name some key terms (Ambrosini & Bowman, 2001). In many disciplines, the notion of tacit knowledge has been insightful since it addresses aspects of learning previously ignored (Duguid, 2005).

In healthcare, a number of studies have explored the use of tacit knowledge. Kothari and colleagues (2011, 2012) undertook a qualitative study in Canada with the aim of obtaining an understanding of how tacit knowledge is used to inform the planning of public health programmes. Designed as a narrative inquiry, interviews and focus groups were carried out in four public health centres using the Ambrosini and Bowman (2001) framework for

eliciting the use of tacit knowledge. Semi-structured interviews were used to elicit individuals' stories of how planning teams used different types of knowledge. The results demonstrated different ways in which tacit knowledge was utilised. For example, knowledge based on previous experience was used in bringing together the planning team and opportunities for initiatives were found by intuition or previous knowledge of the targeted communities. They concluded that tacit knowledge was embedded in many stages of the public health planning process (Kothari et al., 2011, 2012).

The sources of practical knowledge used in nursing care was a secondary theme of two ethnographic case studies examining the research utilisation behaviours of nurses in child and adult care units within four hospitals in Alberta and Ontario in Canada (Estabrooks et al., 2005). Drawing on data from interviews and observation of nursing care, the authors sought to identify the sources of the nurses' practical knowledge. These, they discovered, could be categorised in four ways: documentary sources, experiential knowledge, social interactions and *a priori* knowledge. The results showed that the categories of practical knowledge of most importance to the nurses were social interactions and experiential knowledge. This suggested that the weight of emphasis on research knowledge in the EBM framework is disproportionate (Estabrooks et al., 2005).

More recent work has explored how these sources of knowledge are used in practice. Higgins and colleagues (2011) explored the use of knowledge sources in the implementation of public health initiatives in British Columbia. Twenty-one interviews were conducted with public health staff with the aim of discovering how knowledge is used in decision making. Results revealed that the staff considered experiential evidence and community-process knowledge to be highly significant to their work and of more use than knowledge gained from research documentary sources. This significance of tacit knowledge was mirrored in another recent study exploring how emergency department health professionals use different types of knowledge to make decisions on commencing, continuing or stopping cardiac resuscitation (Brummell et al., 2016). This ethnographic study involved participant observation of resuscitation in two emergency departments in the UK. In-depth interviews with doctors, nurses and paramedics who had taken part followed the resuscitation attempts. The findings showed that staff constructed cardiac

arrest categories using tacit knowledge and experience. These categories aided decision making in combination with technical monitoring data and clinical observation. The results of these studies, highlighted above, suggest that tacit knowledge plays a significant role in many different healthcare situations and that both tacit and explicit knowledge are integral to clinical practice.

Thus, different types of knowledge have to be integrated, taking account of the context of the specific patient. EBM, with its tools, rules and frameworks does place a certain dependence on formal knowledge but over-reliance on scientific knowledge is not sufficient (Greenhalgh, 2010). Equally, relying only on tacit knowledge, experience and intuition has its dangers since these can be built on ineffective practices and customs (Nutley et al., 2003).

The mindlines concept

The clinical encounter is a complex, interpretive and interactive process involving factors such as values, communication and experiences (Davies et al., 2008; Greenhalgh & Weiringa, 2011; Davies et al., 2015) How, in an individual medical mind, are different knowledge strands brought to the fore and combined in order to make judgements and decisions, whilst still accounting for other conflicting goals and responsibilities? How is this messy terrain navigated, ordered and updated? The concept of "mindlines" was proffered by Gabbay and le May (2004, 2011) to account for a personalised repository of flexible knowledge strands (both explicit and tacit knowledge) from education, experience, interaction with others as well as the current practice environment, which intertwine to act as an internalised guideline for practice in context.

In 2004, Gabbay and le May published their ethnographic work with a large general practice in the UK. Over a number of years, they followed GPs, nurse practitioners and other professionals attached to the practice, as they went about their daily work. They intended to discover and understand how health professionals obtained and used the different types of knowledge. They observed clinic visits, home visits, nursing clinics, practice meetings as well as observing generally how practice life was conducted. They also supplemented their observations with interviews to validate their observations and

reviewed relevant documents. What they observed about how clinicians gained, used and revised knowledge for practice, was conceptualised as “clinical mindlines”.

Mindlines in essence are an individual clinician’s “internalised guidelines”. These grow from formal knowledge gained from training, research, clinical guidelines and the like, inextricably mingled with varied experiential knowledge and cultural and behavioural norms (Gabbay & le May, 2011). However, clinicians, when asked, find it hard to explain from where their decisions arise, reflecting previous work on tacit knowledge in healthcare (Greenhalgh, 2002; Rycroft-Malone et al., 2004; Higgins et al., 2011; Kothari et al., 2011, 2012; Brummell et al., 2016). So, it seems mindlines are not easily explained entities nor easily transferable pieces of evidence. Rather, they are, it is suggested: “a shorthand reminder of the complexity of social and psychological processes that one is trying to alter when implementing research findings” (Gabbay & le May, 2011:195).

How mindlines grow and are cultivated depends heavily on social interaction with others: patients, opinion leaders, fellow clinicians, pharmaceutical personnel. Hence, they have been described as taking a social constructionist approach to knowledge (Gabbay & le May, 2011; Weiringa & Greenhalgh, 2015). This does not seem at odds with illness being cast partly as a social construction (Wright & Treacher, 1982; Conrad & Barker, 2010) and that the definition and treatment of illnesses are influenced by social, ideological and other external considerations (Nettleton, 2006; Moreira et al., 2009). The many actors involved in “illness”: patients, doctors, researchers, regulators, health service managers, policy makers, each have a different socially constructed interpretation which gives different meaning to any particular illness (Mol, 2002). This guides what they do, how they act and how illness is defined and managed.

Weiringa and Greenhalgh (2015) conducted a systematic review of the work on mindlines in the ten years from 2004-2014. The review suggested that the mindline perspective on knowledge in clinical environments was essentially unexplored empirically. Furthermore, opinions of how the different types of knowledge in healthcare were obtained, combined and used, remained wedded to a rationalistic notion of knowledge. They proposed that, to widen the understanding of what counts as evidence and how different types of

knowledge combine, a new research agenda is needed. Environments, such as guideline development, heavily biased towards the concepts of evidence-based medicine, were proffered as possible fruitful areas within which to research how mindlines emerge and are negotiated (Weiringa & Greenhalgh, 2015).

In summary, there are different "knowledges" and ways of knowing that play into the clinical environment. Tacit knowledge gained from experience as well as scientific research knowledge is brought to a clinical encounter. Equally important to acknowledge are patient values and experiences in making judgements about the best treatments for individual patients. Having reviewed in Part 1, the clinical guidelines literature and forms of knowledge in the clinical arena, many of which are integral to guidelines, Part 2 now moves to discuss specific influences on the guideline development process.

2.3 Part 2: Influences on the guideline process

This part of the literature review considers influences on the guideline development process in two ways. Firstly, within-group influences are discussed. This includes the composition of guideline groups by profession and role, group functioning factors and influences on group dynamics, conflict in groups such as these and how group facilitation leads to consensus decision making. Following this, the review concentrates on factors external to the guideline group that have the potential to impact how the group functions and completes its task. The networks literature is drawn upon since guideline groups act within a wider network of players and the networks literature offers a number of valuable insights into how a group operates within such a network.

2.3.1 Within-group influences

Group composition

One influence on group functioning in guideline development is the composition of the guideline group. The participants generally include clinical specialists and generalists, allied health professionals, technical and methodology specialists and there is, usually, lay representation. Some have indicated that there is poor representation by

epidemiologists and economists which, given the emphasis on evaluating cost-effectiveness of treatments, is a gap that should be rectified (Sniderman & Furberg, 2009). Evidence suggests that the group composition has an impact on the eventual content of the guideline and is, therefore, important to take into account (Hutchings & Raine, 2006; Eccles et al., 2012). Hutchings and Raine (2006) undertook a systematic review (22 studies) of the factors influencing the impact of professions and therapeutic speciality on judgement in guideline development consensus scenarios. The study demonstrated that individuals who routinely performed a certain procedure in their clinical practice were more likely to endorse that procedure.

Their work also highlighted five studies comparing single speciality groups with multi-disciplinary groups. In every study, the multi-disciplinary groups made more conservative judgements indicating a modifying effect of fellow participants hailing from different specialities. Despite one of the IOM (2011) standards for "trustworthiness" of guidelines being multi-disciplinary panel composition, many guideline groups remain heavily biased towards uni-speciality clinicians even though it is suggested that involvement of more than one speciality would be beneficial (Leape et al., 1992; Guy & Wardlaw, 2002; Shaneyfelt, 2012).

In healthcare, some have questioned whether multi-disciplinary teams are advantageous to collaboration (Powell & Davies, 2012; Liberati et al., 2016). Despite a view that such representation can lead to large groups which may be impractical if all are to contribute to decision making (Kunz et al., 2012), there now appears to be consensus that, for guidelines, multi-disciplinary representation from key stakeholders balances any individual biases (Fretheim et al., 2006a; Eccles et al., 2012; Kunz et al., 2012).

The last 20 years has seen an increasing interest in closing the gap between evidence producers and service users by engaging patients and the public in healthcare decisions (Wynne, 2006; Evans, 2014; Boaz et al., 2016). The advantages of such engagement are seen as improvements in scientific accountability, more relevancy of research to service users, better use of the experiences and expertise of patients, and improvements in healthcare outcomes (Oliver et al., 2004). This shift in intent and in the practice of patient

and public involvement has also been seen in the development and implementation of clinical guidelines. In line with Rowe and Frewer's (2005) typology of the mechanisms of public involvement, engagement in guidelines is by direct participation (as guideline group participants), consultation (advising on specific issues, usually via surveys) and communication (consumer-focused guideline versions are produced). The effect of such involvement is a closing of the gap between evidence and patient values and preferences (Schünemann et al., 2006). There has been, though, little guidance as to what a public and patient involvement programme with respect to clinical guidelines should look like.

Légaré and colleagues (2011) conducted a synthesis of over 2,000 articles and reports concerning patient and public involvement in clinical guidelines. The review indicates that involvement is most often by direct participation in guideline development groups or as consultants on specific issues. Furthermore, the findings indicate that patients involved found it difficult to understand often very technical evidence and to impart their views and experiences in the face of this. A need for specific training in evidence appraisal and other technical aspects was highlighted. There was also a concern that the small number of lay people on guideline groups could not appropriately represent large sections of the population. However, feedback from participants themselves indicated a positive experience. Légaré and colleagues (2011) concluded that public and patient involvement took many forms in clinical guideline development and that its impact was that the guidelines produced were relevant and understandable to patients but that any impact on health outcomes was not clear.

The involvement of patients as guideline stakeholders is still inconsistent across guideline development agencies but a number of developers have instituted systems that are inclusive of such representation (Legido-Quigley et al., 2012). For example, NICE has adopted a comprehensive patient and public involvement programme. This mandates that patients, patient advocates or other interested lay parties should always be included on guideline development groups. NICE ensures that patients are included as stakeholders during consultation periods and have set up a specific internal Patient Involvement Team to manage all public participation in their guidelines. NICE also publishes a version of each guideline for public information. Furthermore, to counter issues such as difficulty

understanding technical evidence, NICE supplies and encourages patient representatives on guideline groups to attend technical/scientific training. NICE are also clear that patients are not expected to represent a large population but are valued for their individual experiences and expertise in the relevant disease topic (NICE, 2014, updated 2017).

Roles played

The literature on groups/teams and group/team roles is broad and diverse. As such, a comprehensive review of all that literature would be beyond the scope of this research. Instead, the focus is on a number of models or typologies that may offer insight into group roles in the guideline environment.

Group roles appear ubiquitously in the literature in various guises: from task groups to group behaviours to group diversity and taxonomies of group roles. For example, Belbin (1993) identified group roles at work using executive management groups. The roles were "asking", "informing", "proposing", "opposing", "delegating", "commenting" and "building". This typology is now commonly used to design or assess groups, balanced by role, in organisations (Pritchard & Stanton, 1999; Aritzeta et al., 2007; Blenkinsop & Maddison, 2007; Meslec & Curşeu, 2015). That group roles appear in many guises in the literature is not to be dismissive of the different typologies since roles, and how they are played, affect group functioning and group effectiveness (Salas et al. 2015; Driskell et al. 2017). More than 150 separate roles have been reported but it may be that similar roles are afforded different nomenclature (Driskell et al., 2017).

One model, recently described in the literature, is the Tracking Roles In and Across Domains (TRIAD) model. This combines existing taxonomies into a model with three behavioural dimensions: dominance (individual prominence), sociability (positive affect towards others), and task-orientation (goal facilitation) (Driskell et al., 2017). The model maps 154 roles and has derived a core set of 13 role clusters: leader, task motivator, power seeker, critic, attention seeker, negative, social, coordinator, follower, teamwork support, evaluator, problem solver and task completer. These are summarised in Table 2.7 below which also details the behavioural dimensions of each cluster. The behavioural dimensions are notated: DOM (dominance); SOC (sociability); TASK (task orientation).

Table 2.7: TRIAD clusters

Cluster	Descriptive behaviours	Behavioural Dimensions
Leader	Guiding, controlling and facilitation activities	High DOM Average SOC High TASK
Task motivator	Prods the group to action Encourages and energises the group	High DOM Average SOC Average TASK
Power seeker	Is aggressive to others Interrupts other Opposes the leader	High DOM Low SOC Average TASK
Critic	Negative and cynical Goes against group Disagrees and opposes	Average DOM Low SOC Low TASK
Attention seeker	Seeks attention without responsibility Withholds information	Average DOM Average SOC Low TASK
Negative	Nothing to contribute Gripes and complains Erodes team spirit	Low DOM Low SOC Low TASK
Social	Mediates disagreements Relieves tension with jokes Supports others	Average DOM High SOC Average TASK
Co-ordinator	Clarifies task relationships Facilitates participation of others Coordinates activities of group	Average DOM High SOC HighTASK
Follower	Effective listener Conforms to assignments Seeks cooperation	Low DOM High SOC Average TASK
Teamwork support	Implements plans Puts information together Prepares for team meetings	Low DOM Average SOC High TASK
Evaluator	Analyses Evaluates Focuses on facts and figures of task	Average DOM Low SOC High TASK
Problem solver	Orientates group to task Points out inconsistencies Clarifies	Average DOM Average SOC High TASK
Task completer	Focuses on deadlines Conscientious and orderly Adheres to responsibilities	Average DOM Average SOC High TASK

Adapted from Driskell et al., 2017

The rating of “high”, “average” or “low” for each of the behavioural dimensions was derived from a Likert-like scale of 1-7 for behavioural characteristics of the roles. These

clusters reflecting roles are useful as an insight into potentially recognisable roles in the guideline group context.

There is a differentiation between group roles and functional roles (Stempfle et al., 2001; Belbin, 2010). A functional role is dependent on the skills and knowledge of an individual who is employed in a group because of these skills. Thus, the clinical experts on guideline groups are expected to utilise their professional clinical expertise for the group task, the project manager uses coordination skills to achieve completion of the task and the chair acts as leader, controlling activities and guiding the group to complete the task. A functional role may be assigned before group work commences, such as that of clinical expert, and may influence assignment, articulated or not, of group roles.

Group roles adopted by group members in any particular setting for a certain task outcome are based on personality, preferred role and the task requirements (Stewart et al., 2005). Group roles, adopted by individuals tend to evolve and new roles emerge during the life of the group. This can be due to group interaction and communication; indeed, some authors have identified group roles as communicative acts and, therefore, have placed such interaction at the centre of group functioning (Kauffeld & Lehmann-Willenbrock, 2012; Lehmann-Willenbrock et al., 2016). Changes to the group role adopted by an individual may also be as a result of a disruptive event, such as a strategic task redirection or the replacement of one group member (Summers et al., 2012). In these cases, the consequent change in role structure of the group can be disruptive to group work (Arrow et al., 2000; Summers et al., 2012).

There are many examples of empirical work studying roles within healthcare groups. For instance, there are studies on how health professionals enact their roles in multi-disciplinary groups (Brown et al., 2000; Van Soeren et al., 2011; Kilpatrick et al., 2012), research into individual interpretation of roles in a group and how this influences collaboration with others (Freeman et al., 2000), and work highlighting the different roles played within healthcare teams in different settings (Presseau et al., 2009). Although group roles in guideline groups are defined and described in guideline process manuals and more widely in the literature (Shekelle et al., 1999; Pagliari & Grimshaw, 2002), there

is little research discussing *how* the different guideline group roles influence the process or shape collaboration within the group.

Group functioning factors

A number of theoretical frameworks support an understanding of how groups function. For example, there is the input-process-output framework (McGrath, 1964; Kozlowski & Ilgen, 2006). Here, inputs can include group composition, individual attributes and the task framework; outputs are group effectiveness, performance and individual satisfaction; processes are actions and interactions that enable groups to meet their goals (Mathieu et al., 2008; Reiter-Palmon et al., 2017). Tuckman's (1965) framework of group socialisation is also frequently used for empirical work on group functioning. The framework describes linear stages of how groups come together and how they function over time. Stages of socialisation are described as: "forming" when the group first comes together and learns about the task at hand and each other; "storming", a stage of conflict and confrontation as members settle into their roles; "norming", as the group focuses on the job in hand; "performing" when all group members' energies are directed to succeeding in their project. A further stage, "adjourning", added later (Tuckman & Jensen, 1977) describes the phase during which the group disbands.

Drawing from various parts of group process literature, four areas of particular interest to this thesis are highlighted in the sections that follow: group dynamics, the influence of group diversity on functioning, conflict in groups, and facilitation and consensus decision making.

Group dynamics

The social and organisational psychology literature as well the organisational behaviour literature provides much information relevant to the study of small group dynamics. Group dynamics are actions and processes and changes that occur within a group and between linked groups (Forsyth, 2018). As described above, Tuckman (1965) ascribed labels to groups according to their state of socialisation over time. The stages were set out in a linear fashion but it was recognised that the group can cycle back and forth depending on functioning at any particular time (Tuckman, 1965; Tuckman & Jensen,

1977). Tuckman's socialisation changes are an example of a change of the internal group dynamics. However, the fluidity of groups has increased in recent times due to the collaborative nature of organisations with many external links and an expectation that collaboration occurs across multiple boundaries (Mortensen, 2015). Thus, group constructs are subject to more rapid change now, for example due to environmental contextual forces, than in traditional groups (Cronin et al., 2011).

The fluidity of groups is, in part, due to the many levels of influence that may impact group functioning. Groups are influenced by the qualities and characteristics of individuals (micro level), qualities, such as cohesiveness, of the group itself (meso level), and by organisations and communities that surround the group (macro level) (Forsyth, 2018). Allmendinger and colleagues (1996) demonstrated the importance of multi-level considerations in assessing group dynamics in their study of why some professional orchestras outperformed others. They studied individual musicians, the orchestras as groups and the macro-level variable of location of the orchestras (US, UK, East and West Germany) which set the social and cultural context. Their work revealed complex interactions between the three levels. The skill of individual musicians influenced the quality of performance of the orchestra but the talent of the musicians was dependent on the financial health of the orchestra. This study demonstrated that a multi-level perspective should be taken into account when describing or analysing group dynamics (Allmendinger et al., 1996; Hackman, 2003). There has been criticism that previous research on groups has been on static structures rather than on dynamic interactions (McGrath et al., 2000; Cronin et al., 2011; Humphrey & Aime, 2014). This may be because dynamic interactions are difficult to study and require acknowledgement of these multi-level influences (Cronin et al., 2011).

Groups are social entities and the relationships of members with each other and with external persons or other groups, influences task success (Forsyth, 2018). The sociologist R.F. Bales (1950, 1999), after many years observing groups, concluded that there were two types of interactions in groups: those that are directed towards interpersonal relationships and those that are directed towards the task. Thus, task success is influenced by interactions of group members. Criteria for evaluating the success of work groups are

completing the task, benefit to individual group members, and maintenance of relationships (Hackman, 1987; Levi, 2015).

Some research, although limited, has indicated that group dynamics, as described in the literature, are manifest in guideline groups and, further, that psychosocial factors, such as conformity, professional and social status play an important role in how the group functions (Pagliari et al., 2001; Pagliari & Grimshaw, 2002). Pagliari and colleagues (2001) considered small group processes in guideline development, highlighting key psychosocial factors. Their work was based on a literature review and the practical experiences of the authors. In summary, they found psychosocial influences such as groupthink, compliance and obedience, conformity, persuasion, and status to be factors in how the group functioned and that professional hierarchies, inherent in multi-disciplinary groups, may distort group dynamics. They pointed out the need for leaders in these groups with skills in managing situations where these influences played out. Pagliari and colleagues (2001) reviewed key factors affecting group level processes but, there is little research on dynamic interactions *between* guideline group members and how these change over time.

Group diversity

There is much research that demonstrates that group diversity can have both a positive and negative effect on group functioning and performance (Williams & O'Reilly, 1998; Horwitz & Horwitz, 2007; van Knippenberg & Schippers, 2007; van Knippenberg & Mell, 2016; Guillaume et al., 2017). For example, Williams and O'Reilly (1998) suggest that diversity is a disruptive factor for interpersonal interactions but has a positive effect on performance since diversity is associated with higher informational resources. This links back to hierarchies in multi-disciplinary groups affecting group dynamics. Later research also reveals both positive and negative effects of diversity on performance; positive effects are aligned with informational integration processes and negative effects with social categorisation of being "in-group" or "out-group". Further, these effects interact in the diversity – performance relationship (van Knippenberg & Schippers, 2007).

Citing a wealth of primary studies on how diversity has positive and negative outcomes, Guillaume and colleagues (2017), used a different approach to assessing diversity effects. They conducted a literature review looking at variables that moderated the effects of diversity on social integration, performance and well-being of group members. One finding was that, if demographic diversity was not to negatively impact social integration, performance and well-being, diversity management strategies should be in place to mitigate against disruptive organisational change. Further, high quality leadership was key to ensuring these strategies were successful. Also, having clear objectives and roles for individuals and removing any status differences not based on merit, was agreed to be essential to facilitate social integration and well-being.

A qualitative, systematic review on group diversity was undertaken by Güver and Motschnig (2017). This included 139 studies, carried out between 1959 and 2016 and used descriptive interpretation of the studies. Factors moderating the consequences of diversity in work groups are time, task, leadership style and mind set about diversity. The perception of, or attitude to, diversity differs among group members. Being in a minority in a group is associated with more sensitivity to diversity. In line with other authors, they concluded that there is no single accepted effect of group diversity on performance, nor is there an uncomplicated relationship between diversity and group dynamics. However, the studies analysed tended to demonstrate a positive effect on decision making and problem solving and a negative effect on cohesion, integration and communication. The guideline literature suggests a multi-disciplinary group is more beneficial to guideline group performance than a uni-disciplinary group. This is because multi-disciplinary groups have the potential to consider options more widely and multiple stakeholders contribute to, and support, the guideline outcome (Lomas, 1993; Hutchings & Raine, 2006; Eccles et al., 2012). Thus, compositional diversity in guideline development is important.

Conflict in groups

Another factor affecting group functioning, conflict in groups, has also garnered much attention with the main focus on two types of conflict: task-related and relationship-related. Task conflict has been positively associated with performance while relationship

conflict is negatively associated (Simons & Peterson, 2000; Bradley et al., 2011). However, De Dreu and Weingart (2003) found a negative association for both task and relationship conflict with group performance and satisfaction of group participants.

The task/relationship conflict correlation with performance is not simple. One study demonstrates a moderating effect of relationship conflict on the task conflict-performance dynamic. There is a curvilinear correlation when relationship conflict is low, but a negative linear correlation when conflict is high. This translates into moderate task conflict having a positive effect on performance when interpersonal interactions are good, but a deleterious effect at times of high task conflict and poor interpersonal relationships (Shaw et al., 2011).

Elucidation of the type of interpersonal dynamics that give rise to, or moderate, conflict is less well documented. A number of authors have pointed to trust, both individual-level and intra-group, as being a key moderator in relationship conflict (Simons & Peterson, 2000; de Jong & Elfring, 2010; Lau et al., 2010; Salas et al., 2015). Many studies have demonstrated a beneficial effect of trust on performance in well-established versus short-term groups (Costa, 2003; Rispens et al., 2007), although the definition of established and short-term is not only related to time, but also to the intensity and duration of their interactions. Trust is important for performance since it precedes exchanges between group members that lead to decisions or task outcomes. Group exchanges involve risk, in that contributions to group discussions/tasks will, or will not, be accepted. Trust enables group members to accept the risk with an expectation of a positive outcome (Rousseau et al., 1998). Processes or actions that may mediate trust in groups include behaviours, such as deliberate attempts to cause conflict or, more positively, ensuring group members who need assistance with a task, are provided with it (de Jong & Elfring, 2010).

A number of sources suggest that guideline groups may experience conflict in their intra-group interactions and that leaders should have the necessary skills to manage such conflict (Pagliari et al., 2001; Fretheim et al., 2006b; IOM, 2011; Eccles et al., 2012). However, exactly how this conflict should be mitigated or managed and what group processes are positive or negative to the emergence of conflict, is unclear. Furthermore,

there has been limited attention in the literature to assessing how trust arises, or how it is identified, in guideline groups or to its effect on conflict within the group and on its performance.

Facilitation and consensus decision-making

The presence of a strong group facilitator is key to managing group processes in guideline development (Fretheim et al., 2006b; Kunz et al., 2012). This is so that all voices are heard and balanced before agreement is reached on the many decisions that must be made. These are decisions such as the relevance and acceptability of the evidence presented, the way the evidence can support a recommendation or the wording of the recommendation. An evidence-gathering review, performed for the World Health Organisation as background to healthcare recommendation advice, suggested that, in healthcare panels, having an identified leader and a strong facilitator is essential to support the group processes and manage conflict (Fretheim et al., 2006b). The style of that leader may impact the decision making of the group positively or negatively as it is the key role that directs the group, identifies and manages conflict and leads the group to consensus (Kunz et al., 2012). Two types of leaders emerge, those focused on the task and those focused more towards socio-emotional processes. A leader focused on either the task or the socio-emotional processes exclusively, influences the process negatively. A leader focusing in the task tends to be overly directive and does not incorporate all viewpoints. One whose focus is on social-emotional processes tends not to be directive enough so clarity and focus on the task at hand is lost (Pagliari et al., 2001).

Decision making during guideline development, whether concerning the applicability or acceptability of evidence in forming recommendations, is supported by the notion of consensus and collective decisions where all group members are heard and all agree to endorse the resultant guideline recommendations (Fretheim et al., 2006b). Consensus methods can be formal or informal. Formal methods most commonly in use in guideline development are the Delphi technique and the Nominal Group method (Murphy et al., 1998; Fretheim et al., 2006b).

The Delphi technique was developed by the RAND corporation in the 1960s to court expert opinion about new technologies (Dalkey, 1969). It has since had a variety of uses in healthcare, for example, for setting research priorities for trauma nursing (Bayley et al., 1994), and the selection of healthcare quality indicators (Boulkedid et al., 2011). The technique involves seeking views from participants, who do not have any direct interaction, by questionnaire. These views are analysed statistically to arrive at a group judgement. The Nominal Group method, developed in the 1970s by Delbecq and Van de Ven (1971), for use in committee decision making as a structure for committee interaction, is similar to the Delphi technique. Individual responses are elicited and collated and a group judgement (again using statistical methods) is agreed on. However, interaction between participants is face-to-face. The Nominal Group method has also been applied in healthcare, for example, for setting priorities for health promotion (Brown & Redman, 1995) and assessing triage and management of pregnant women in the emergency department (Harvey & Holmes, 2012).

Burgers and colleagues (2003a) surveyed 18 guideline organisations to investigate their structures and working processes. The survey included organisations from the US, Canada, Australia, New Zealand and nine European countries, including the UK, but did not include NICE. The results showed that a mixture of consensus methods is in use in guideline development and 7 of the 18 guideline organisations used formal methods to formulate guideline recommendations (ibid). Factors such as evidence availability and group functioning dictate whether informal or formal methods are used in guideline development. (Legido-Quigley et al., 2012). Formal methods tend to be used in circumstances where there is a lack of evidence or there is disagreement among group members (Burgers et al., 2003a; Hill et al., 2011).

One study compared the two formal consensus methods commonly used in guideline development, the Nominal Group method and the Delphi method (Hutchings & Raine 2006). Over 200 clinicians participated in rating four treatments for three conditions. The conditions chosen (chronic back pain, irritable bowel syndrome and chronic fatigue syndrome) are notably contentious for their origins and treatments. Using these conditions for their research, the authors said, was because guidelines based on consensus are most

useful for problems such as these. Closeness of consensus was higher in the Nominal groups than in the Delphi groups but the latter was more reliable (measuring agreement of median ratings between pairs of groups), with no difference with respect to concordance with research evidence. The authors concluded that combining these methods in a hybrid model may bring the advantages of both to guideline decision making (Hutchings & Raine, 2006).

Various consensus methods are permitted in NICE guideline development and "there are no rules that set out which approach should be used in which circumstances" (NICE, 2014, updated 2017:49). NICE does not dictate which formal method should be used in which circumstance, only that the method used is documented. However, the decision on whether formal methods are appropriate in a given scenario is made by NICE staff and not the chair of the specific guideline group (NICE, 2014, updated 2017). In a multi-actor setting, different perspectives mean that, although agreement may be reached, complete consensus is unlikely (Nutley et al., 2013). It is unclear, either from the guideline process manuals or from limited empirical literature, what happens when there is not consensus in the guideline group and how this then plays into the guideline's recommendations.

There are, then, various influences, reviewed above, that impact guideline group functioning specifically. However, the guideline group does not operate within a vacuum; it is linked to a wider set of players and organisations. For example, there are the organisations that individual group participants belong to, such as patient interest groups and charities. There are also many public bodies linked to NICE, such as the Department of Health and the National Health Service. All of these play a role in the guideline development process. As such, the guideline group and NICE are part of a broader network and the next section draws on networks literature to provide insight into the influences of such a network.

2.3.2 External influences on the guideline process

The broader network

Network forms and research into network structures and functioning have increased exponentially since the 1970s (Borgatti & Foster, 2003). This reflects a switch away from hierarchical organisational structures to more messy governance arrangements which are impacted by relational and contextual factors (Borgatti & Foster, 2003; Lecy et al., 2014). It also aligns with the evolution of commerce becoming more global and unstable, requiring flexibility in organisations and between organisations (Powell, 1990; Ebers & Oerlemans, 2016). Academics have looked to theoretical frameworks, such as "networks", in an effort to describe these complex structures and interactions (Salamon & Elliott, 2002; Lecy, et al., 2014). The vision of a network as a structure of interdependence with multiple parts, involving many subunits with a common interest but few formal ties has provided a convenient description of many of the characteristics of the different types of networks described in the literature (O'Toole, 1997; Rhodes, 2007; O'Toole, 2010). Here, the focus is on networks in healthcare, as well as networks in the public policy arena since guidelines cross this divide. This section reviews the turn to network forms in public policy and networks in healthcare. It discusses some of the challenges in using a network structure for governance and decision making and how these insights help to understand some of the external influences on the guideline process.

The turn to networks in the public sector

Polycentric governance provided an early vision of networks in the public policy arena The concept was introduced by Ostrom and colleagues (1961) in a review of the organisation of government in metropolitan areas with separate political jurisdictions. 'Polycentricity' connotes formally independent centres of decision-making that may enter into various cooperative projects or use central mechanisms to resolve issues. The centres function in a coherent manner and display predictable patterns of interactive and effective behaviour (Ostrom, et al., 1961). This was at odds with the wisdom prevailing at the time which suggested that only centralisation of public services would improve efficiency (McGinnis & Ostrom, 2012).

The concept was examined in several studies of water industry performance in 1960s (Ostrom, 1965, 1967; Weschler, 1968), and in the police service (Ostrom & Parks, 1973; Ostrom, et al., 1973; Ostrom & Whitaker, 1974). The studies specifically looked at the ways public and private players co-operated and co-ordinated efforts to manage water resources and whether economies of scale could be gained by centralising police services for urban areas. The research demonstrated that the different players managed to find productive ways of working together for efficient management of the resources despite their independent nature. Further, operating a large, centralised police department rather than smaller departments serving smaller conurbations did not result in economies of scale and an increase in efficiency (Ostrom et al., 1978; Ostrom, 2010). The polycentric concept and Ostrom's empirical research pointed to an interrelated structure in policy formation and implementation, where elements are not necessarily formally linked but in which beneficial relationships are formed. More recently, the literature has provided evidence of a positive relationship between different levels of governance and outcomes. For example, Grassmueck and Shields' (2010) study of government fragmentation and growth in the United States revealed that regions with more fragmented governments had relatively higher growth than those using a more collaborative model.

Technological advances, leading to less dependence on geographical proximity of organisational actors and increasing complexity in organisational forms, heralded a move away from centralised bureaucratic systems of governance and policy (Raab & Kenis, 2009). In such decentralised structures, central governmental control over local areas decreased with a concomitant shift in power and resources (Rhodes, 1997, 2007). Locally situated players became more important to policy outcomes than in the traditionally hierarchical structures and different forms of governance structure were required to manage the policy process and implementation (Raab & Kenis, 2009). As public policy problems became increasingly convoluted, so-called "wicked problems" (Rittel et al., 1973), requiring coordination between many organisations, network forms of multiple players with multiple dependencies and linkages became more common (O'Toole, 1997).

Policy decisions, often made in crisis situations and based on linear, mechanistic decision making, can have negative consequences on indirect, but connected, areas (Agyepong et

al., 2012). A different way of thinking, taking account of these connected parts which are elements of a dynamic system, is required to manage effective policy change (Sterman, 2006). Network-centric approaches are thought to be beneficial for promoting innovation and integration in such systems in the public policy arena (Willis et al., 2012). They offer a way of approaching complex policy problems, take account of indirect policy effects, offer structures useful for strengthening relationships between component parts, and bring stakeholders together to effect change (Adam & de Savigny, 2012; Willis et al., 2012). Some, though, have criticised network approaches as lacking in theoretical foundations, ignoring the role of power in assuming co-operation and collaboration in networks and being devoid of evaluation criteria (Klijn & Koppenjan, 2000).

The rise of the network form in practice has been paralleled by an upsurge of research into these forms. An examination by Isett and colleagues (2011) of networks scholarship in public administration, places networks research into three main areas. Policy networks research explores how networks aid public policy development and decision making. Collaborative networks research examines how government bodies and non-profit/for-profit agencies combine to deliver a public service. Governance networks research analyses the combination of public goods and services with collective policy making. Whilst research into how networks develop, what forms they take and what influences them, is valuable in understanding them, certain issues have been identified by Isett and colleagues (2011), which makes such research challenging. These include the definition of what a network is, how the term is used and the unit of analysis chosen for the research. These choices have implications for what is inferred from such research. Acknowledging these issues, the next section turns to what research has revealed about networks in the healthcare sector.

Networks in healthcare

The proliferation of network forms in healthcare has mirrored that in other public policy sectors and there is now a considerable body of work on networks in healthcare from managed service-provision networks in various disease areas to networks in health policy arenas and health professionals' knowledge networks. The growth of networks has come about because health organisations are unlikely to be able to deal, in isolation, with multi-

factorial problems and one way to improve health is by pooling innovations, strategies and resources (Woulfe et al., 2010; Provan et al., 2011).

Networks in healthcare appear to be a mixture of mandated (form decided prior to set up) and natural (emergent) networks. Mandated networks are more common in health policy scenarios and where service provision requires co-ordination of different organisations. Natural networks emerge from, for example, collaborations between healthcare groups which enhance delivery of care (Braithwaite et al., 2009). Whether mandated or natural, it is the sharing of knowledge and knowledge integration across service areas that is important in the provision of cost-effective care (Provan & Milward, 1995; Provan et al., 2011). Evidence-based guidelines support managed networks' activities by providing evidence-based knowledge for health policy or provision decisions. However, questions have arisen as to the nature of this support and what underlies it, especially due to the relationship between knowledge and power.

Drawing on Foucault, a number of authors have pointed to a power/knowledge nexus in medicine (Ferlie et al, 2012b; Ferlie & McGivern, 2013). The nexus indicates that power and knowledge are related, and are not separate entities; thus, power is a function of knowledge and knowledge is an exercise of power. The nexus ties state bodies and related operating apparatuses with professionals and their knowledge bases (Foucault, 2007; Ferlie & McGivern, 2013). An example of the potential effect of this nexus in healthcare is provided by Ceci (2004) who explored, from a Foucauldian perspective, aspects of knowledge and power in an inquiry into the deaths of children following heart surgery in 1994 in Canada. Nurses, involved in the care of the patients, were concerned about an individual surgeon's practice but their concerns were not acted upon by other professionals or people in positions of authority. The credibility of knowledge claims by certain individuals and groups is examined. Ceci (2004:1881) suggests that the "truth" (or what really happened) is distinct from "knowledge" (giving reasons for one's beliefs). This knowledge is constructed by "networks of claims" held to be collectively true. The knowledge is accepted by one community but not by others and the weak power of nurses led to their concerns being dismissed by communities in more authoritative positions.

Ceci (2004) also comments that such exchanges are possibly typical, rather than unusual, between health professionals.

Ferlie and McGivern (2013) examined macro-level governance in EBM and the power/knowledge nexus behind guidelines using a NICE case study. They utilised an Anglo-governmentality[1] perspective to explain steering mechanisms in this context. The membership of guideline groups is dominated by medical professionals. This is combined with technical scientific expertise in the NICE technical team attached to each guideline group (and other technical expertise available more widely in the NICE organisation). The authors suggest that the core of the power/knowledge nexus in evidence-based guideline formation is with the scientific networks which define the technical knowledge and methods of guideline development. The state has a steering role (setting the agenda for guideline topics, for example) but the task is enacted by the scientific networks, the professional advisors and the technical apparatuses. In effect, this is a clinical professional/managerial governing hybrid.

While health professionals form part of these governing hybrids, they are also part of specific professional networks which can impact the way decisions are made (Cohen et al., 2013). Professional networks are uni-professional and represent the views, beliefs and interests of a particular profession (Rhodes & Marsh, 1992). The characteristics of a professional network include high stability, restricted membership, vertical interdependence and a tendency to separate themselves from other networks (Rhodes, 1990). Professional networks abound in many areas but medicine is often cited as an exemplar of a professional network (Rangachari, 2009). Guideline groups consist of different types of healthcare professionals and, as such, guideline group participants are likely to belong to different professional networks which may expect them to act, and interact, in different ways. Being part of a professional network has an influence on clinical decision making by providing an advantageous social and professional context for the capture and dissemination of clinical knowledge (Cohen et al., 2013), but it may

[1] Governmentality – a term introduced by Foucault concerning the practices of government and their relationship to the way "truth" is produced in political, social or cultural contexts. Anglo – after the group of scholars who further developed the concept of governmentality

also decrease the uptake of evidence-based information (Mascia & Cicchetti, 2011). Indeed, Parchman and colleagues (2011) suggest a reason for the low implementation of guidelines is because professional networks, and interactions within these, are more influential in practice decisions than guidelines themselves.

Challenges of networks

Conceptually, hierarchical models are easy to understand: there is a leading actor, or group of actors, at the top of the hierarchy, recognised as having all the information and power, who leads other actors in the decision-making process. The hierarchical model assumes that there is uniformity within and between organisations, actors are receptive and open to superiors' suggestions, and the hierarchical structure is stable with little dynamic movement in the organisational units (de Bruijn & ten Heuvelhof, 2018). Network structures are said to have mutual dependencies, are closed to hierarchical signals and are dynamic. The horizontal nature of networks requires multiple organisational and individual interactions across boundaries to be taken into account (Brass et al., 2004; de Bruijn & ten Heuvelhof, 2018).

As with structure, decision-making processes within a network may be contrasted with that in a hierarchy. In a hierarchy there are regular, sequential steps with a clear start and end point, the decision making is consistent and predictable and usually occurs in one arena. By contrast, decision making in networks is irregular with no recognisable sequence, the actors behave unpredictably, and decisions are made in several arenas (de Bruijn & ten Heuvelhof, 2018). In networks with many actors, the chance of finding an individual to co-operate with is high and there is a higher chance of innovation as groups act collectively to solve problems. Conversely, variety may stifle decision making: the intervention of any actor has limited effect in a large network and there are reduced opportunities for bespoke interventions (de Bruijn & ten Heuvelhof, 2018). Complex interdependencies between network actors can increase opportunities for exchange or act as a motivation for co-operative behaviour. However, many interdependencies make for opacity in who is dependent on whom and this can paralyse decision making (McGuire & Agranoff, 2011).

Network management is characterised as activities or strategies that centre on organising interactions and improving collaboration between actors in complex networks (Klijn & Koppenjan, 2012; Klijn & Koppenjan, 2016). There are various enabling strategies for network management. There is the initiation of interaction processes or "games" to solve particular problems (Kickert et al., 1997); restructuring of the network to better fit the task as a structure rarely ideally fits all required tasks (Scharpf, 1978); creation of "new" content such as testing scenarios or exploring new ideas (Koppenjan & Klijn, 2004). An inference from this is that the skills required to manage such strategies are those of influencing and negotiation, as well as leadership, since the actors required to effect these tasks are not in hierarchical management lines. Thus, network management requires the actors in the network to have the ability, desire and urgency to solve interactional problems. Those facilitating network operations require the skills to manage these processes across various organisational layers in many different institutional forms.

Trust is cited as a moderator of interactional conflict in the group processes literature and has been highlighted earlier in this chapter. Trust is also seen as important in the network management literature as a mediator, reducing uncertainty and fostering sharing of information (Klijn et al., 2010). A higher level of trust within a network seems to have a positive effect on performance (Provan et al., 2009; Klijn et al., 2010). It is not, however a common characteristic of networks, rather, it is a desirable asset to have which facilitates collaboration between actors with diverse, often conflicting, concerns (Klijn & Koppenjan, 2012).

A number of future challenges are envisaged to the way networks are managed. One challenge is the influence of the media on social and cultural institutions. Decisions, especially political ones, are played out often on a global stage (Hjarvard, 2008). There has also been, in recent times, the phenomenon of "fake news" or false stories circulated to distort truthful inferences (Allcott & Gentzkow, 2017). When media representation is unfavourable, there is a negative effect on network performance (Korthagen & Klijn, 2012). Further, there are the effects of social media technology. These lead to virtual networks within networks and can influence actor understanding and behaviour. The use of such technology makes it possible for an individual to proffer an opinion without

having to support their arguments with any evidence (Allcott & Gentzkow, 2017). All these are disruptive influences on the flow of information to networks and extra analytical skills are required to operate in such environmental noise.

The guideline environment has characteristics that lend it to being described as a network. Multiple parties have vested interests, or parts to play, either in the input to or the development of the guideline. Many actors are involved: there are data analysts who provide the evidence, technical staff that synthesise the research, the guideline group that forms the recommendations, NICE, (the underpinning organisation) and multiple external stakeholders who influence the process. External influences on the core guideline development group can be from group participants' own professional networks, from external organisations linked to individuals, from governance influences, and from the power/knowledge nexus of scientific networks. Taking a networks perspective, then, aids an understanding of the challenges of guideline development and the nature of the external influences on the process.

2.4 Summary

What is presented in this chapter sets out the theoretical foundations of this thesis, provides a persuasive case for this research and highlights the areas to which this thesis contributes. What is clear from the literature is that guidelines continue to be an integral part of healthcare. They are a strategy to link the best-available research evidence to clinical practice, with the aim of reducing inequalities in treatments. They provide pre-packaged assemblages of information for clinicians, and others, to guide medical practice. There are now sets of standards for guideline development (AGREE Collaboration, 2003; Brouwers et al. 2010; IOM, 2011), although guidelines continue to be produced in many healthcare systems by different organisations with differing adherence to these standards (Legido-Quigley et al., 2012).

The methodologies of guideline development are afforded much space in the guideline literature; so too is research about implementation of guidelines. The literature asserts that the uptake of guidelines by clinicians remains low with barriers to guideline adherence including the volume of guideline information being unmanageable, the

guidance being too rigid and the information not being applicable to many real patients (Greenhalgh, 2017). There are a number of other concerns too about guidelines highlighted in the literature, such as, bias within the supporting evidence, (McGauran et al 2010; Hart et al. 2012; Mangin 2012), conflicts of interest for guideline group participants (Guyatt et al., 2010; Gale, 2011; Kung et al., 2012), and not recognising co-morbidity as a factor in treatment strategy (Hughes et al., 2013; Upshur, 2014).

Certain areas of interest around guidelines, and their development, are under-represented in the literature. These include the social processes of guideline development and the influences on these. Thus, empirical research in these areas will contribute to the understanding of guidelines. Key areas for exploration are the factors affecting the social interactions of the guideline group, how the group uses the available evidence, and the key influences (internal and external) on group functioning. In particular, there is a need to explore the wider environment within which the core guideline development group operates because guidelines are not produced in isolation; they influence, and are influenced by, many actors and organisations in healthcare, not least by patients as service users.

The next chapter focuses on how insights from the literature were incorporated into a conceptual framework to underpin this research. It discusses how the framework was conceived, how it evolved during the research, and why using multiple perspective lenses was an active choice. The research questions, both the primary and subsidiary questions, which were developed from the framework are also discussed.

Chapter 3: Conceptual Framework and Research Questions

3.1 Introduction

This chapter provides a discussion of the multi-perspective framework underpinning this research and how the research questions were developed from exploring key themes in the guideline literature. The literature review in the previous chapter has revealed that a key area under-represented in the guideline literature concerns the social processes of guideline development. This includes how guideline groups interact as they assess and appraise evidence, as well as the influences shaping these interactions. The conceptual framework was built to capture multiple perspectives on these interactions and influences. As such, its purpose is to guide the research, including the questions asked, the data collected and the analysis of this data.

The chapter begins with a discussion of how the framework was conceived and developed. It then describes elements of the framework. This includes detailing the lenses chosen as the most appropriate to explore the guideline development process. How the framework evolved after the early stages of the research is also described. There is information on the perceived advantages and limitations of the framework and the final section sets out the research questions that have emerged as most pertinent to understanding the social processes of guideline development.

3.2 Development of the framework

There is usually a multitude of concepts, theories and literatures that researchers can draw upon and multiple possible directions to take to address particular research questions. Given this labyrinth, it is important to have a conceptual framework to guide the research and act as an anchor (Miles et al., 2014; Ravitch & Riggan, 2017). A conceptual framework defines the research problem and the approach to solving the problem (Lederman & Lederman, 2015). It characterises what will be included, what will not; it provides a means of describing relationships within the framework and directs what data to gather and how to analyse it to answer the research questions (Miles et al., 2014; Ravitch & Riggan, 2017).

The starting point for this research was an interest in the guideline development process: how guideline groups use evidence, interact and make decisions. Early in the literature review, questions arose such as: how does the guideline development group interact to assess evidence; what types of evidence are considered; how is evidence interpreted and what assumptions underlie this; how are decisions made on what the guideline recommendations should be and what are the influences on the group that is involved in the design and development process?

Thus, exploring the social processes involved in developing a guideline did not lend itself to a single theoretical underpinning. For example, a review of the environment within which UK guidelines are developed by NICE, suggested that the nexus of people involved in guideline development could possibly be considered a form of policy network. An initial focus, therefore, was on policy networks. However, as the literature review proceeded, and the view of the research landscape matured, concentrating on any particular form of network was felt to be too narrow a boundary to elicit rich detail about the guideline process. Obtaining rich detail required an exploration of guideline group structure and functioning, how the group used evidence and how all this was influenced by the broader network within which the guideline development group operated. This, then, was the rationale behind the decision to use a multi-perspective framework.

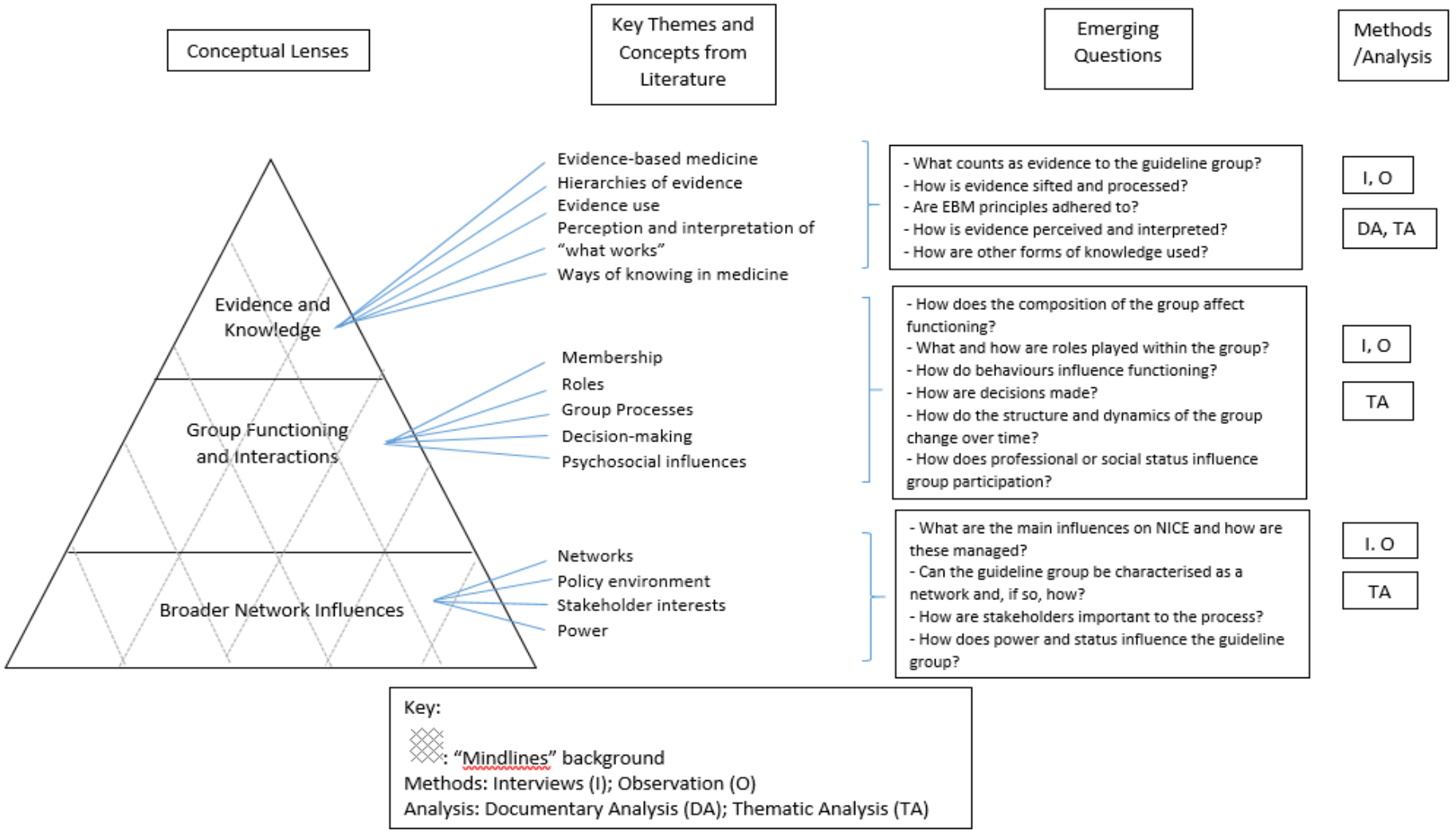
Despite possible difficulties of comparing data informed by different perspectives, it has been advocated that "multiple theoretical triangulation", the combination of multiple theories in single investigations, is advantageous as no single way of viewing a subject of research can capture all that is relevant (Denzin, 2009b). Estabrooks and colleagues (2006) also suggest that, at least for knowledge translation processes (of which the guideline process can be considered an example in that research is translated into guideline recommendations for practice), multiple perspectives are more powerful than a predominant theory. It was felt that, in this research, the use of a multi-perspective framework was appropriate as it would provide an in-depth picture of the guideline process where boundaries of healthcare, policy, practice and knowledge are crossed.

The main conceptual lenses guiding this research are: Evidence and Knowledge (in the clinical environment), Group Functioning and Interactions, and Broader Network Influences. The next section describes the framework and its elements and why they, in particular, aid an understanding of the terrain of the guideline process

3.3 Description of the framework and its elements

The conceptual framework is depicted in Figure 3.1. It sets out the conceptual lenses chosen and the key themes from related literatures most germane to an exploration of the guideline process. There is information about the research questions that were developed from the literature. The methods of data collection and analysis chosen for this research are also highlighted in the framework. These are aligned with the researcher's world view, the underpinning epistemology and the research design, all of which are discussed in detail in Chapter 4 (Methodology and Methods).

Figure 3.1: Conceptual framework for studying clinical guideline development



The pyramidal shape around the conceptual lenses in the framework is significant: it represents a progressive broadening of influences from individual to external. The first conceptual lens is "Evidence and Knowledge". This has both an individual and a group-level element. How evidence is used at NICE involves group level discussion, but it is also an individual process. This is because assumptions about evidence, and how these impact interpretation of evidence, are personal. Personal interpretation, then, plays into group debates. Evidence and knowledge are highly important to the guideline process and this is considered to be a key conceptual lens. The second conceptual lens, "Group Functioning and Interactions", examines the processes and dynamics of the guideline group. The final lens is "Broader Network Influences", which considers those influences that are external to the guideline development group, but still impact its functioning and output.

The conceptual framework developed over time as new understandings were gained. Originally the framework contained four conceptual lenses, the fourth being the "mindlines" concept. This was chosen as a key lens as it offered a way to show how the many ways of knowing - explicit, intuitive, tacit - are blended as a consequence of social interaction with others (Gabbay & le May, 2004; 2011). It was considered that the concept would aid understanding of interactions in the guideline group network and influences on the decision-making processes in a more encompassing way compared with viewing the processes from only one knowledge lens. There were also calls for research on how mindlines impacted guideline development (Weiringa & Greenhalgh, 2015). This is because it is still not clear what the foundations are for integrating evidence-based and other types of knowledge in EBM decision-making scenarios, such as formulating guideline recommendations (Malterud, 2006; Jonas, 2009). However, mindlines are a process that health professionals find hard to articulate and observing the process occurring in a research scenario is difficult (Gabbay & le May, 2011). This was recognised early in this case study, along with awareness that observing a change of mindlines in individuals (manifested as a change in practice) would not be possible since the actual practice of the guideline group participants was not within the boundaries of this case. Hence, the mindlines concept moved to the background within the framework, remaining a link between individuals' interpretations of evidence, the interactions within

the group and the factors affecting these, rather than it being a key conceptual lens. The three key conceptual lenses chosen are now discussed in more detail below.

Conceptual lenses

Evidence and knowledge

Guidelines are grounded in the concept of evidence-based medicine (EBM) (Timmermans and Mauck, 2005; Greenhalgh, 2017). In part, the EBM movement came about to strengthen the scientific base on which clinical decisions are made as well as to address studies which demonstrated wide variation in practice patterns (Timmermans & Kolker, 2004; Greenhalgh et al., 2014). So evidence (of many types and classifications) relevant to the disease-specific area is at the heart of guideline development. Therefore, in order to understand why and how guideline recommendations are made, an understanding of the evidence used is necessary. What counts as evidence to members of the guideline group, how evidence is perceived and interpreted, how the hierarchy of evidence is applied, and how qualitative data are used, were all questions of interest and central to this research. In guideline development, systematic research outputs seem to be privileged over other evidence such as observational research and expert opinion but "research does not speak for itself" (Thistlethwaite et al., 2011:455); research data requires human input to translate it and to situate it using experience and tacit knowledge. Expert opinion, based on the experiential and tacit knowledge of guideline group members, is involved in the interpretation of the research data, despite its lowly status at the bottom of the evidence hierarchy. As a result of this, types of knowledge other than research data were included as part of this conceptual lens within the framework.

Group functioning and interactions

Guideline development involves a social process as well as a technical one. Part of the impetus behind this research is that the technical aspects of guideline development have been well elucidated but the social processes have been given less attention (Pagliari et al., 2001; Michie et al., 2007; Legido-Quigley et al., 2012; Atkins et al., 2013). The quality of the social processes in guideline development are dependent upon both group

composition, functioning and dynamics of the Guideline Development Group (Eccles et al., 2012). This, therefore, is a salient conceptual lens for this research.

Group composition is seen to play a role in guideline group discussions and in the final recommendations made (Hutchings & Raine, 2006; Kunz et al., 2013). There is some agreement that guideline development groups should be multi-disciplinary with key stakeholders, such as clinical experts, healthcare professionals specific to the guideline topic, clinical providers and patients all represented (Pagliari & Grimshaw, 2002; Eccles et al., 2012). A mix of professionals, providers and patients is prescribed for guideline groups within guideline methodology manuals (IOM, 2011; Legido-Quigley et al. 2012; NICE, 2014, updated 2017), although the exact balance may be dictated by the topic and availability of participants. This research explores group composition, and changes to that, as well as the balance of the group (professional, gender, age, role) and how this affects their interactions. Also of interest was the influence of status amongst the professional participants, what roles were taken on by the participants and how they changed over time.

Research from the social and organisational psychology literature and the organisational behaviour literature has provided insights into small group processes. There is some research that has indicated that group processes, as described in the literature, are evident in guideline groups and, further, that factors, such as professional status, play an important role in how the group functions (Pagliari et al., 2001; Pagliari & Grimshaw, 2002). However, there is little research on dynamic interactions between guideline group members and how these change over time. Key themes to explore for the macular degeneration guideline group were, then, group processes and interactions (were the processes from the literature recognisable and what influenced them?), how these changed over time, decision-making (how were decisions made and by whom?), and psychosocial influences.

Broader network influences

NICE guidelines are developed by a network of actors, stakeholders, advocates and interest groups all bounded within a political subsystem. The landscape is depicted in Figures 5.1 and 5.2 and described in Chapter 5. The rationale for choosing this conceptual

lens is that, given the increased emphasis on evidence-based healthcare being delivered in an interconnected system of people, policy and politics (Best & Holmes, 2010; Shepherd, 2014), understanding the policy environment, the wider networks and external factors impacting the research subject is important. The broader network influences are also of interest as the guideline chosen covers both diagnosis *and* management of a disease and, hence, a range of stakeholders from clinicians and allied health professionals to service commissioners to patient interest groups and charities are involved and interested in the outcome of this guideline. Further, the guideline studied has created much external interest as funding for macular degeneration treatments is mired in controversy (BBC 2015; Cohen 2015a, 2015b; 2017; see also Chapter 6.2.2). The attentiveness of external parties to the outcome of this particular guideline process has been high and so the impact of this on the guideline group making final guideline recommendations was another point of focus for the research. The key themes and concepts extracted from the literature include the policy environment and boundaries, networks, stakeholder interests and power. The questions emerging from the key concepts identified in the literature aim to examine the main external influences that shape the guideline recommendations as well as consider the characteristics of the broader network.

3.4 Reflections on the framework

The main advantage of a multi-perspective framework is that it enables a research subject from to be viewed from multiple viewpoints. As such, it gives a complementary understanding of a phenomenon which can have practical implications in multiple contexts (Denzin, 2009b; Jacobs, 2012; Hoque, et al., 2013). This advantage is particularly relevant to the healthcare context where one theory is unlikely to fit all contexts since the healthcare terrain is complex (Estabrooks et al., 2006). Since the aims of this research included looking at guideline development from many aspects, the choice of a multi-perspective framework is appropriate.

Being multi-perspective, this research has quite a lot of secondary questions (see Figure 3.1 above and discussion in the next section). This is intentional despite some authors suggesting too many research questions can suffocate innovation and discovery (Richie

& Lewis, 2003). The subsidiary questions are directed at the different aspects of this inquiry and add to the holistic view of the guideline process that emerges from this study.

Adhering to a single conceptual perspective avoids potential epistemological tensions that can arise with the use of a multi-perspective framework. For example, there may be epistemological differences in how scientific evidence-based research is conceived compared with other forms of knowledge, such as tacit knowledge. Much research in the medical arena has a positivist underpinning and assumes that knowledge is created which is value-free and objective (Bunniss & Kelly, 2010; Howick, 2011). However, some have pointed out that there are other more interpretive ways to understand scientific, medical data (Upshur, 2000). Furthermore, viewing evidence from a positivistic standpoint only, removes all social context from medical practice (Goldenberg, 2006). Exploring clinical guidelines means crossing multiple boundaries of knowledge, policy and practice, and venturing into competing epistemological paradigms is largely unavoidable. However, drawing on multiple concepts with different underlying epistemologies, as for this research, permits examination of the subject from different viewpoints (Hoque et al., 2013), adding to the rich picture of the guideline process.

3.5 The research questions

The process of constructing research questions involves a variety of elements such as immersion in the literature, the influence of various stakeholders and the background and experience of the researcher (Agee, 2009; Sandberg & Alvesson, 2011). “Gap-spotting”, or finding an area in a body of literature that has been overlooked in some way, is a dominant method of question construction (Sandberg & Alvesson, 2011). Gap-spotting is a way to create the opportunity for a meaningful contribution to a body of literature (Locke & Golden-Biddle, 1997; Golden-Biddle & Locke, 2007). This is the approach followed in this research. The literature review undertaken of the clinical guideline landscape revealed a lack of empirical data concerning the social processes of guideline development. Thus, the development of the research questions was directed towards this area. As outlined in Chapter 1, the overarching question that was developed for this research is:

"How does a multi-actor group, responsible for developing clinical guidelines within the UK, interact and use evidence?"

Further exploration of the literature led to the choice of the lenses with which to examine this question. Three subsidiary questions were developed which aligned with the main lenses. These were:

1) How is evidence perceived, interpreted and used by the guideline group during the guideline process?

2) How does the group interact and what are the main within-group influences?

3) How does the broader network, surrounding the core development group, influence it or impact the process?

In order to examine the overarching research question and each of the subsidiary questions, further detailed questions were developed (Table 3.1). The questions had a number of functions: they provided direction in terms of design and also clarity for specific research issues. They also served as the basis for the design of the interview protocols (Appendices i and ii). The first interview protocol (Appendix i) framed the interview questions for the initial four key conceptual lenses. The second interview protocol (Appendix ii) is the framework for interview questions used after the removal of the mindline concept as a key lens.

Table 3.1: Emerging questions aligned to the three main conceptual lenses

Lenses	Emerging Questions
Evidence and Knowledge	What counts as evidence to the guideline group?
	How is evidence sifted and processed?
	Are EBM principles adhered to?
	How is evidence perceived and interpreted?
	How are other forms of knowledge used?
	Are there identifiable gaps in the evidence base and, if so, how are they filled?
Group Functioning and Interactions	How does the composition of the group affect functioning?
	What, and how, are roles played within the group?
	How do behaviours influence functioning?
	How are decisions made?
	How do structure and group dynamics change over time?
	How does professional or social status influence group participation?
Broader Network Influences	What are the main influences on the guideline process and group and how are these managed?
	Can the guideline group be characterised as part of a network and, if so, how?
	How are stakeholders important to the process?
	How does power and status influence the guideline group?

3.6 Summary

Both the conceptual framework and the research questions have been set out in this chapter. A multi-perspective framework using three key lenses has been chosen to guide this research. There is one overarching question concerning how a guideline group interacts and uses evidence for development of a clinical guideline and three subsidiary questions derived from the conceptual lenses. The overarching question gives direction and captures succinctly the major aims of the research. The subsidiary questions then funnel the broad focus of the overarching question allowing detail to be captured (Agee, 2009). For research to be coherent, these research questions need to be aligned with the underlying philosophical assumptions and methodology. These assumptions, the

methodology and methods of data collection and analysis utilised for this research are discussed in the next chapter.

Chapter 4: Research Methodology and Methods

4.1 Introduction

The purpose of this research is to examine further clinical guideline development with a special focus on the social processes involved. The research questions, set out in the previous chapter, frame and define the focus of the research: how the group of actors responsible for clinical guideline development, interact and use evidence to come to consensus decisions. The research is a qualitative inquiry using single case study methodology underpinned, epistemologically, by 'weak social constructionism'.

This chapter discusses the choice of research methodology and methods. First, there is consideration of the philosophical stance of the research. Then, case study methodology as the research strategy is considered. The remainder of the chapter discusses the choice and implementation of a case study methodology in this research, including the methods of data collection and analysis used.

4.2 Locating this research within philosophical paradigms

There are layers of philosophical and methodological alternatives to consider in order to get to the core of what data to collect and how to analyse it. Preferences of underlying philosophy must be explained and there are choices to be made of methodological strategies and of techniques of data collection and analysis. The intrinsic beliefs and values of a researcher influences all these choices and guides the research (Denzin & Lincoln, 2011; Moses and Knutsen, 2012; Creswell, 2013).

The philosophical perspective taken in this research is within the interpretivist paradigm. This is due to the nature of the research questions which seek an understanding of how social interactions within the guideline group impact the guideline process and the researcher's ontological and epistemological leanings. The ontological position taken is that reality is a product of interactions with others. These interactions occur at many levels and create a web of complicated socially constructed structures, for example, cultural, political, organisational. This accords with the view that interpretive researchers do not accept that there is a social reality that exists irrespective of people and their social

interactions (Tuli, 2011). The epistemological assumption in this research is that producing knowledge about the social world depends on understanding better how participants construct their social reality. Interpretive approaches allow researchers to analyse their respondents' views and understand how their social reality in their particular social and cultural context is constructed (Darlaston-Jones, 2007) and the aims of this research align with this approach. The underlying epistemology justifies and evaluates the knowledge gained as well as influencing the methodological choice by which to gain this knowledge. The methodology chosen, in turn, justifies and guides what methods are used to produce the data. Within the interpretivist paradigm, this research is underpinned by social constructionism and this is discussed in the next section.

Social constructionism underpinning

A social constructionist perspective maintains that different people construct different views of the same issue in specific social contexts (Burr, 1995; Andrews, 2012; Cruickshank, 2012). Social worlds, or their social "reality", are constructed through social processes and interaction (Young and Collin, 2004; Andrews, 2012; Efran et al., 2014). In social constructionism, the focus is both on the process by which meaningful experiences are created, negotiated and sustained (Schwandt, 2000; Baert et al., 2011), and on how these meaningful experiences are informed and motivated by the social and historical contexts within which these take place (Baert et al., 2011).

Social constructionism has four underlying assumptions (Burr, 2003): firstly, a critical position is taken that challenges the assumption that knowledge is based only on an objective view of the world. This aligns with the ontological assumption that reality is subjective and multiple. Secondly, that culture and history shape the way we understand the world. Thus, nothing remains static and our understanding will change over time (Young & Collin, 2004). Thirdly, that social processes sustain knowledge and it is impossible to create and revise knowledge without socially interacting with other people. The final assumption is that social action and knowledge are intertwined; human response is influenced by the knowledge created by interaction with their world and, as a result, social action changes when this new or revised knowledge is created.

Social constructionism is often confused with social constructivism. The similarity is that the main focus is on making meaning of the world. However, social constructivism refers to how individuals cognitively make sense of the world in a social context, that is, knowledge occurs as an *outcome* of social interaction. Social constructionism focuses on how knowledge is created through shared production, that is, it is constructed *through* social interaction. (Sismondo, 1993; Engler, 2004; Young & Collin, 2004). As the methodological approach and design of this research is aligned with social constructionism, social constructivism will not be discussed further.

There is no single constructionist viewpoint; rather, two camps, "strong" and "weak" social constructionism are often distinguished in the literature (Sismondo, 1993; Sayer, 2000). The main tenet of strong social constructionism is that *everything* is a social construction, underpinned by language, and that nothing of an objective nature exists (Sayer, 2000). Sayer (2000) argues that, if this is the case, then respondents' and researchers' constructions and interpretations of knowledge are alterable at any time and this supports the criticism of extreme relativism in social constructionism. Furthermore, Jacobs and Manzi (2000:38) suggest that this means there is an inability to "discern between competing claims". By contrast, in weak social constructionism, there is not a complete rejection of an objective "reality". This follows Berger and Luckmann's (1966), original orientation to social constructionism that, whilst human interaction shapes the social reality of individuals, there is a degree of objectivity to the world. Weak social constructionists do still align themselves with Burr's (2003) basic four assumptions; they also acknowledge a distinction between concepts of knowledge which are socially constructed and knowledge which has a material existence (Jacobs & Manzi, 2000).

The epistemological position taken in this study is of weak social constructionism. This rejects the extreme stance where *every* "reality" is said to be socially constructed. In the context of this study, the disease topic: macular degeneration exists independently of the mind and is a "real" disease entity. However, how people make sense of it, and the evidence pertaining to it, depends on their previous and present interactions concerning that disease. These different interpretations and perceptions then play into what social "reality" emerges from their interactions. Therefore, multiple social realities will emerge

during the course of the guideline process and a variety of meanings about how the group interacts can be elucidated. In this respect, social constructionism is justified as an underpinning epistemology for this research.

A qualitative study choice

Research within healthcare is frequently dominated by positivism and quantitative methods (Greenhalgh & Russell, 2009; Howick, 2011). The positivism of medicine seeks to reduce the observer to a passive repository of information with no idea that the observer may be a perceiver of his or her world, or further, a conceiver or constructor of that world (Ashworth, 2003; Darlaston-Jones, 2007). In effect, medicine tends not to recognise the ability of a person to see and interpret the world in their own way. However, many authors' accounts of medical diseases demonstrate that interpretation of disease is shaped by the cultural, social and historical world in which the physician and patient find themselves (Gabbay, 1982; Bury, 1986; Conrad & Barker, 2010). Indeed, some authors have suggested that medicine is now moving towards more interpretivist models and qualitative methods which encompass patients' subjective views and incorporate them into individual disease management (Wilson, 2000; Boivin et al., 2010; McCartney et al., 2016).

The choice of qualitative inquiry aligns with increasing acceptance of the value and contribution of qualitative research in healthcare, until recently a poor second cousin to quantitative, hypothesis-testing research (Noyes et al., 2010; Cleary et al., 2014; Drabble et al., 2014). The support for more qualitative research in healthcare was exemplified by an open letter to the British Medical Journal (Greenhalgh et al., 2016), which was signed by 66 senior medical academics from 11 countries. This exhorted the British Medical Journal to consider more such research and increase its priority for publication.

Strengths of qualitative research include obtaining rich accounts of human perceptions and experiences which permit in-depth interpretation about a phenomenon as it occurs in context (Denzin & Lincoln, 2011; Joubish et al., 2011). As this research is concerned with *how* evidence is used in a guideline development group, what the influences are on the social interactions of the group and how these affect decision making, a more quantitative

approach would not have sufficiently elucidated a rich, detailed picture of how guideline recommendations are achieved. Qualitative research aims for the understanding and illumination of a subject (Joubish et al., 2011), and it is exactly this that this research seeks to provide.

4.3 Research strategy - case study methodology

A number of possible qualitative methodologies were considered for this research including grounded theory and ethnography but these were considered inappropriate or unfeasible. Grounded theory, for example, assumes no previous understanding of the subject (Glaser & Strauss, 1967; Glaser, 1998). This was not tenable due to the researcher's long association with healthcare and the therapeutic area of the guideline. Ethnography, whilst attractive in that it focuses on the social interactions of one cultural group (Erickson, 2011), would have necessitated immersion in the guideline process as a participant. This was not possible as NICE would not allow researcher participation in the group meetings. Case study methodology was selected for this research where an in-depth exploration may provide answers to "how" or "why" questions and where the focus is on the search for meaning (Merriam, 1998; Yin, 2012; Merriam & Tisdell, 2016).

The case study method has been widely used within the social sciences (Tight, 2010; Starman, 2013) in a variety of different disciplines (such as education, family studies, business, social work, nursing and medicine, psychology), but continues to sit in contested terrain concerning its definition, the approach to it, and its underpinning epistemology (Yazan, 2015). Case study work has been variously referred to as a method, a way of collecting and analysing research data (Yin, 2014), or a design (often confused with ethnography or fieldwork) (Punch, 2013; Yin, 2014), or a research strategy (Eisenhardt, 1989, Stake, 1995; Verschuren, 2003). Others have argued that the defining characteristic of a case study is that the focus of inquiry can be bounded; thus it is the unit of analysis that characterises a case, not the subject of the investigation nor the underlying approach (Merriam, 1998; Stake, 2005; Merriam & Tisdell, 2016). It should be noted that in this research the case study is considered a research strategy. This is based on having a congruent set of methods and processes for generating and analysing empirical material

of a real-life situation in order to describe inter-related phenomena (Verschuren, 2003). The intent is to attain a rich and holistic understanding of the case under study.

There are different typologies of case studies within the literature (Stake, 1995; Jensen & Rodgers, 2001; Thomas, 2011; Yin, 2012). These categorise case studies on parameters such as time-frame, the number of cases studied, the specific focus of the research or the researcher's intention. Yin (2012) notes three categories of case study: exploratory, descriptive and explanatory. Exploratory case studies investigate any point of interest and provide a basis for further research questions or hypotheses. As the name suggests, explanatory case studies aim to explain phenomena and to suggest causality but they have no single clear set of outcomes. Descriptive studies simply describe the phenomenon in a real-life context. Stake (1995) further categorises case study research to highlight the researcher's intention; the three categories are intrinsic, instrumental and collective (or multiple) case study research. Intrinsic case study work studies a case due to interest in that specific case rather than interest in an abstract idea or theory. Instrumental case study research provides understanding of something other than the case; the case itself is secondary and supports the researcher in examining another issue beyond the case or in refining a theory. Finally, collective case study research refers to the use of multiple instrumental case studies where many cases are studied for comparative purposes.

Selection of cases can be problematic. A case is not chosen "primarily to understand other cases" (Stake, 1995:4) but, that in any choice, even with constraints of time and materials, in-depth learning should be maximised. Selection does not preclude cases crossing categorical boundaries, for example, an intrinsic case study, may also be characterised as a descriptive case. This case study of clinical guideline development falls into the exploratory category as well as being instrumental *and* intrinsic, since the case is both secondary to the explorations of evidence use and decision making by the guideline development group and is also of particular intrinsic interest to the medical world, and to the researcher, due to the topic area of macular degeneration.

Qualitative inquiry and case study methodology, in particular, has often been challenged in the literature due to concerns about theory development and research rigour (Eisenhardt,

1989; Hammersley, 2007; Gibbert et al., 2008). Flyvbjerg (2006; 2011) considers these challenges "misunderstandings" rather than limitations. Flyvbjerg's (2006, 2011) five misunderstandings about case studies are detailed in Table 4.1.

Table 4.1: Five misunderstandings about case study research

Misunderstanding No. 1	General theoretical knowledge is more valuable than concrete knowledge
Misunderstanding No. 2	One cannot generalize on the basis of an individual case; therefore, the single case study cannot contribute to scientific development
Misunderstanding No. 3	The case study is most useful for generating hypotheses; that is, in the first stage of a total research process, while other methods are more suitable for hypothesis testing and theory building
Misunderstanding No. 4	The case study contains a bias towards verification, that is, a tendency to confirm the researcher's pre-conceived notions
Misunderstanding No. 5	It is often difficult to summarize and develop general propositions and theories on the basis of specific case studies

Flyvbjerg 2011:302

One misunderstanding concerns single case study research. It advances that multiple case study research is preferable to single case studies in generating theory and having a sounder analytical basis. Yin (2009; 2014) suggests that analysis based on multiple cases will be more robust and powerful and he proffers that there are only five instances or rationales where single case study research is appropriate (Table 4.2). He argues that, unless one of these rationales is met, then multiple case study research will be analytically preferable.

Table 4.2: Five rationales for conducting a single-case study

The case represents the critical case in testing a well-formulated theory
The case represents an extreme or unique or unusual case
The case represents a typical or common case and the objective is to capture the circumstances and conditions of an everyday situation
The case represents a revelatory case where there is an opportunity to research a phenomenon that has not previously been accessible
The case is a longitudinal case and changes over time can be observed and documented

Adapted from Yin 2009: 47-49 and Yin 2014: 51-53

However, there is much support for single case study research. Single cases offer the in-depth observation required to elucidate the complex nuances of a case as opposed to the surface depth obtained when multiple cases are considered (Creswell, 2017). Single cases can be powerful examples used as additional support for a conceptual argument (Flyvbjerg, 2006; Siggelkow, 2007). They can make a conceptual contribution as an illustration of a conceptual framework (Siggelkow, 2007).

Siggelkow (2007) offers more support for single case studies. He gives the example of the "talking pig" to illustrate that whilst it may be but one pig, it is a powerful and unusual example of that subject. Thus, a small sample size in a case study should not be discounted as offering valuable information. He also defends single case studies from the charge of non-representativeness. Citing the case of Phineas Gage, who lost both frontal lobes as a result of an explosion which led to inferences being made about the function of frontal lobes Siggelkow (2007), suggests that no case study subject is picked randomly. Specific cases are chosen for study exactly because they are considered to offer some special insights into a subject.

Also, some small scale generalisation can occur from single case studies (Stake, 1995). Dyer and Wilkins (1991), go further and argue that good story-telling about a single case is a better way to generate theoretical insight than multiple case studies. They offer a counter to Eisenhardt (1989), and to Eisenhardt and Graebner (2007), who have written extensively about using multiple case studies for theory generation with single case studies tending to be confined to verification-orientation rather than hypothesis-

generation. Eisenhardt (1989), and Eisenhardt and Graebner's (2007) notion to use multiple cases to support theory generation is based on replication logic where individual cases serve as their own analytical units and act as replications and contrasts to emerging theory. Dyer and Wilkins (1991), suggest that, paradoxically, this multiple case, theory-generating approach actually includes many features of hypothesis-testing research and misses out on the rich contextual data of the single case. Furthermore, as studies of complex cases provide material rich in detail, the single case study approach can provide a deep insight compared with other methodologies (Jensen & Rodgers, 2001; Siggelkow, 2007; Flyvbjerg, 2011; Crasnow, 2012).

One of the oft-repeated criticisms of case studies, and one of Flyvbjerg's five misunderstandings of case studies (Flyvbjerg, 2006, 2011), is their lack of generalisability. Generalisability refers to the extent to which findings are applicable to other cases, samples or populations and to the belief that theories account for findings within, and outside, of the case setting (Gibbert et al., 2008). Whilst cases studies, especially single case studies, cannot offer statistical generalisation, analytical generalisation is possible (Yin, 2014). Others view the value of case studies in this regard as "situational representativeness" where findings can be exported to cases in comparable settings and contexts (Horsburgh, 2003), or as holistic narratives (Flyvbjerg, 2006; Baxter & Jack, 2008).

Choosing a case study approach brings the responsibility of bounding the case (Merriam, 1998; Miles et al., 2014; Merriam & Tisdell, 2016). Boundaries solidify the research focus and are important in allowing a limit to be applied to the type and amount of data collection (Merriam, 1998; Merriam & Tisdell, 2016). One challenge for the researchers of any type of extended network, such as the guideline development network, is to delineate the boundaries under study; networks may extend limitlessly due to the inter-related nature of people and organisations (Halinen & Törnroos, 2004; Hanney et al., 2010). So, choosing a case study approach in any research where some type of network is recognisable, doubles the challenge and makes boundary setting all the more important. Whilst it may reduce flexibility to take new developments into account, setting boundaries *a priori* is useful. This is because the changing of boundaries during the

research process can make the volume and analysis of data unmanageable (Thomas, 2015). The boundaries for this case study are discussed below where implementation of the case study approach in this research is discussed.

4.4 Implementation of the case study approach in this research

This research was a single real-time case study of the design and development of a NICE ophthalmology guideline focusing on the diagnosis and management of macular degeneration, a degenerative retinal disease. This is the first study to explore ophthalmology guideline development in depth, in a real-time fashion and with a focus on the social interactions of guideline group members during the process. The research aims and questions for this case study could apply to the study of any clinical guideline which raises a question as to why the particular guideline topic was chosen. The guideline topic of macular degeneration was chosen because the study of guidelines in this particular therapeutic area is new and of intrinsic interest to the ophthalmology therapeutic area. Furthermore, the findings may have practical implications for further study of guidelines in eye diseases. In addition, the management of macular degeneration, just prior to the start of the guideline process, created contextual issues for development of this guideline and resulted in conflict within the guideline group during the process. These issues are discussed in Chapters 6 and 7. For these reasons, it was considered appropriate to be specific about the guideline topic as it was influential in this case.

The justification for a single case study for this research was founded on the knowledge that the chosen guideline is both a unique case and represents a case where there is an opportunity to research a phenomenon that has not previously been accessible. This fulfils at least two of Yin's (2009, 2014) rationales for conducting single case studies. Further fit with Yin's (2009, 2014) single case study rationales is that this case study has elements of a diachronic (Thomas, 2011), or longitudinal, study where the subject is studied over a time period with changes expected in processes and functioning. The case was chosen to offer specific insights into ophthalmology guideline development and was used as an illustration of an integrative framework for the clinical guideline process (See Chapter 7).

The selection of this particular case was based on the researcher's own background in clinical ophthalmology. This facilitated access to the NICE macular degeneration guideline group and brought a deep understanding of the subject matter to the research. However, one related, but recognised, challenge was of the researcher's own biases and assumptions due to her prior, extensive knowledge of the research subject matter. In interpretive research, there is a "blurring of boundaries between process and content" (Sultana, 2007: 376) as the researcher is both interpreter and a data source (Sultana, 2007; Bourke, 2014). This was especially true for this research given the researcher's own extensive background in the therapeutic area. The researcher is "not a transparent conduit" of data (Yanow & Schwartz-Shea, 2014:110). Careful reflection and constant questioning of assumptions about findings can help to mitigate any dominant assumptions affecting the shaping of the research narrative. This is discussed in the "Reflections" section of Chapter 8.

This case provided a valuable opportunity to study the process whilst it was on-going. While some favour retrospective studies for reasons of distance from data and time for reflective learning, undertaking retrospective studies may lead to incomplete and inaccurate data or selection bias (Marschan-Piekkari & Welch, 2011; Ben-Zeev et al., 2012). "Real-time" study has many advantages: emerging themes may be used to bring out the nuances of the data, the researcher is less likely to focus on any particular outcome and there is less reliance on interviewees' memories (Mills et al., 2009). There is much more of a time investment required from the researcher for "real-time" study but in this study, it was considered an opportunity to enhance the detail and depth of the data. Furthermore, the macular degeneration guideline process and completion timeline fitted well with the timeframe for the research.

The *a priori* boundaries for this case were initially set around the Guideline Development Expert Group (GDEG) - see Chapter 6, Part 1 and Figure 6.3. This did not initially involve any NICE staff. However, at the start of data collection, further clarification of the individuals intimately involved in the development of one guideline led to an expansion of the case study boundaries to include some NICE team members. These were the associated (mainly technical) staff who assessed, appraised and presented evidence to the

GDEG or managed guideline group operations. Referred to in this research as the NICE Technical Team (NTT), they were included because of their close association with the specific guideline under study and because they attended all group meetings. Thus, they were an integral part of the guideline group. The GDEG and the NTT together constituted the case study subject group but there were also other NICE staff that interacted with the group members. These included teams organised within NICE such as the Evidence Review Team, the Quality Assurance Team, and the Business Analysis Team. Team members from such teams were assigned to the macular degeneration team and can be seen as "other core NICE staff" in Figure 6.3. The GDEG, the NTT and core other staff constituted the macular degeneration guideline development group (GDG). However, the attendance of other core NICE staff at meetings was only when they were required and they were not considered as part of the subject group of this research.

After selection of the macular degeneration guideline group and topic as the subject of the case study, the next step in conducting the research was to gain access to NICE and to the specific guideline group. Attempting to do research within institutions, especially governmental ones, can be problematic with many levels of authorisation required and politics to negotiate (Woolf, 2004; Flick, 2008; Cunliffe & Alcadipani, 2016). Access to research is said to be monitored and guarded by formal (directors or senior people of an organisation) and informal (less senior people within an organisation but, nevertheless, influential) gatekeepers (Brewer, 2000; Clark, 2011). The key "gatekeeper" for this research was the Director of the Centre for Guidelines at NICE. After a review of the research proposal he granted access to the macular degeneration guideline group with a proviso that individual members of the group, and the group as a whole, would also have to approve. This was negotiated by a presentation of the proposed research to the whole group and their consensus agreement was minuted formally in the group's proceedings. Individual participants, who agreed to be formally interviewed (and recorded) for the case study, were from either the GDEG or the NTT. Each gave their individual consent to being recorded and for use of their interview material in this thesis. Despite access for social sciences research becoming more difficult, due, in part to a protectionist stance increasingly taken by organisations (Roesch-Marsh et al., 2011), gaining access to NICE was relatively straight forward. However, although access to observe group meetings was

granted, details of materials used (unless in the public domain), or discussions held, during meetings were to remain confidential. This has precluded the use of verbatim group conversations to illustrate findings in this thesis.

Once the case study design and plan for the research was completed, an application was made to the University Teaching and Research Ethics Committee of the University of St Andrews. Approval was given in line with regulations (Ethics Reference Number: MN 11756). A copy of the approval form is at Appendix iii. All participants were given an information sheet prior to the start of interviews and all consented to the recording, storage and analysis and use of their data.

Research ethics in social science should be concerned with more than just a paper trail of approvals. In interpretive research, the researcher must be aware of ethical concerns emerging throughout the research process (Yanow & Schwartz-Shea, 2014). Reflexivity of the researcher is key here to remain alert to, and respond appropriately to, ethical issues should they arise as the research proceeds (Guillemin & Gillam, 2004; Yanow & Schwartz-Shea, 2014). In the context of this research, there appeared to be little possibility for any kind of harm to participants during the data collection process. However, measures, such as stopping the recorder during interviews on request or not transcribing parts of interviews, were in place. This was used only once during an interview and involved the views of one participant concerning the macular degeneration treatment issue (see Chapters 6 and 7 and Appendix ix).

There was a concern about how data from this case study would be anonymised given that the disease topic of the guideline was made apparent for the reasons given previously. Measures were put in place to give anonymity to the participants of the guideline group. This included the use of codes for individuals with no reference being made to the geographical locations of participants and use of “Interview 1”, “Interview 2” etc. as notation for the sources of interview quotations used in Chapter 6. However, on occasions, in order to hear the differences in voices between the experts and the NICE technical staff, the illustrative quotations are ascribed either to “GDEG member” or “NTT member”. A further measure to ensure anonymity for participants was use of genderless terms, such

as using “s/he” or “their” when referring to individuals in this thesis. Finally, any names of individuals mentioned during interviews were removed from the interview transcripts.

Finally, there were no financial conflicts of interest for this research. The researcher was partly self-funded with some support from the University of St Andrews for tuition fees and travel expenditure. There was no contract with NICE with regard to the findings ensuing from the research.

4.5 Research design and methods

Broadly conceived, a research design should be structured to focus on the research questions, the purposes of the study and which methods would be the most appropriate to fulfil the objectives (Miles et al., 2014). This is a qualitative case study design that aims to understand better the clinical guideline process and characterise the major influences on it. It utilises a multi-perspective framework and, as such, there was the potential for large amounts of data to be collected. It is incumbent on the researcher to employ methods of data collection and analysis that are robust enough to ensure data is manageable but that can be used successfully to fulfil the overall aim of the study (Miles et al., 2014). The next section, then, discusses the research design with respect to data collection and the analysis methods used.

Data collection

When deciding on data collection methods, Newell and Burnard (2006) recommend asking which sort of data will help answer the research questions and aims and what is the most appropriate method for collecting those data. Deliberations need to encompass issues relating to time, access and finance (Meyer, 2001), as well as those concerning qualitative research rigour (Miles et al., 2014). Multiple data collection methods, not only enable the answering of different research questions, but are also an accepted way to increase research rigour. One measure to improve research rigour is triangulation. This will be considered before moving on to the specific data collection methods used in this study.

Triangulation refers to making use of more than one method to gather data and establish converging evidence. Patton (2015:674) argues that triangulation: "increases credibility and quality by countering the concern (or accusation) that a study's findings are simply an artefact of a single method". Others consider that triangulation enables confirmation and completeness of the data, ensures rigour and enriches it (Casey & Murphy, 2009; Denzin & Lincoln, 2011; Houghton et al., 2013; Cronin, 2014). A number of types of triangulation have been described (Denzin, 2009b; Miles et al., 2014): data source, investigator, theory, methods of data generation and data type. These are detailed in Table 4.3.

Table 4.3: Types of triangulation

Type of Triangulation	**Features**
Data source	Persons, places, times
Investigator	Multiple researchers
Theory	Multiple theories or paradigms
Methods of data generation	Different methods such as interview and observation
Data type	Texts, documents, videos

Source: Denzin, 2009b; Miles et al., 2014

While many see triangulation as permitting corroboration which improves credibility of research findings, others consider it to have a problematic nature in that such multiplicity can cause confusion and conflicting findings (Moran-Ellis et al., 2006; Cohen et al., 2007; Hammersley, 2008). For this research, it was thought that triangulation would improve reliability and add to the credibility and completeness of the data. Triangulation used in this study was theory triangulation (discussed in Chapter 3) and triangulation by different methods of data generation.

The methods of data generation for this research combined direct observation of the guideline group, semi-structured interviews of group members to validate observations, and documentary review. Document analysis ensured the researcher understood the evidence base which the subject group were discussing and that the documents produced aligned with decisions made by the group.

An overview of the methods employed and the types of data collected for each method is seen in Table 4.4 and the specific methods and their application in this research are discussed in the next section.

Table 4.4: Types and amount of data collected for each method

Interviews	**Observation**	**Documentary Review**
Verbatim transcripts of recorded interviews *22 formal interviews range: 28 mins to 73 mins*	Observation of committee meetings *Attended 15 meetings of 8 hours each: 120 hours*	Minutes of committee meetings *15 sets of minutes*
Notes taken during formal interviews *22 pages notes*	Fieldwork notes of direct observation of committee meetings *148 pages fieldwork notes*	Scope of guideline *1 document: 10 pages*
Field notes post-formal taped interviews *22 pages field notes*	Fieldwork reflections *76 pages fieldwork notes*	Review question evidence documents *25 sets of evidence*
A*d hoc* interviews *25 ad hoc interviews* *25 pages field notes*		Evidence tables and statements, draft recommendations *Over 900 pages reviewed*
		Disclosure of interests register *1 document: 14 pages*
		Draft Guideline *1 document: 244 pages*
		Final published Guideline *1 document: 244 pages*

Direct Observation

Observation is a mainstay of data generation in many types of qualitative research where researchers are observers of both human actions and the physical places where these occur (Angrosino & Rosenberg, 2011). This naturalistic setting for observation adds richness to data by documenting events and interactions while taking account of contextual factors

(Flick, 2008; Morgan et al., 2016). It also provides data for circumstances where respondents are unwilling to verbalise their thoughts or are unable to recall events (Angrosino & Rosenberg, 2011; Morgan et al., 2016). The strength of observation as a data collection method lies in directly seeing how a subject acts rather hearing of that act secondarily in interview (Mays & Pope, 1995; Morgan et al., 2016); the method is especially useful when roles and behaviours are a focus (Walshe et al., 2012). Another strength of observation is that discrepancies between data collected at interview and interactions observed directly can be explored in follow-up interviews (Angrosino & Rosenberg, 2011; Newman, 2014).

Following Gold's (1958) typology of roles that characterise naturalistic observation, the researcher can adopt one of several stances which describes their relationship with the observed. Table 4.5 details these roles with regard to the degree of participation in observation, their features and the advantages and disadvantages of each different role.

Table 4.5: Observational roles

Roles	Features
Complete participant	Covert observation. The observer becomes a part of the group being studied concealing her role. Opportunity to perceive the case from the perspective of the subject but loss of perspective as a researcher. Possible observer bias.
Collaborative partner	As for complete participant but the researcher is known to the participants. Researcher and participants are equal partners. Possible observer bias.
Participant as observer	Overt observation. Researcher known to participants. Opportunity to perceive the case from the perspective of the subject but high level of trust required to obtain in-depth information. Possible observer bias.
Observer as participant	Observation is primarily for data gathering; peripheral participatory role. Interaction can be close enough to establish an insider's identity but there is less familiarity with the culture of the group and the level of information imparted is often controlled by the respondents. Possible observer bias.
Complete observer	No participation. Researcher may be hidden from participants. Unobtrusive data gathering. Unable to fully appreciate the participant perspective

Adapted from Gold, 1958; Herr & Anderson, 2014; Merriam & Tisdell, 2016

As previously explained, in this research, there was no opportunity for the researcher to be a participant observer. This was due to the NICE guideline process being closed to people who are not part of the guideline group. The role for the researcher, therefore, was as a complete observer. The researcher was allowed to be in the same room, sitting quietly at the back while proceedings of the guideline group unfolded. However, despite this background role, the presence of an observer and the observational process itself may affect social interactions and alter group processes – the so-called "Hawthorne" effect (Wickström & Bendix, 2000; Newman, 2014). The guideline group participants knew of the researcher's ophthalmology background by her being introduced at the start of each meeting and, occasionally, reference would be made to the researcher during the meetings. This was usually a clinical expert trying to gain endorsement of their point of view. This, in effect, included the researcher in the group's discussion despite there being a lack of response from the researcher. The implications of this on the research and the discomfort felt by the researcher are explored more fully in the "Reflections" section of Chapter 8.

There are a number of methods of collecting observational data: taking field notes and creating a narrative from what is seen, heard and sensed, using a formal observational rating instrument or using technological devices such as digital tape recordings (Angrosino & Rosenberg, 2011). The use of a formal observational rating device was considered inconsistent with the qualitative study design as most of these instruments favour quantitative analysis. Tape recordings or other technological solutions would have produced a faithful reproduction of proceedings but using that alone may also have precluded gathering valuable data on thoughts and feelings of the researcher (Angrosino & Rosenberg, 2011). Recordings of the day-long meetings were, anyway, not allowed by NICE and field notes became the main source of observational data. Note-taking can be problematic: if the period of observation is long, the task can be onerous and taking detailed notes at the time capturing all events, interactions, behaviours is difficult (Schensul & LeCompte, 2013; Merriam & Tisdell, 2016). Thus, the approach was to make scribbled short summaries of situations and interactions, occasionally writing down whole conversations, and then, as soon as possible afterwards, recalling and capturing events and reflections in a more detailed fashion. The field notes collected for this research were categorised into *descriptive*, describing what happened during the meetings,

reflective, commenting on key behaviours, interactions and an impression of events and *reflexive*, exploring the researcher's own reactions and feelings and how these may have affected the observations made.

Table 4.6 sets out the *a priori* conceptual interests for observation. This provided a partial filtering lens for observation although what to observe on the occasion of each meeting varied by the agenda of the meeting and previous meeting events.

Table 4.6: *A priori* conceptual interests for observation

Interests	Observation
Evidence	What evidence is discussed? How is evidence interpreted and discussed? Who contributes to each debate? What challenges arise?
Group functioning	What is the mood of the group? How does the group as a whole interact (including changes over time)? How do various individuals interact? (including changes over time)? How does the GDEG interact with the NTT? What roles[2] are participants adopting? Are there participants who are not part of the core GDG and how does this impact functioning? What issues arise and how are they dealt with?
External network	How do external stakeholders influence the meeting today? What are the challenges and how are they overcome?
Other	What is of particular note today? What is there to follow up and with whom?

The decision for the particular focus of interest in any meeting came about both from the conceptual framework and from events that arose in previous meetings. There was flexibility, however, to change observation focus in meetings. So, for example, when the group was not quorate for one meeting (see 6.4.4), the focus changed from observing

[2] The TRIAD model (Driskell et al., 2017), discussed in Chapters 2 and 7, would have been a useful *a priori* framework for exploring the roles adopted by participants. However, the model was published only towards the end of the study and was not utilised during data collection.

interactions between patient and expert members of the group to how the group dealt with conflict and anger felt towards absent fellow participants.

Interviews

The interview as a data collection method provides one of the most important sources of data for a case study (Stake, 1995; Yin, 2012). Interviewees provide detailed insights into the case in which they are positioned through relating their opinions, perceptions, attitudes and feelings (May, 2011). They may be used as a stand-alone data collection method for investigation of an historical event or where behaviour cannot be observed or used in a confirmatory manner to corroborate observed events (May, 2011; Merriam & Tisdell, 2016).

A semi-structured interview design was chosen for this research. This was based on the design being considered to provide richer detail, with every interview being unique as each interviewee has a distinct experience of, and place within, the case (May, 2011; Merriam, 1998; Merriam & Tisdell, 2016). The main topics for discussion during the interviews were guided both by the research questions and the conceptual framework themes. From these an interview protocol was developed which evolved during the course of the research (Appendices i and ii). The main change in the protocol was to remove questions thought to be able to elicit mindline formation and revision. This was as a result of the mindline lens being removed as a main conceptual lens. Alvesson (2003, 2010) suggests that interviews should not be afforded just an *a priori* framework of a protocol but emergent themes should be explored too. For this reason, while the interview protocol themes were followed, any related, or tangential, themes arising during the interview were explored as well.

A constructionist conception of the interview is that data are co-produced by the respondent and the researcher (Silverman, 2011; Roulston, 2010), with the researcher, the interviewees and the research process itself in a mutually influencing relationship (Yates, 2013). Whilst this type of co-construction was not the main focus of this research, it does align with the epistemological underpinning of this study. There were two areas pertaining to this to consider. Firstly, to acknowledge that the interaction between

interviewee and interviewer created the product of the interview especially as the interview was of a semi-structured format. There was an interview protocol to follow but this did not preclude following subjects of interest. These subjects could be from either the interviewer or interviewee, although mostly they arose from the interviewer. Occasionally it meant tangential themes were explored and, sometimes, it was difficult to re-focus the interview to research subjects. However, it did allow the researcher to understand more deeply the participants' views and values. Secondly, it was important to recognise that the researcher's therapeutic experience had an impact on questioning during interview. This was generally advantageous in that nuances concerning macular degeneration did not have to be explained but it did mean that the researcher's own assumptions underpinned the questioning.

How many qualitative interviews is enough? Baker and Edwards (2012), report the views on this from 14 established social scientists and 5 early career researchers. The answer is that "it depends" - on the aims of the research, the resources available and practicalities. Other authors suggest saturation, or when no further data of interest are being discovered, is reached after just 12 interviews (Guest et al., 2006). Table 4.7 sets out the details of the 22 formally-recorded interviews and 25 *ad hoc* interviews for this study.

Table 4.7: Interview details

Formal interviews (22) (Average: 40 mins; range: 28-73 mins)	*Ad hoc* interviews (25) (All 5-10 mins)
<u>GDEG members:</u> 13 interviewed once	<u>GDEG members:</u> 13 interviewed once 2 were interviewed twice
<u>NTT members:</u> 5 interviewed once 2 interviewed twice 2 interviews for replacement staff	<u>NTT members:</u> 4 interviewed once
	<u>Other core NICE staff:</u> 6 interviewed once

That question of how many interviews is enough was a slight concern at the outset of the study with respect to having sufficient interview data to help answer the research questions. All the participants of the guideline group were interviewed, some twice at

different time points and there were many *ad hoc* mini-interviews and conversations to pin point views on specific issues. This, along with over 120 hours of meeting observation has provided data enough to answer the research questions. Interviewing all participants formally after the conclusion of the guideline development for their retrospective opinions of the whole process would have, perhaps, added to the detail of the findings of this research. However, this was not possible because of time and resource constraints with unforeseen delays introduced during the process, the difficulties of interviewing on days of the meetings due to time limitations and the disparate locations of the interviewees. Where there were not formal interviews at the end of the process, *ad hoc* interviews/questions were asked of respondents. These focused on their thoughts about the whole guideline development process.

A common dilemma for interviewers is whether to tape record the interview or rely on notes taken either during, or after, the interview (Kvale, 2007; Rabionet, 2011). Recording the interview will give an accurate recording which can be reviewed at any time but may create a distraction, may cause the interviewee to modify his or her responses and is time-consuming afterwards to systematically listen to and transcribe (Merriam & Tisdell, 2016). Having the facility to review the accurate detail of interviews plus to utilise verbatim comments in the analysis of the data and the formation of the research narrative, led to a decision to proceed with tape recording all formal interviews in this study.

Conducting face-to-face interviews has long been considered important to cement the relationship between the researcher and interviewee (Rubin & Rubin, 1995; Kvale, 2007). Face-to-face interviews permit non-verbal cues to be picked up and allow more detailed exploration and probing of opinions during the interview (Kvale, 2007; Perakyla & Ruusuvuori, 2011). However, the use of telephones and other video technology for interviewing has gained popularity (Holt, 2010; Hanna, 2012). Indeed, research has suggested that there are practical benefits, such as lower cost due to a reduction in travelling, being able to interview easily or anonymously in special and sensitive situations, and where differences in social status of interviewer and interviewee do not

impact the conduct of the interview (Stephens, 2007; Holt, 2010; Irvine, 2010). Further there is little reduction in quality of data produced (Sturges & Hanrahan, 2004).

With this in mind, both face-to-face and telephone interviewing were deemed suitable. The aim was to conduct face-to-face interviews in the first instance to allow rapport to be built between the researcher and the interviewees. Most interviews, (nineteen of twenty-two), were conducted face-to face. Three interviews were telephone interviews conducted as such due to time and geographical constraints. One of these was initially a face-to-face interview but this was concluded after five minutes when a fire alarm went off in the NICE offices. A telephone interview was arranged and then conducted at a later date. The telephone interviewing worked reasonably well, except on one occasion where interference on the line disrupted the recording temporarily. However, face-to-face communication was considered more important to permit observation of non-verbal language and, where possible, interviews were conducted in this way. Other sources of data were sought to support information given in interviews and from observation of guideline group meetings. This was in the form of review of relevant guideline documents and this is now considered below.

Documentary review

Documentary review in social science research is a widely used method with a wide variety of sources available (Bowen, 2009). The way documents are used is considered a methodological choice although critical discourse on its advantages, or disadvantages, in this respect, especially in qualitative research, is somewhat sparce (May, 2011). Documents may be used to provide contextual background, to generate further research questions, to complement and corroborate other forms of data, such as interviews, or to track development of an issue through a process (Bowen, 2009). The value of using documents as a source of data is that they are what Merriam and Tisdell (2016) describe as "stable", that is, the researcher cannot alter the source and so they remain independent of a research agenda. Documentary information is thought relevant to most case study topics (Yin, 2014). In this, they augment understanding of the case and provide a means of comparing the researcher's interpretation of events with what is recorded in case-related material (May, 2011).

Scott's (1990) categorisation of twelve types of document provides a means to characterise the various documents reviewed in this case study. It is useful since guideline development uses documents of many different types, Scott (1990), characterises documents by authorship (origin of document) and access (availability to people other than the owner) (see Table 4.8).

Table 4.8: Classification of documents

Access	Authorship		
	Personal	Official	
		Private/Non-state	State
Closed	1	5	9
Restricted	2	6	10
Open-archival	3	7	11
Open-published	4	8	12

Scott, 1990:14

Authorship can be personal which includes items such as personal letters or diaries, or official. The official category is split between state/governmental and items pertaining to non-state organisations. Closed documents are limited and seen only by those eligible; restricted documents are generally closed to those not eligible but can be seen after special dispensation is granted. Open documents may be seen by anybody with the difference between open-archival and open-published being that the latter are published specifically for public consumption (Scott 1990).

The documents reviewed for this research included the guideline topic referral, internal and external guideline group documents, the scoping document, the evidence base used by the guideline group and the draft and final guideline. Most of these documents were official documents, falling into the "open" categories and were accessible through the NICE website. Other documents falling into the open-published category, such as guidelines produced by other organised bodies like the Royal Colleges of the UK, were reviewed as appropriate. Some documents, notably the NICE protocol review questions evidence base, the health economic modelling assumptions data and the pre-edited

guideline recommendations fell into the restricted category. They were, nonetheless, available to review in this research although their use in this thesis was permitted only in their final published formats. Given the large amount of documents involved it is useful to classify them with regard to access and authorship. Table 4.9 maps the documents reviewed against the categories within Scott's (1990) classification.[3]

Table 4.9: Mapping of documents accessed

Access	Authorship	
	State (NICE)	*Private (non-state)*
Restricted	Review question evidence documents	Evidence (Commercial health economic data plus other data provided by GDEG members)
	Evidence (NICE health economic modelling assumptions)	
	Pre-edited guideline recommendations	
Open	Minutes of committee meetings	Evidence (published articles)
	Guideline topic referral	Guidelines of other relevant organisations
	Scoping document	
	Disclosure of interests register	
	Final evidence tables	
	Draft guideline and final published guideline	

Documents may be considered primary or secondary sources of data: primary sources are where the author of the document is recounting the focus of interest of the research first-hand. Secondary sources are those complied by authors who have not directly experienced or been involved in the phenomenon of interest (Merriam & Tisdell, 2016). Altheide and Schneider (2013) offer a third category of document, the "auxiliary" document. Here a document is used as a supplement to understanding the case but is not the main focus of

[3] The "restricted", "open", "state" and "private" categories are not those in use, nor recognised, by NICE

the research. The approach taken to documentary review in this research was aligned with Altheide and Schneider's (2013) auxiliary category: the documents provided a background scaffold to reflect what was being discussed during guideline group meetings, a record of the outcome of decisions made and a longitudinal record of the guideline process.

Data analysis

"Qualitative research works up from the data" (Richards, 2015:85) and data analysis, which involves opening up the data to explore ideas and themes, is one of the most challenging and exciting parts of qualitative research. Case study analysis is possibly one of the most important but least developed aspects of case study design with consideration of analytical approaches often coming a poor second to the development of the study/interview protocol (Yin, 2012). Whilst other research methods tend to follow routinised analytical protocols, qualitative case study analysis methods are more variable (Merriam & Tisdell, 2016). What is routine is that the data are first organised, often on some thematic basis using manual or computer-assisted technology, before being further explored and a narrative built. There is an argument that thematic analysis is simplistic and does little to critique the complexities of social processes. Despite this, thematic analysis was chosen for this research as it highlights salient constellations of both manifest and hidden meanings (Joffe, 2012) and has as its focus, identifying and describing both implicit and explicit ideas (Guest et al., 2012). It, therefore, aligns with this research's overarching interest in social processes. The thematic analysis approach of Braun and Clarke (2006, 2014) was followed for both the observation and interview data and the analysis process followed is now discussed more fully in the following section.

Thematic analysis

The thematic analysis was undertaken manually in this research as this was regarded to be the optimal way to maintain close contact with the data. Proprietary software coding tools have gained in popularity (Gilbert et al., 2014; Sotiriadou et al., 2014) and proponents of these packages for coding and content analysis suggest that using this approach provides a more transparent view of the data and an holistic audit of the analysis

process (Welsh, 2002; Rademaker et al., 2012). However, using such software leads to being guided in a particular direction, may add a quantitative element to qualitative research and increases the distance of researcher from the data (Rademaker et al., 2012), all reasons for the choice of manual analysis.

The approach of Braun and Clarke (2006, 2014) starts with familiarisation with the data and generation of codes. Searching for and naming themes follows, after which there is production of a report which presents the analysis with extract examples and relates the analysis to the research questions and literature. In this research, Chapter 6 (Findings) and Chapter 7 (Discussion) constitute the report.

The first phase, familiarisation with the data, involved initially transcribing the interview data. Transcription, while being the bane of some researchers' lives, offers the benefit of itself being an interpretive act and a key phase of data analysis within interpretive qualitative methodology (Bird, 2005). Transcription allowed the researcher to "re-hear" participants' voices and visualise the interview. This, sometimes, led to recollection of non-verbal cues and, since interviews were transcribed as the research proceeded, allowed further questions to be asked of the participants. Transcription was, therefore, a method of analysis.

There are various conventions for transcription offering differing levels of detail in the transcribed text and the convention or method used should fit the purpose of the analysis (Edwards, 1993). For this research, the aim was an orthographic transcript: a verbatim replica of all verbal speech and some non-verbal utterances such as coughs, or pauses where appropriate (Braun & Clarke, 2006). This provided, not just a faithful record of the interview, but also gave the researcher the opportunity to reflect on her interview technique and assess and refine the interview questions for subsequent interviews.

All transcripts were in the same format with no headers and footers and each participant was ascribed a code. A password-protected list was kept of the participants' details including name, location, and professional role, and role on the guideline committee. Although each respondent was not identifiable by name within the transcript, others'

names were often mentioned in the interview, as was the name of the researcher. This Tolich (2004) calls a breach of internal confidentiality or deductive disclosure (Kaiser, 2009) where individuals can become identifiable in research transcripts. This points to the challenges of anonymising qualitative data in sensitive contexts (Kaiser, 2009; Saunders et al., 2015). The ways of anonymising data in this study were described earlier in this chapter (see 4.4).

The transcripts were read and re-read before the start of coding. Also, a number of the interviews were listened to again in order to fully understand the context and tone of the conversation. The observation field notes were all typed up so that these also could be coded manually and extracts accessed easily using electronic word searching.

The generation of initial codes followed the Braun and Clarke process but other authors were drawn upon. Miles and colleagues (2014) suggest a number of ways of creating and categorising codes. Firstly, what are called "researcher" or "deductive" codes are generated *a priori* using the conceptual framework and research questions as a prompt. Secondly, what are termed "inductive" or "in-vivo" codes come from the data: these are phrases, words or terms used repeatedly by respondents during the course of interview and deemed interesting or important in the context of the research. One method may suffice in some types of research, grounded theory using only inductive coding, for example (Glaser & Strauss, 1967), but some have suggested that using both types of coding demonstrates rigour in analysing qualitative research (Fereday & Muir-Cochrane, 2006). For this research, both methods were employed.

Miles and colleagues (2014) also suggest further categorisation of coding can be achieved by considering how the data fits into the following groupings – descriptive coding, process coding, emotion coding, values coding. This method too was encompassed during the process of coding for this analysis.

For the first few interviews (5) and meetings (2), after the readings of the transcripts and observation notes, individual words, phrases and paragraphs were highlighted in the text. Coding involved a process of reading, and re-reading, transcripts and field notes while

asking the question: “what is this about?”. Codes were then assigned using the categories “descriptive”, “process”, “emotion” and “in-vivo” (or verbatim). Apart from the “in-vivo” category, codes were developed by the researcher with a focus on explicating both explicit and implicit ideas. Different colour highlights reflected what the researcher decided related to deductive or inductive codes. Coding notes were made in the margins and an overall transcript coding memo was generated. These highlights, notes and memos were converted into a first level coding framework which was then used for subsequent interview transcripts and observation notes. This is seen in Appendix iv.

The first level codes were condensed into higher level codes, collating data relevant to each code, to make the dataset more manageable. The higher level coding can be seen in Appendix v. For both the first-level and higher-level phases, as more data was generated, codes were changed or more added. It was an iterative process that continued throughout data collection and analysis (prior to theme generation).

After the coding, the search for themes commenced. This was an active process and themes constructed, rather than merely discovered, by reducing or clustering codes with reference to the research questions and chosen conceptual lenses. The themes should highlight meaningful and coherent patterns within the data and say something important about the data (Braun and Clarke, 2006). In order to facilitate theme generation, each code was transferred to an individual post-it note and placed onto blank sheets of paper attached to large boards. This was not necessary to start generating themes but visually helped the researcher organise the data. Codes were grouped in various ways: by deductive and inductive categories, by using the coding methods of Miles and colleagues (2014); by researcher consideration and intuition about how codes may combine and so on. The definition of themes was an iterative process with codes grouped into themes and then themes into meta-themes. Thematic maps were generated and relevant extracts collated. A thematic map example can be seen in Appendix vi.

When presenting the findings of this thesis, verbatim quotations are used to illustrate respondents’ perceptions, views and opinions of the guideline process. Verbatim quotations are said to be useful to illustrate what was said in different contexts and to

provide support for the researcher's interpretations. This allows readers to make their own judgement on the appropriateness of the researcher's interpretations (Anderson, 2010). However, there should not be multiple quotations with no common thread (Richards, 2015). With this in mind, the quotations selected were those that were thought to best illustrate the data themes whilst keeping a balance in terms of opposing viewpoints and using the whole range of study participants. The analysis results for this thesis are discussed in Chapters 6 and 7.

4.6 Summary

This chapter has outlined the research methodology, research design and methods adopted for this study. A researcher may have methodological preferences but the chosen methodology should be aligned with the type of research questions asked. This research was grounded in the underlying assumption that perceptions and individuals' social realities emerge from interactions with others. As such, a qualitative case study approach to elucidate the nuances and detail of the social processes of a guideline group and how they use evidence, interact and come to consensus decisions, was determined to be the best approach. Multiple lenses were used to view the guideline process and this introduced a certain degree of complexity to the study. Hence, it was useful to concentrate on a single case.

The case study approach for this research incorporated interviews of key guideline group participants and observation of guideline group meetings as well as documentary review of various guideline documents. The data gathered and analysed provided sufficient material to meet the aims of the research and answer the overarching research question.

Concerns about case study methodology within social sciences have been outlined but these are often unjustified. As Thomas (2015: x) puts it: "a case study provides a form of inquiry that elevates a view of life in its complexity".

Having set out the research questions and the methodology and methods used to answer these questions, the next chapter presents the generic NICE clinical guideline process to orientate the reader to the process before the findings of the study are presented.

Chapter 5: NICE and the Guideline Process

5.1 Introduction

This chapter provides contextual background for the case study. It details the environment within which NICE guideline groups operate and their usual membership and operation. The chapter starts with a section on NICE as the primary UK organisation that develops guidelines. The choice of NICE as a research setting has been touched upon in the Introduction Chapter and understanding how NICE and its broader network may influence guideline development is addressed in the Chapter 2 of this thesis; here, what NICE is and what it does is the focus. Given that NICE does not operate in isolation, it is set within the broader practice and policy setting of the health system in England and Wales. The remaining section of the chapter deals with the generic guideline development process.

5.2 NICE, the UK guideline developer

NICE is the primary body charged with developing guidelines within the UK although there are also regional bodies with which NICE interacts: GAIN – Guideline Audit and Implementation Network (in Northern Ireland) and SIGN – Scottish Intercollegiate Guidelines Network (in Scotland). The latter two bodies produce guidelines for their specific jurisdictions. Occasionally these are de novo guidelines but, more often, they revise and adapt an existing NICE guideline to the local situation. Guidelines on various topics also emanate from health professional organisations such as the Royal Colleges or from *ad hoc* advisory bodies funded by pharmaceutical companies or other organisations with vested interests in specific disease topics.

NICE is government funded but operates independently and has, since its inception in 1999, published guidance on hundreds of medicines and technologies (Steinbrook, 2008; Legido-Quigley et al., 2012), ranging from diabetes to blood transfusion to various cancers (NICE Guidance, 2017). NICE was established to provide consistency in access within the NHS to efficacious and cost-effective medicines and technologies. There are several forms of guidelines in various topic areas: clinical, social care and public health guidelines and other forms of guidance, (for example, Health Technology Appraisals

(HTAs)[4], interventional procedures and diagnostics guidance). Further services offered by NICE are development of quality standards and performance metrics in addition to a range of information tools for commissioners of health, social care and public health services. Where NICE recommends a treatment as part of a HTA, the NHS is legally required to fund that treatment should a doctor consider it clinically appropriate for their patient. All other guidelines and guidance produced are recommendations rather than practice mandates, although the Care Quality Commission, which oversees quality standards in healthcare practice, has an expectation that NHS health professionals will abide by NICE guidance in their clinical management (Rawlins et al., 2010).

The target audience for NICE guidance is wide: it spans individual health professionals to health service providers, to commissioners, to policy makers, to patients and their carers. There is no unified model for implementation of guidelines; each relevant local NHS or service organisation takes the guidance and implements it in its own way to fit its preferred pattern of working. NICE does, however, provide an "Into Practice Guide" which gives practical implementation advice.

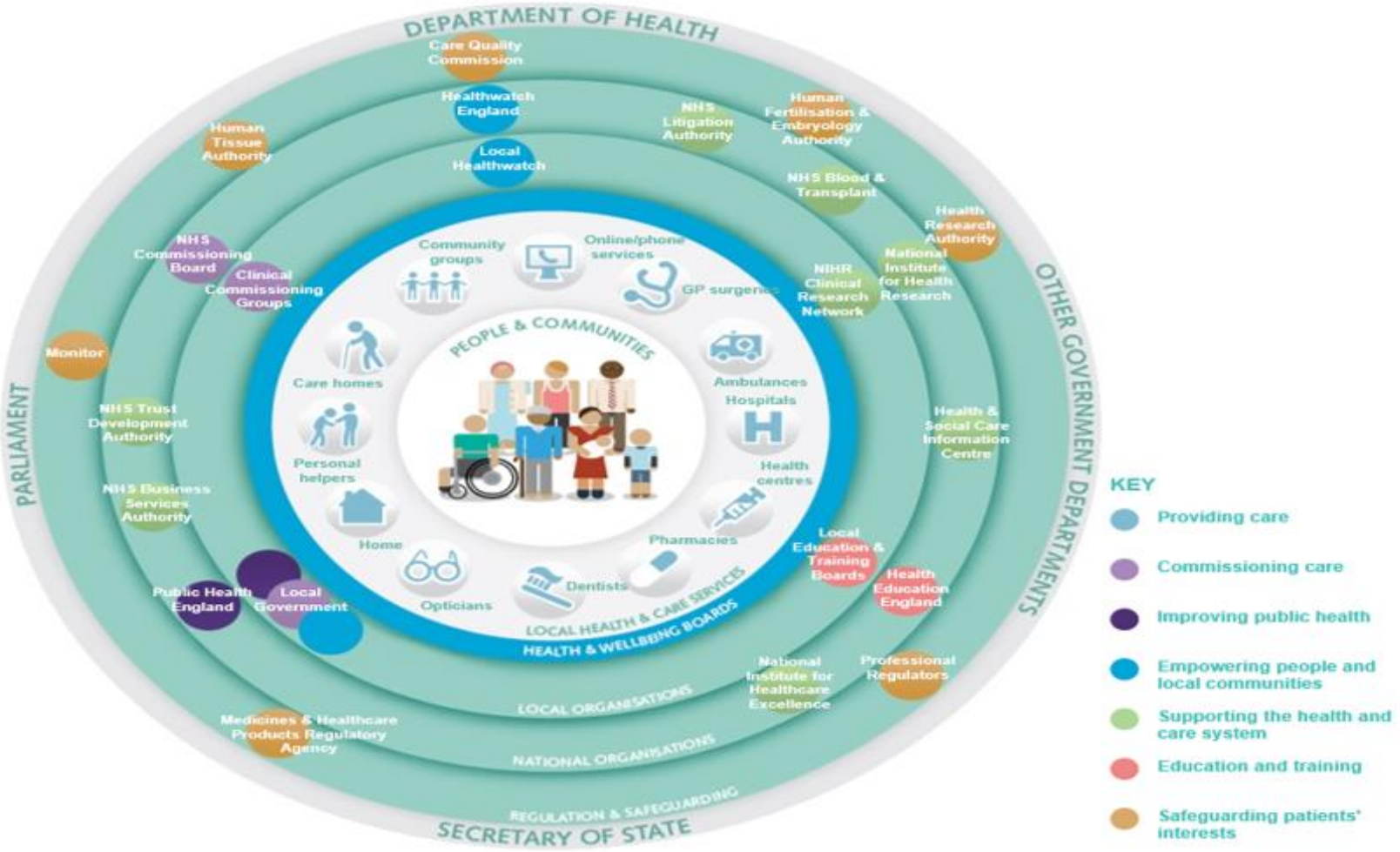
Taken together, NICE has a broad-ranging remit and far-reaching influence on the way health and social care is practised and provided in the UK. Whilst considered to undertake development of clinical guidelines and its other activities in an independent way, NICE does not exist in a vacuum; many actors can impact and influence the process. The health system in the UK is complex, not least because healthcare provision is devolved to the governments of Scotland, Wales and the Northern Ireland Executive in this country. Multiple systems, therefore, operate simultaneously although political and practical factors influence all the different systems similarly. Explaining all the nuances, similarities and differences of the healthcare systems operating in every part of the UK is beyond the scope of this thesis and, instead, the focus is on the wider healthcare system in England.

[4] Health technology appraisals are recommendations on the use of new or existing interventions within the NHS. They can be medicines, medical devices, diagnostic techniques or surgical procedures or health promotion activities

The last major re-organisation of the health system in England occurred in 2013. Figure 5.1 illustrates all the components of that system with NICE, situated in the bottom right of the diagram, linked closely to the Department of Health and subsumed in the "Regulation and Safeguarding" layer.

The new structure was put in place to deliver services to patients according to the Department of Health, Health and Social Care Act (2012). Patients are at the centre of the system provided for by local services such as GP surgeries, community health hubs, hospitals and care homes. These services are bought for patients by local Clinical Commissioning Groups, comprised of local doctors, nurses and allied health professionals. Local councils have taken the responsibility for promoting public health and health and well-being boards in each local area ensure services are dovetailing efficiently. National bodies such as NHS England, Public Health England and Health Education England provide national support and expert services for local agencies. Organisations, like NICE, within the "Regulation and Safeguarding" layer, provide centralised guidance and monitoring services.

Figure 5.1: The healthcare system in England



Department of Health (2013)[4]

Individual healthcare institutions will not be reviewed in detail as most are not directly relevant to this thesis[5]. Rather, a number of key shifts in policy and other external issues which have impacted, or will in the future, the way healthcare is delivered, are highlighted. These are the ones that relate to this PhD topic in that they may alter the way NICE operates.

Firstly, as illustrated in Figure 5.1, patients are at the centre of healthcare. There is much empirical research to suggest that patient involvement in planning and delivery of healthcare is beneficial to outcomes and cost containment (Crawford, 2002; Coulter, 2005, Batalden, 2016). However, critical voices have pointed to contested areas of this consumerist agenda, such as, the meaning of "choice" in public services delivery and operationalisation problems (Jung, 2010). In spite of this and guidelines remaining disease-focused rather than patient-focused (Shaneyfelt, 2012), NICE has responded to the need for greater attention to a patient perspective on healthcare: lay members (patients, carers, family members) are included in NICE guideline decision-making groups to relate their direct experience of the disease. Further, one form of the guideline produced is specifically for patients and the general public. Also, NICE has recognised that the internet and other forms of communication are used by patients as alternative ways to access health information; thus, another format of each guideline is a web-based interactive map.

In 2014, various partner organisations were involved in developing the "NHS Five Year Forward View" (NHS England, 2014), a vision of how health strategy would have to change in the future if the gaps between population health, social care and available funding were to be narrowed. Full integration of health and social care by 2020 is the aim although the complicated nature of achieving this has already been demonstrated by the failure of the primary integration initiative in England, The Better Care Fund, to meet its benefit objectives in its first year of operation in 2015/6 (National Audit Office, 2017). NICE has also acknowledged the closer alignment of health and social care by

[5] More information and description of the new system may be found at www.gov.uk/government/publications/the-health-and-care-system-explained

amalgamating the guidelines methodologies into one common methodology for clinical, social care and public health guidelines. Furthermore, NICE guidelines in development now include service provision, compliance with treatment regimens and patient experience.

Pressures on resources have led to calls for greater participation for third sector organisations in contributing to services as well as playing a role in service policy and planning (Wyatt, 2002; Department of Health, Cm 6737 2006; Baggott & Jones, 2014; Bull et al., 2014). It is currently unclear how the charitable sector should integrate their efforts with the health and social care services. Despite some suggesting their involvement is open to government or professional manipulation (Baggott & Jones, 2014), it is likely that voluntary organisations will play a higher-profile role in the future, thus changing the landscape of the health services and with uncertain implications for NICE.

Finally, in June 2016, one major factor emerged that will have profound effects on health services: that of the UK leaving the European Union, so called "Brexit". These effects too are unclear as yet, but Brexit issues affecting the health services such as staffing and working regulations, funding and finance and cross-border co-operation on disease control will need to be addressed at a time of political and economic uncertainty (The King's Fund, 2016, Costa-Font, 2017).

Having reviewed what NICE is and set it in a broader context, the next two sections detail the generic guideline process followed by NICE and the generic guideline group membership and structure.

5.3 The clinical guideline process

Guideline development follows a generic process which is now common for clinical, social and public health guidelines. The process is laid out in explicit detail in the NICE manual of processes and methods (NICE, 2014, updated 2017). This is a guide developed mainly for NICE staff and contractors (such as those commissioned to do evidence reviews) and expert group members. However, it also has a wider audience, such as other guideline developers and stakeholders who participate in the guideline process; its impact

and relevancy thus extends out with the immediate NICE environment. Described here is each step of the process to orientate the reader to the formal guideline process followed in the macular degeneration guideline development. Each step in described but more detail is provided for the step where the interactions of the guideline group under study, and their use of evidence, are salient in determining guideline recommendations. This step is: "Guideline Development". All sequential steps in the process can be seen in Table 5.1, adapted from the generic NICE process pathway (Appendix vii).

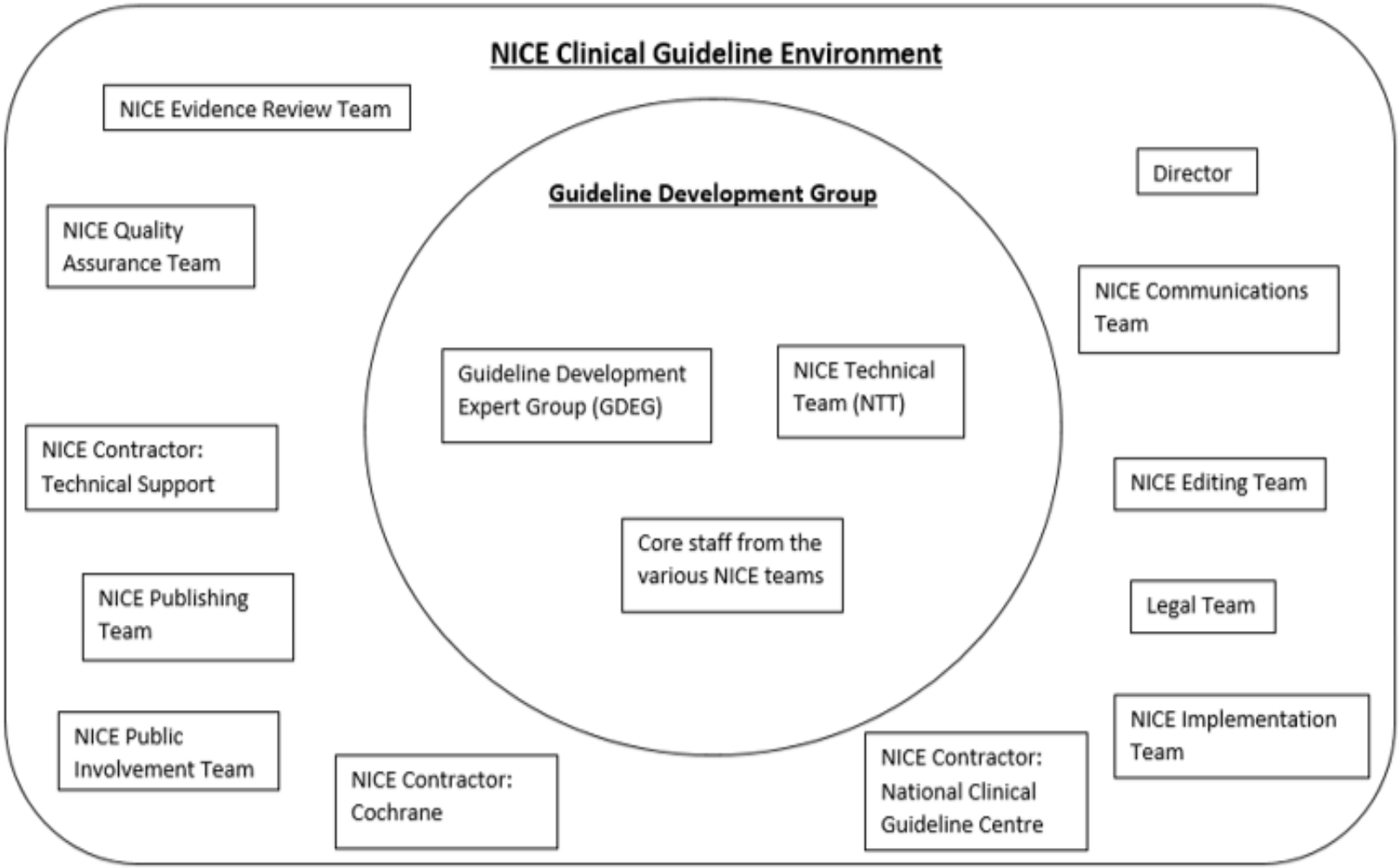
Table 5.1: The sequential steps of the clinical guideline development process

Steps	Title	Description
1	Topic referral	The disease subject for guideline development referred to NICE by the Department of Health
2	Scoping	The boundaries for guideline development are set by NICE with input from experts and other stakeholders
3	Guideline development	Questions to be addressed are agreed, literature gathering and evidence reviews undertaken, recommendations are drafted
4	Draft guideline consultation	The draft guideline is put out to stakeholders for consultation
5	Guideline revision	Stakeholder comments are reviewed and, where appropriate, the guideline recommendations are amended
6	Guideline sign-off	The NICE Guidance Executive signs off the guideline for publication
7	Publication	The guideline is published in various formats alongside resources to support implementation
8	Updating	The guideline is reviewed regularly and updated appropriately according to the usual process

Adapted from NICE Manual 2014, updated 2017

The explanation of the generic guideline process will reference several teams and groups involved. In this case study, the Guideline Development Group (GDG) is a key focus. Figure 5.2, below, depicts how this group sits within the immediate NICE environment.

Figure 5.2: The guideline development environment at NICE



Each guideline topic is assigned to a GDG. This is the central group managing the guideline process for one guideline topic but the group interacts with various internal NICE teams or other external bodies contracted by NICE. There are various external stakeholders (not depicted in Figure 5.2 as they are too numerous), such as the Royal Colleges, the Department of Health and pharmaceutical companies, who input to the guideline or interact with the GDG and other NICE teams. There are many linkages between all these groups, for example, between various NICE teams and the GDG, between the Department of Health and the Directors of NICE, between contractors and NICE teams. Again, the linkages are too numerous to depict without the figure becoming confusing and are, therefore, not included in Figure 5.2 [6].

Topic referral (Step 1)

Suggestions of topics for new guidelines come from a number of sources, for example, NHS England, the Department of Health, or health professionals. Selection panels, administered by NICE, review and discuss these topics for possible guideline commissioning. An annual programme for the development of NICE guidelines is agreed with the Department of Health, taking into account work capacity of NICE teams and contractors. Long and short lists of topics are prioritised by considering alignment with national priorities, impact on outcomes frameworks in healthcare, social care and public health, or the disease topic being a significant burden of care with increased mortality or reduction in quality of life. Once agreed, a new guideline is commissioned and formally referred to NICE from the Department of Health and becomes part of the annual NICE programme (NICE Manual 2014, updated 2017).

After referral, guideline development is either managed by an internal NICE team or contracted out to specialist guideline development centres. For acute and chronic clinical conditions this is the National Clinical Guideline Centre (NCGC), funded by NICE and hosted at the Royal College of Physicians in London. Even where the main development is undertaken by an internal NICE team, the NCGC may be contracted to assist with part of the guideline work.

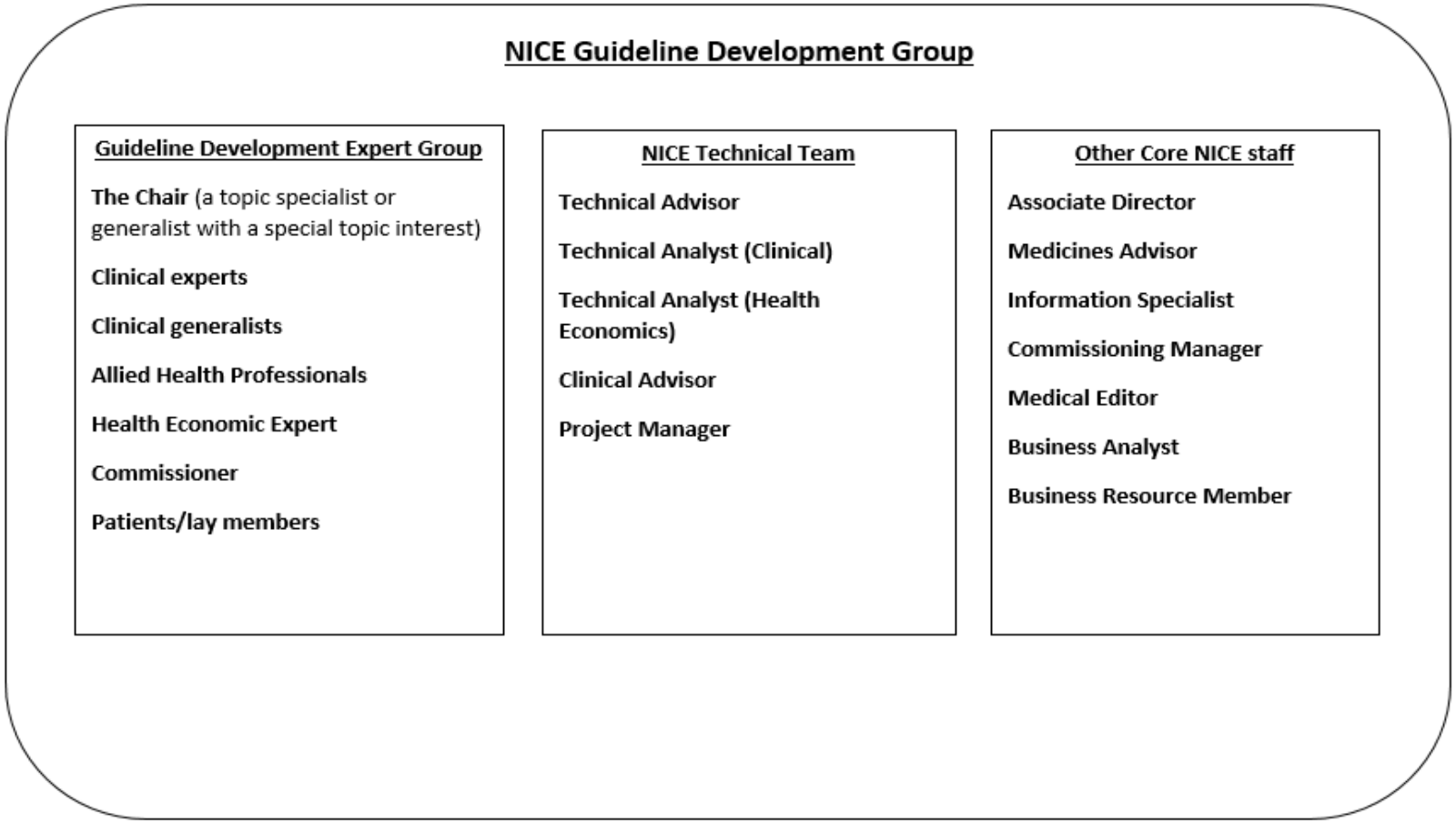
[6] For more information see: www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf

Scoping (Step 2)

Scoping makes clear what will be included, and what will not, in the guideline. The scope focuses on key issues/questions and the economic perspectives to be used and defines the populations and settings to be included. The scope is drafted by NICE staff from the specific guideline group, the chair of the Guideline Development Expert Group (GDEG) plus one other expert participant from the group, both of whom contribute topic expertise, and other NICE staff from the various teams assigned to each GDG. The draft scope is signed off by a senior member of the NICE Quality Assurance team and is then sent out to registered stakeholders for input on whether the key issues/populations identified in the scope are accurate and relevant. The final scope, amended as appropriate, is again signed off by a senior Quality Assurance official and no changes should be made to the scope from this point except in exceptional circumstances such as withdrawal of a relevant drug from the market.

Recruitment of the other experts who sit on the GDEG is on-going during Step 2. The GDEG sits alongside the NICE Technical Team (NTT) specific to one guideline and these two groups, together with other core NICE staff, constitute the GDG for one guideline. Figure 5.3 illustrates a generic NICE Guideline Development Group.

Figure 5.3: The generic NICE guideline development group



The GDEG is made up of a group of professionals who are independent of NICE. The GDEG is a decision-making body and draws on multi-disciplinary members with expertise in areas defined by the scope. Members include topic experts who bring knowledge and expertise (but do not represent their organisations) and lay persons with relevant personal experience or knowledge of those affected by the disease. Other individuals are recruited for their experience in health service provision, for example, commissioners of services, or for their expertise in health economics or epidemiology. Each participant has equal status in decision making and the expertise and knowledge of each person is formally acknowledged as being at the same level in contributing to the process (NICE, 2014, updated 2017:42). Appendix D of the NICE manual (NICE, 2014, updated 2017) sets out the terms of reference for guideline group expert members and this includes, not only advising on the effectiveness of interventions, action and measures, but also offering advice on best practice where research evidence is absent or poor. Each member should be free of any conflicts of interest such as receiving remuneration from relevant drug manufacturers. There is a NICE policy and process in place (NICE Policy on Conflicts of Interest, 2014) to maintain the impartiality of GDEGs and each member must declare, at the start of the guideline process and at the start of every guideline group meeting, possible conflicts of interest. Declarations of interest are published with each set of minutes and in the final guideline. The exact composition of the GDEG is tailored to the guideline topic and NICE "aim for diversity in membership, an objective in NICE's equality policy" (NICE, 2014, updated 2017:42). GDEG members are not paid for participation but do receive travel and accommodation expenses.

The GDEG works alongside various staff from NICE. The most important group of staff have been named as the "NICE Technical Team" (NTT), although this is not a recognised NICE "term". This group mainly comprises technical people and this is what differentiates them from the group labelled as "other core NICE staff". Most of the NTT are assigned to one specific guideline although some of the individual members may contribute to more than one guideline, for example, the clinical advisor and project manager. The NTT are responsible for collating and presenting evidence, providing input on technical aspects of the evidence and the NICE process, and managing the recommendation/guideline formation. There are at least two technical analysts in the NTT:

a clinical evaluation expert and a health economist. The work of the technical analysts is overseen by the technical advisor. The NTT are complemented by individuals from other core NICE teams offering advice and expertise when required.

Guideline development (Step 3)

At this stage, the full GDG has been formed and the most important part of the guideline development process commences. At this point, the review questions are shaped, the evidence to address the questions is gathered, presented and debated, and guideline recommendations are drafted.

Review questions

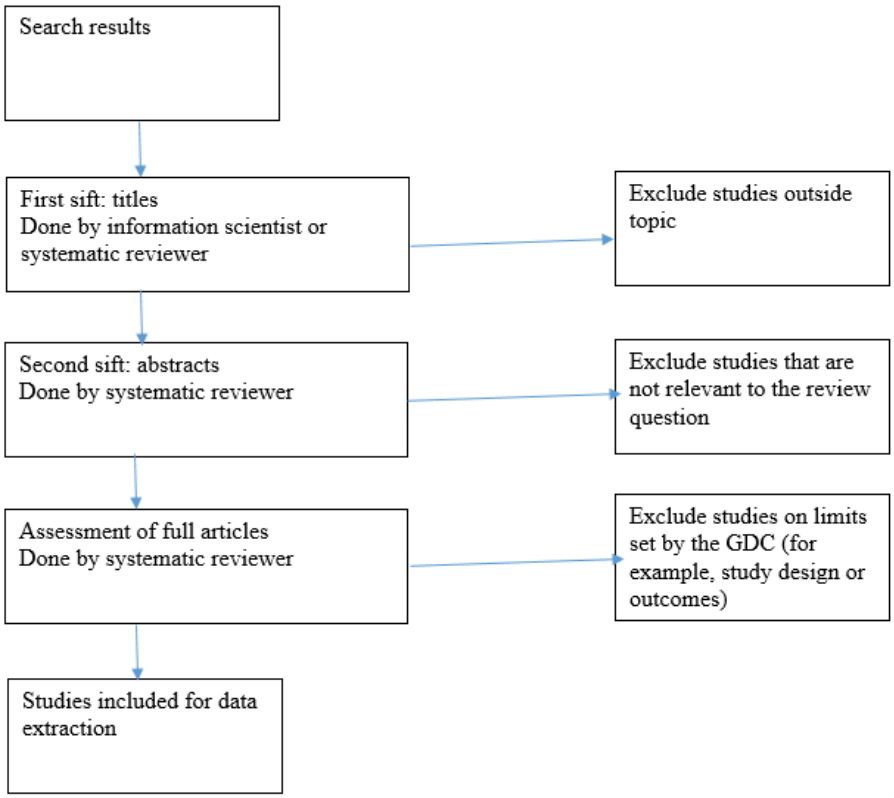
These are developed from the key issues identified in the scope and define the boundaries of each specific guideline process. They act as the framework for the literature searches, inform the evidence review and guide the setting down of recommendations. They are developed by the NICE technical team with refinement by the GDEG. A "Patient, Intervention, Comparison, Outcomes" framework (Richardson et al., 1995) is used for structuring the questions and ensuring enough specificity for a comprehensive literature search.

Literature review

According to the NICE manual (NICE, 2014, updated 2017), evidence to support guideline recommendations may be obtained from a number of sources including randomised controlled trials, cohort and observational studies and expert opinion. The manual also sets out the type of evidence that is used for different review questions: quantitative studies are the primary source of evidence for questions concerning effectiveness of interventions and qualitative studies for patient experience and views on different treatments and services. For each review question, a systematic review is conducted by members of the Evidence Review Team working with the NTT. The process for economic evaluation is similar to that for clinical evaluation in that databases are searched for relevant economic evaluations and a systematic review is conducted. The economic evaluation differs from the clinical evaluation in that, where data is sparse or inconclusive, priority areas are selected for economic modelling. A schematic, adapted

from Hill and colleagues (2011) of how NICE selects studies, is shown in Figure 5.4. This was published in 2011 and NICE processes continue to evolve but the schematic remains aligned with current NICE processes (NICE, 2014, updated 2017:81).

Figure 5.4: Diagram of the NICE literature search and selection process



Hill et al., 2011:754

Numerous databases, such as the Cochrane Database of Systematic Reviews, Embase, Medline, NHS EED (Economic Evaluation Database), are searched with the intent that the search will reveal sufficient data specific to the review question but not an overwhelming amount of material. Usually a few thousand titles are sifted at the initial stages and articles are rejected on the basis of being outside the topic or not having inclusion criteria or outcomes that are relevant or not having an appropriate study design or publication mode. Other criteria such as language other than English or date of publication or participant age or unpublished data may also preclude inclusion in the search results. Further evidence may be sought from on-going trials that have yet to be

published. This would be in a situation where NICE staff or the experts believe the evidence may be helpful to address the review questions. In this case a "call for evidence" is sent out to the relevant stakeholders. The selection of data for inclusion privileges randomised controlled trials especially where the review question concerns the effectiveness of an intervention (Higgins & Green, 2011). However, this does not preclude other types of studies being considered (NICE, 2014, updated 2017).

An assessment is made of the quality of the evidence gathered to improve confidence in making guideline recommendations. A number of formal evidence grading systems are in use (Schünemann et al., 2003, 2008) and the NICE assessment uses two approaches. Individual studies are rated using a checklist appropriate to the study design (NICE Manual, Appendix H, 2014, updated 2017). Quality ratings are shown in Table 5.2.

Table 5.2: Individual study ratings

++ All or most of the checklist criteria have been fulfilled, and where they have not been fulfilled the conclusions are very unlikely to alter.
+ Some of the checklist criteria have been fulfilled, and where they have not been fulfilled, or are not adequately described, the conclusions are unlikely to alter.
– Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

NICE Manual 2014, updated 2017:96

The second approach uses GRADE (Grading of Recommendations, Assessment, Development and Evaluation) criteria (Atkins et al., 2004). GRADE assesses quality by outcome across multiple studies. Prior to the GRADE assessment, each outcome to be considered is assigned a relative importance to decision making. For each "critical" and "important" outcome in intervention studies, the features shown in Table 5.3 are assessed.

The effect size, the effect of all plausible confounding factors and evidence of any dose-response relationship are also considered for observational studies. The quality of

evidence is then rated as “high”, “moderate”, “low” or “very low”. The description of each of these ratings can be seen in Table 5.4.

Table 5.3: Evidence features assessed

Study limitations (risk of bias) – the internal validity of the evidence inconsistency – the heterogeneity or variability in the estimates of treatment effect across studies **Indirectness** – the degree of differences between the population, intervention, comparator for the intervention and outcome of interest across studies **Imprecision** (random error) – the extent to which confidence in the effect estimate is adequate to support a particular decision **Publication bias** – the degree of selective publication of studies.

NICE Manual 2014, updated 2017:97

Table 5.4: GRADE quality ratings

High – further research is very unlikely to change our confidence in the estimate of effect. **Moderate** – further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low** – further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low** – any estimate of effect is very uncertain.

NICE Manual 2014, updated 2017:98

Summaries of the evidence together with quality assessments and economic analyses are then prepared for the GDEG to review, debate and come to consensus about how the evidence will support guideline recommendations.

Formation of recommendations

A published guideline contains the recommendations made by a guideline group, the evidence on which they were based and the methods used to develop them. Included are

details of how a guideline group reached its decisions, the rationale for their recommendations and the considered impact on practice. In short, as the NICE Manual puts it, "The guideline recommendations are the distillation of the Committee's development work", (NICE, 2014, updated 2017:161). In the guideline publication, there is an "Evidence to Recommendation" table for each review question addressed. Here, how the guideline group reached its decisions from the evidence is set down, as well as any issues impacting the decision. The categories addressed are detailed in Table 5.5.

Table 5.5: Evidence to recommendation categories

Category	**Considerations**
Relative value of different outcomes	Which outcomes were considered and their relative value; any issues with selected outcomes
Trade-off between benefit and harms	The importance and magnitude of the benefits and harms of an intervention and whether there is any potential for unintended consequences; whether the recommended intervention supersedes an existing one; whether recommendations made impact on health inequalities
Trade-off between net health benefits and resource use	How costs, resource implications and economic considerations were made; this may be by use of a model or more informal considerations
Quality of evidence	GDG agreement for the Evidence Statements; uncertainty of the evidence and details of any biases
Other considerations	Potential impact on population health; any extrapolation to other populations; any ethical issues or policy imperatives taken into consideration

Adapted from NICE Manual 2014, updated 2017

Once the evidence is debated, the guideline group start to draft recommendations. Recommendations are formed on the quality of the evidence but the group must also consider the strength of the recommendation they are making. NICE has used the GRADE system previously but now favours reflecting the strength of a recommendation by the wording used. Guideline groups are aided by a NICE "Writing Guide" (NICE Style Guide, 2016) which describes what each verb used means. So, for example, NICE uses "offer"

to express a strong recommendation and "consider" to reflect evidence with a less certain benefit. The wording "must" or "must not" conveys a legal duty to apply the recommendation and is the strongest language used in recommendations. Where there is little, or no, evidence on which to base a recommendation, either a research recommendation or no recommendation can be made.

The clinical and health economic evidence is presented by the NTT to the GDEG in several closed meetings. The core participants of these meetings are the GDEG and the NTT plus others as required, for example, co-opted experts in health economics or members of other NICE teams. No draft recommendations can be agreed unless the GDEG is quorate, that is, there is 50% or more of the membership present. Several iterations of a recommendation are common with input from the NICE Editing Team and with some of the discussion occurring outside of the meetings. The recommendations addressing each review question are finalised and collated, together with the evidence, to form the draft guideline.

Consultation, revision and sign off of draft guideline (Steps 4, 5 and 6)

NICE undertakes a validation process for draft guidelines to allow peer review and quality assurance. The draft guideline is posted on the NICE website for consultation by registered stakeholders for a period of six weeks. Alongside the draft guideline, there is a set of questions for the stakeholders; these questions seek specific views, such views on potential inequalities or excessive costs of the guideline recommendations. The stakeholders include organisations who produce relevant medicines such as pharmaceutical companies, organisations led by people using services or representing the interests of people with the condition, and commissioners and providers of health services.

There may also be targeted consultation where NICE seeks views on the feasibility of implementing the draft recommendations. This is known as "fieldwork" where NICE tests the recommendations directly with patients affected or service providers to see how the recommendations might work in practice. NICE may also commission a review of the health economic and statistical data of the guideline or ask for further expert input during the period of consultation.

All stakeholder responses are collated by the NTT and presented to the GDEG. The comments are considered by the GDEG and changes incorporated in the recommendations, as deemed necessary. Each stakeholder comment is responded to directly by the NTT with information included about whether their comment changed the recommendation or, if not, why not.

The guideline is then subject to a quality assurance process within NICE. This includes a check of any changes to the guideline recommendations and that responses to stakeholder comments are appropriate. The NICE Guidance Executive, comprising NICE Executive Directors, the Centre for Guidelines Director and the Communication Director sign off the guideline as ready for publication.

Publication of final guideline (Step 7)

The final guideline is released two weeks in advance to stakeholders who have commented on the draft guideline. This is to give them an opportunity to highlight any substantial errors and prepare themselves, and their organisations, for publication and subsequent implementation of the guideline. It is not a further opportunity for comment. The final guideline and supporting documents, such as tools for implementation are published on the NICE website simultaneously. The GDEG and NTT work with the NICE Communications team on strategies to promote the guideline. NICE raise awareness of the guideline by such means as press releases, notifications to stakeholders of its publication and publicising its release through newsletters and social media. Four versions of each guideline are published for different audiences: the full version details all the evidence, methods and the links between evidence and recommendations, the short version (also confusingly termed “The NICE Guideline”) contains the recommendations only. There is an interactive, web-based map version called “Pathway” and a version containing easily understandable language for patients, carers and the general public.

Updating guidelines (Step 8)

NICE is committed to ensuring that guidelines remain current and accurate. Therefore, a check of the need to update a guideline is usually undertaken every two years, or at least four years, from initial publication. The intent is to identify recommendations within the

guideline that have become outdated by changes such as new treatments arriving onto the market or alterations in policy or legislation. The checks include a review of the literature and "intelligence gathering" (NICE, 2014, updated 2017:196) which encompasses responses to questionnaires, external enquiries, related NICE guidance and quality standards and medicines licensing information. Topic experts are also surveyed for their opinions on the current relevance of published guidelines or their knowledge of anything new that could impact the guideline recommendations. A number of options for updating guidelines are available: no update, a partial update within the scope of the published guideline, a partial update with a modified scope, a refreshing of the wording of recommendations, withdrawing some recommendations or the whole guideline, a full update within the scope of the published guideline or a full update with a modified scope. The final decision on the need and type of update is taken by NICE's Guidance Executive. Updates to guidelines follow the same philosophy of transparency and robustness and follow the same methods and processes as described in earlier sections of this chapter.

5.4 Summary

This chapter has set out the generic NICE clinical guideline development process. It has detailed the steps of the usual guideline process with specific focus on the guideline development step of the process. This focus is because this step is the main one where interactions of the guideline group members occur. The chapter has detailed too who, and what, constitutes the central group responsible for the guideline process, the Guideline Development Group. The group contains the Guideline Development Expert Group and the NICE Technical Team, (these constituting the main study subject in this thesis) plus other core NICE staff from various NICE teams. It has also placed the GDG within the NICE environment which includes all the various NICE teams who may also contribute to the guideline process. As NICE does not work in isolation and is influenced by its environment, the chapter has given information about how NICE sits within the wider health policy and government context in England. The next chapter moves on to the findings of this case study of the development of one guideline: the Age-related Macular Degeneration, Diagnosis and Management guideline.

Chapter 6: Findings

6.1 Introduction

This chapter sets out the main findings of how a multi-actor group, responsible for developing a clinical guideline for macular degeneration interacted and used evidence.
A multi-perspective framework was utilised for data collection and analysis and this framework is used to organise the findings. Each part of the chapter is organised by themes derived from the data analysis. Illustrative verbatim quotations are sourced mainly from participant interviews and from the researcher's reflections diary. Verbatim data from group meetings are not detailed due to issues of confidentiality. The chapter is structured in four parts.

The first part starts by setting out the key timelines for this case study. Then information is given about the specific guideline topic of macular degeneration. The provision of certain treatments for macular degeneration is controversial so this is covered in detail. This is to orientate the reader and set the scene for the main findings that follow. This part of the findings chapter also characterises the study subject group. The group's structure, and changes to it over time, their motivations for participation in the guideline process and their perceptions of guidelines are set out here.

The second part of the chapter addresses findings related to the evidence on which the guideline is based. Described are the sources of evidence used as the support for guideline recommendations, the availability and acceptability of that evidence, the application of a strict hierarchy of evidence, and the use of expert opinion as evidence.

The third part details findings related to how the group functioned and interacted during the guideline's development. This includes the roles adopted by group members and how the guideline process was facilitated, how evidence was converted to guideline recommendations, and how the group functioned and interacted during the guideline development period.

The fourth part of the chapter examines how the broader network influenced the guideline outcome. Key influences, such as the political/legal environment, the availability of resources and the impact of external stakeholders on this case study are described.

6.2 Part 1. Specific case characteristics

This part of the chapter starts with the key timeline events and a discussion of the disease topic addressed by this guideline. It then moves on to detail the characteristics of the guideline group with respect to its composition (including changes to this over time), the motivations of individuals to participate, and their perceptions of what guidelines are and for whom they are written.

6.2.1 Key timeline events

The key events of the development of the macular degeneration guideline are shown below in Table 6.1. The NICE manual (NICE, 2014, updated 2017) sets out a timeframe of 12-27 months for development of a guideline from the scoping stage to final publication. For this guideline, the time taken was 37 months in total, indicating the breadth of the guideline subject. It also reflects specific issues impacting the guideline timeline, for example, a delay occurred due to the General Election in June 2017. This is highlighted in the timeline below and addressed further in 6.5.2 of this chapter and in Chapter 7. This case study research followed the events between Oct 2015 (second formal guideline group meeting) and Jan 2018 (publication of final guideline).

Table 6.1: Key events during the development of the guideline[7]

Date	Event
1 Dec 2014	The topic referral received from the Department of Health as part of NICE's work programme.
8 Jan 2015 – 8 May 2015	Guideline scope developed
8 May 2015 - 8 Jun 2015	Draft scope consultation period.
27 Oct 2015	Scope published
4 Sep 2015 - 13 Feb 2017	Guideline development group meetings: discussion of the 25 review questions (Appendix viii). Guideline recommendations developed.
2 Mar 2017	Pre-consultation documents released
18 Apr 2017	Consultation dates and publication date for this guideline revised to account for further development work.
June 2017	Consultation for this guideline postponed, in part due to the General Election
13 Jul 2017	Draft guideline put out for consultation of stakeholders
24 Aug 2017	End of consultation period
6 and 18 Sep 2017	Post-consultation guideline group meeting
23 Jan 2018	Final guideline published

6.2.2 Specific topic discussion - macular degeneration

Macular degeneration is a degenerative retinal disease affecting part of the retina, the macula, upon which incoming light is focused. A competent macula is crucial for clear central vision and fine image detail and quality. A diseased macula results in loss of central sight such that an affected person has a large black area in the middle of their field of vision (Figures 6.1 and 6.2).

[7] Note: prior to this guideline topic being referred to NICE, macular degeneration treatments had been the subject of a Health Technology Appraisal (TA155). Further information may be found at https://www.nice.org.uk/guidance/ta155

Fig 6.1: View of person with normal vision

Fig 6.2: View of patient with macular degeneration

Photos credit: J Hughes

It results in loss of the ability to read, use a computer, drive and many other activities of daily life. Thus, macular degeneration causes considerable disability (Lotery et al., 2007; Soubrane et al., 2007).

Whilst a number of different pathogenic states can cause macular degeneration at any age, the overwhelming majority of sufferers have age-related macular degeneration (AMD) causing changes in the layers of the retina and loss of sight. Indeed, in the developed world, it is the leading cause of irreversible blindness in patients over 60 years of age (Lim et al., 2012; Wong et al, 2014) and is the ophthalmic disease with the greatest growth prediction (seekingalpha, 2013), mainly due to the changing population demographic.

Prevalence estimates are difficult to produce since there are differing stages of the disease, various classifications systems are in use, not all those with the disease choose to be registered, or even qualify for sight-loss registration, and studies used to generate the data have varied characteristics (Owen et al., 2012; Ferris et al., 2013). However, various studies and meta-analyses have shown the prevalence to be increasing (Klein et al., 2010; Owen et al., 2012; Wong et al., 2014). In the UK, Minassian and colleagues (2011) estimate the number of patients afflicted with macular degeneration to rise to more than 750,000 by 2020. This has clear implications for healthcare provision strategies and planning especially with regard to cost containment.

The management of macular degeneration consisted, until recently, of lifestyle modification (smoking is a major risk factor), ingestion of anti-oxidant vitamin supplements or laser treatment (Jager et al., 2008). The main cause of visual loss in macular degeneration is the growth and bleeding of friable new blood vessels in the eye (called neovascular AMD). In 2008, a treatment was introduced: inhibitors of Vascular Endothelial Growth Factor or anti-VEGFs. They are also known as "anti-angiogenic"[8] agents and this term is used throughout this thesis. These drugs are injected into the eye under local anaesthesia, sometimes on a monthly basis, where they counteract the exudation from the leaking blood vessels. However, improvement in vision occurs in only a third of patients and 10% of patients do not respond at all (Moutray & Chakravarthy, 2011). Further, the costs of these injections are very high.

Treatment with anti-angiogenic agents has caused much controversy in the UK and has raised questions about how regulatory rules and legal positions can shape clinical management (Lock, 2014; Cohen, 2015a). The controversy is centred on two main anti-angiogenic agents: ranibizumab and bevacizumab. The former has a marketing licence held by the pharmaceutical company Novartis and an approval by NICE for treatment (and reimbursement) of neovascular AMD in the UK. Bevacizumab is licensed for other conditions, such as cancer, where new vessel growth is also an issue but it does not have a licence for AMD. Novartis also has the marketing licence for bevacizumab for these other indications. Bevacizumab is increasingly being used "off-label" (outside its licensed indications) for AMD by clinicians in the UK, supported by a Cochrane report comparing the two agents which suggested there were no major differences in visual outcomes (Solomon et al., 2014). However, the major difference highlighted by the report is cost. Estimates of cost for ranibizumab per injection are £1500 versus £40 for bevacizumab and the use of bevacizumab rather than ranibizumab could free more than £100M per year for other health services (Dakin et al., 2014; Cohen, 2015a). Publicly-funded trials of the effect of bevacizumab in AMD have sought to provide an evidence base for a NICE recommendation for its use but that path has not been smooth with accusations that the trials are being thwarted by the pharmaceutical companies, in some cases, in conjunction with vision charities (Cohen, 2015a)

[8] Anti-angiogenic: prevents abnormal blood vessels forming

It is against this background that in December 2014, the referral from the Department of Health was received by NICE to develop the first comprehensive clinical guideline for AMD: "Age-related Macular Degeneration: Diagnosis and Management". With respect to the controversy concerning anti-angiogenic agents, there was a note within the guideline scope, reproduced in full below:

> *"Note that guideline recommendations will normally fall within licensed indications* [conditions for which a drug is licensed]; *exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients. Although bevacizumab is in use in the UK and elsewhere for the treatment of neovascular AMD, the Medicines and Healthcare Products Regulatory Agency regards it as unlicensed for this indication because its use requires the formulation of the licensed product to be divided into separate smaller doses (to produce multiple aliquots) for injection into the eye. Licensed alternatives (such as aflibercept, pegaptanib sodium, ranibizumab and verteporfin) are available. Although there is evidence (including research funded by the National Institute for Health Research) demonstrating the safety and efficacy of bevacizumab for treating AMD that will be referred to in the guideline, our ability to refer to its use in routine clinical practice for this condition is constrained by its licensing status. Therefore, while bevacizumab will be included in the evaluations carried out to develop the guideline, and information on its properties and use may be included in the final guideline, no recommendation for its use will be made in any case where there is a licensed alternative.*"
>
> Source: NICE AMD Appendix B: Guideline Scope 2018:3

This illustrates the difficulty for the guideline development committee in that bevacizumab is in routine (off-label) use and there is evidence available of its efficacy and safety. Furthermore, while the guideline group had been given instructions to include the drug in their deliberations, they were also told that they could not make any formal recommendations about its use. The effect of the controversy around anti-angiogenic

treatments for macular degeneration on the functioning of the guideline group and this guideline process is discussed within section 6.5.1 of this chapter and in Chapter 7.

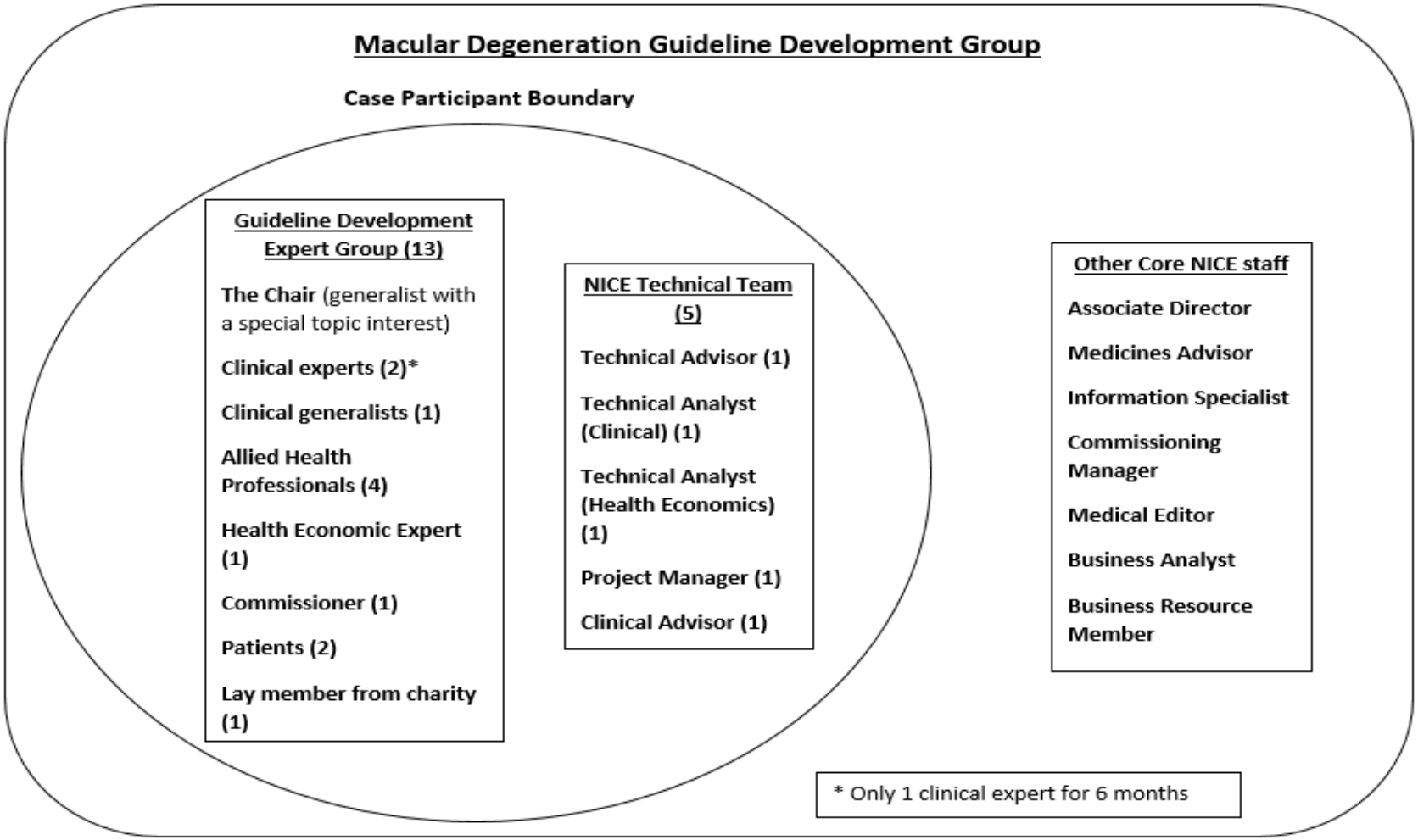
6.2.3 Group characteristics

Group structure

Building on the generic structure of a NICE Guideline Development Group (Figure 5.3 of the preceding chapter), this section details the actual composition of the GDG for the macular degeneration guideline[9]. The structure of the group can be seen in Figure 6.3.

[9] As a reminder, abbreviations used throughout this thesis are GDEG (Guideline Development Expert Group), NTT (NICE Technical Team) and GDG (Guideline Development Group). The GDEG and the NTT plus other NICE staff who contribute to the guideline process, comprise the GDG. GDEG and the NTT together constitute the main case study subject.

Figure 6.3: The macular degeneration guideline development group



The boundary set for recorded participant interviews and for observation of committee meeting interactions was placed around the GDEG and the NTT. Other NICE team members assigned to the macular degeneration guideline, as shown in Figure 6.3, only occasionally attended group meetings but members of the GDEG and the NTT were constant attendees. Drawing this boundary limited the number of participants to a manageable level but ensured that those who were closest to proceedings were interviewed and observed during the research process. However, this did not preclude *ad hoc* interviews with other NICE staff. Consistent attendance at guideline group meetings allowed relationships to build steadily between the participants and between the researcher and the participants. It ensured practical fieldwork issues, such as limited accessibility to participants, were minimised as participants were almost always present for guideline group meetings.

There were 13 members of the Guideline Development Expert Group and 5 members of the NICE Technical Team. The chair of the GDEG was a General Practitioner (GP) with a special interest in ophthalmology and a background in commissioning, plus experience in chairing various committees. There were two hospital-based, clinical ophthalmologists and one GP with a special interest in ophthalmology and in teaching. Four allied health professionals included two optometrists, one specialist nurse and one clinical liaison officer. The two optometrists practised in different areas of optometry: one was in general optometry with links to the Royal College of Optometry and the other was a low vision specialist. There was one expert health economist with a background in public health and ophthalmology and one commissioner of eye services. There was a representative from a charity and the two patients included in the group had macular degeneration but were at different stages of the disease. Furthermore, they had had different experiences of disease management which offered a patient view from both ends of the disease spectrum.

The NTT consisted of the technical advisor who had a background in health economics and whose role was to oversee the input from the NTT as well as providing health economic expertise. There were two technical analysts, one clinical and one health economics analyst, one clinical advisor for more clinical input and a project manager to manage operational proceedings.

Other core NICE staff included representatives of NICE teams that support guideline development. They are assigned to guidelines under development and contribute when required. For instance, there was a Medical Editing Team representative who attended group meetings at the point when guideline recommendations were being formulated or when recommendations that had undergone the editing process were being presented to the GDEG again. The information specialist member, who is part of the literature gathering team, attended meetings mainly at the beginning of the guideline development period. There was also an associate director who had overall responsibility for the guideline's development.

Group composition changes

Figure 6.3 above represents the GDG composition by the end of the process. The composition of this group was subject to a number of personnel changes during the development period. For instance, a clinical expert left after one meeting and was replaced only at Meeting 7; the NICE clinical technical analyst was replaced after Meeting 5; a new NICE project manager arrived at Meeting 4; an experienced NICE health economics technical analyst was replaced by a more junior health economist at Meeting 10. The reasons for the departure of some GDEG/NTT members and the arrival of others were many and varied: a clinical expert left for "unforeseen personal circumstances" (NICE AMD Guideline Meeting 2 Minutes, 2018); the first project manager was only temporary while a permanent project manager was being recruited; the NICE clinical technical analyst departed to full-time studies. The personnel changes that occurred were generally substitutions of individuals for a variety of reasons rather than extra additions to the group. One member had a medical problem which precluded their frequent attendance and s/he became a "co-opted member" rather than a full member of the GDEG. Co-opted members contributed often to very specific topic discussions, but did not have voting rights within the group.

Many participants considered the composition of the group to be unbalanced, especially concerning the clinical experts, of which there was only one for six months of the development period:

"My biggest concern [with only one clinical expert] *is will the committee be seen as credible being an unbalanced composition?"*

[Interview 5]

"....obviously they are deferred to a lot, aren't they, the clinical experts? So, it is a problem when there's only one there, I think."

[Interview 14]

The impact of being a sole clinical expert was not lost group members. Here, one expressed concern at the power of the position the individual found themselves in:

"I don't know what they will do with the Ring of Gyges yet."

[Interview 5]

Others had a slightly different perspective, suggesting that more clinical experts (more than two) might disrupt group functioning, rather than enhancing it.

"I don't know if many more would have been better in terms of clinical experts because there'd be a real tendency for that group to completely dominate the committee."

[Interview 21]

Further imbalance in the group was seen in the gender ratio with more female GDEG members than males (9:4). For the NTT, at the end of the development period, there were slightly more females to males (3:2), although at the start of the development period before personnel changes, the ratio was reversed (2:3). The gender imbalance was noted by participants but was not thought to be a significant issue in how they functioned. There was also imbalance in the age spectrum represented in the group with the majority of the GDEG being over the age of 40 years. This was also thought not to be significant, especially as the topic of the guideline was age-related macular degeneration, although some did express a desire to see younger participants included. This was because younger patients can develop forms of macular degeneration which are treated in similar ways.

Regional spread of participants and variation in practice

The NICE staff were based in London or Manchester only but there was a reasonable geographical spread across England for members of the GDEG. NICE prefers that GDEG members come from different parts of England but does not exclude membership from experts in other countries of the UK too, especially as NICE guidelines are adopted in Wales and used as the basis for guidelines in Scotland and Northern Ireland. However, there was no representative from these parts of the UK on the macular degeneration GDEG.

A geographical spread of participants ensures diversity in practice experience and precludes guidelines reflecting only practice in one small location. One group member noted:

> *"....there is a lot of variation between how patients are treated, how they're managed, how they're diagnosed; it's huge."*
>
> [Interview 9]

A similar view from another group member:

> *"Also, I've noticed a number of times, what has come up is the differences in practice around the country and, therefore, if you have people from the Northwest or the Northeast or a heavy preponderance of those people, perhaps you'll get one certain view. I don't know whether that's considered when NICE are putting together the group or not. I've been quite amazed by the difference, the variation in practice around the country."*
>
> [Interview 14]

The geographical locations of the GDEG members were not widely dispersed but neither were they all centred in one place. Therefore, there were contributions from different practice areas.

One perspective on differences in practice was that guidelines can be too dogmatic. In this way, they do not take into account these variations of practice and, furthermore, such variation *should* be acknowledged:

*"It is difficult and that's always the danger between being too prescriptive and saying this is what you **have** to do, versus, recognising that there **is** variation in practice."*

[Interview 18]

6.2.4 Motivations for participation

Recruitment of the GDEG follows NICE's policy and procedure for recruitment and selection to advisory bodies and topic expert groups (NICE Recruitment and Selection Policy, 2015). In accordance with this, GDEG positions are advertised on the NICE website and other appropriate places, such as websites of the Royal Colleges and other stakeholders. There may be instances when individuals are approached by NICE, rather than themselves apply via advertisements, but this is still in accordance with the policy. All candidates are required to submit a Curriculum Vitae, or application form, details of two referees and a declaration of interests to guard against conflicted individuals participating in the process. A shortlisting and interview process is undertaken before committee members are appointed. Table 6.2 indicates the routes via which the 13 GDEG members made their applications.

Table 6.2: Route of application for guideline development expert members

Method of Application	Number
Applied directly (applied directly but only after being directed to advertisements)	**5** (2)
Applied at request of another party - employer or other stakeholder	**5**
Approached by NICE	**3**

There were as many applications as a result of interactions of participants with their employers, or aligned institutions, as there were individual applications. Also, even where applications were made individually, only three were as a result of those individuals themselves seeing the advertisement on the NICE website; the others were made aware of the advertisements by different parties. As one interviewee put it, when commenting on the recruitment advertising and how to find it:

".....it almost feels like a bit of a closed shop, not a purposefully closed shop, but something hidden in plain view."

[Interview 15]

The route by which GDEG members applied aligned with their individual motivations for participation. So, for example, those seeing the advertisement themselves and applying directly were positively motivated to join the committee. Many reasons were altruistic: volunteering for something worthwhile and wanting to make a difference to practice at a national level. Others gave reasons of self-education, illustrating that they thought NICE offered a way of learning about the most up-to-date research:

"So the motivation really was quite selfishly keeping myself and my skills honed. It was a way to find out more about it again, because, I suppose it's that thing about it: if there's something out there that can benefit, then, where's the best place to be? Well, actually, in the middle of it. So, it's finding out if there's more to be done and if there's some research coming out that, you know, how else would you find out about it?"

[Interview 7]

An opportunity to counteract excessive pharmaceutical influence in practice guidelines was a motivation mentioned by three group members. This is from one respondent describing their interest in participating in this specific guideline and what they saw, in their opinion, as pharma taking away choices from those affected:

"[It's] *not just a kind of crusade against big pharma but……the decisions are sitting with a body* [pharma] *which has no responsibility to our population and our people and we want to be able to make our own choices."*

[Interview 16]

Those approached directly by NICE, or representatives of NICE, to be included as a GDEG member tended to be for positions that were proving difficult to fill, such as, clinical and health economics expert positions. Here, participation was also generally seen as positive, an education and a source of recognition, even kudos with colleagues:

> *"I mean it is a motivation, I guess, as well to get recognition and, yeah, kudos with your peers."*
>
> [Interview 18]

> *"I think, for me, it's an educational experience and I think that's what really sold it to me."*
>
> [Interview 6]

Some individuals were encouraged to apply by employers or other stakeholders; here, the motivation and enthusiasm with which they viewed their role varied. Some felt pleased to be made aware of the opportunity to represent patients and embraced participation enthusiastically, feeling it beneficial to be able to contribute from their own specific ophthalmology area. Others were resentful of the time and effort required. This is from one participant about giving up (unpaid) time:

> "*I'm getting no freebies out of this that would stand for personal gain; it just seems problematic to give up one's holiday* [for participation]."
>
> [Interview 5]

In conclusion, motivations for participation varied. Often the motivation depended on the mode of application to join the process and the majority cited positive reasons to participate.

6.2.5 Perceptions of guidelines

The guideline committee, being a multidisciplinary group with different institutional affiliations, demonstrated a variety of views on guidelines. Responding to questions, such as, who and what are guidelines for, who are they important to and whether they change practice, a majority of respondents were of the view that the guidelines had to be many things to many people. They were pieces of advice for clinicians and other health professionals, recommendations for commissioners on which to base prescribing decisions and information for patients and carers. The number of diverse groups that guidelines are intended to serve indicate to many people that their influence cannot, therefore, be substantial in any one sector and this limits their value.

One group member, on being asked who they believe guidelines are written for, suggested that the production of guidelines for different parties and institutions is a difficult task for NICE and that a solution that fits all is unlikely to be achieved:

> **Interviewee:** *"I think NICE likes to think they're written for patients. I think they're written for clinicians (laughs) because they're the people who are going to be using them, so, I think there's an audience mismatch."*
>
> **Interviewer:** *"Do you think NICE understands there's an audience mismatch?"*
>
> **Interviewee: "** *…… I don't know whether they do or it is an impossible circle to square: writing for a patient but really it's a clinician* [as the intended recipient]. *They ……. want to be wholly evidence-based, as well as use expert opinion, but still not upset regulatory frameworks. It's a very difficult balance to strike, isn't it? It's a very narrow tightrope to walk. Do NICE understand that there's a difference between the audiences? I think that they probably do but I don't think they're ever going to solve it. I don't think they can."*
>
> [Interview 15]

The positive effect that a guideline could have on practice was seen to be mitigated by certain features of guidelines. These included guidelines being pieces of advice only, rather than being mandated policy, and that clinical autonomy could still be exercised whatever the guideline recommended. Further, the evidence which supports guideline recommendations was considered to speak only to a narrow subset of patients, usually those without chronic disease or multiple conditions. This was said to be true especially for treatment guidelines for patients in primary care. The language of guideline recommendations was also adjudged to be a barrier to their successful implementation. The quote below is from a member of the group questioning the impact guidelines have on practice and suggesting the language used, derived from the strength of the evidence base, is an issue:

> *"I find it very hard to point to any instances where they have substantively changed practice and I think that is a function of a couple of things. It is firstly about topic expert committees: if you're gonna substantively affect practice, then you have to be making recommendations that say:* ***stop*** *doing things this way,* ***do*** *it this way. It is seldom the case that topic experts have that clear a view of an*

evidence base that enables them to do that, even when the evidence points in a certain direction. So that militates against any meaningful changes in practice."

[Interview 20]

For some there was an unhealthy emphasis on cost during the guideline discussions. This precluded certain treatment recommendations being made and which could be detrimental to patient choice. Others thought that considerations of cost are mainly an issue for commissioners and for NICE, but not for clinicians. However, it was felt that discussions of cost relevant to the guideline were entirely appropriate. For example, from one group member:

"…..at the last meeting we were talking about cost-effectiveness and things that come up with proposed guidelines which are not necessarily what clinicians would come up with because their main concern is not cost. I think, I see that [issues of cost] *as their* [NICE] *role. Basically it doesn't surprise me because that's what they're there for, that's what they do."*

[Interview 18]

Despite some misgivings as illustrated above, guidelines were positively received as an important part of health information sources. They were seen to be of value as a resource for different health professionals, as a tool to educate patients, the public and clinicians about best practice, as a method to standardise practice across different regions and to improve quality of overall healthcare provision. The following quotes, from interviews with two group members, reflects many of the positive perceptions of guidelines:

"I do generally think they have a positive impact. It is there as a resource. People know where to go to, clinicians know where to go. I think more generally, broadly, in areas where there are no guidelines, where there's mixed practice across the country: that's bad. The guideline becomes really valuable to point out who's doing it right and standardises that across the country. I think that is a really positive outcome."

[Interview 21]

"I think NICE probably had a lot of criticism from, say, GPs and primary care, professionals because a lot of the guidance was squarely aimed at the secondary care sector. Therefore, there was criticism that the guidelines were not applicable

to them but I think that the senior Board at NICE have started pushing changes through to involve primary care and also involve other people. I think that's a welcome move."

[Interview 10]

The guideline group's perceptions of guidelines indicated that guidelines have a number of uses for different parties who have contrasting agendas and they are useful as a practice resource ensuring equitable care. However, concerns remain that they are too numerous to be impactful in all practice situations.

6.3 Part 2. Evidence in the guideline process

This part of the chapter describes what evidence was considered by the guideline group. Firstly, the types of evidence for the evidence base are detailed. This is followed by sections on how variable the evidence base was in terms of quantity and quality of the evidence and on the availability and acceptability of the evidence. Further sections detail the importance of health economics data and the application of a hierarchy of evidence. The final section reviews the use of expert opinion in the development of this guideline.

6.3.1 Types of evidence

Prior to setting out the findings about evidence, it is useful to highlight the different types of evidence used in this guideline. These can be seen in Table 6.3.

Table 6.3: Types of evidence used in the macular degeneration guideline

Type of Studies	Sub-categories
Quantitative studies	Individual RCTs Systematic reviews Meta-analyses
Qualitative studies	Interpretive phenomenological studies Surveys
Cohort studies	Longitudinal studies Retrospective studies Prospective studies
Case studies	Nested case-control studies Retrospective case studies Case series
Observational studies	Before-and-after, treatment-switching studies Retrospective studies Prospective studies Cross-sectional studies
Expert evidence	GDEG contributions Consensus recommendations from expert panels
Other evidence	Medisoft hospital data Other guidelines Retrospective audit Health economic models

Source: NICE AMD Guideline, Appendix E: Evidence tables, (2018)

The evidence gathered and appraised by the guideline group was from wide and varied sources. The meanings of all the different sub-categories are not described here although many of the different sub-categories of evidence have been discussed in Chapter 2. Some are referred to below in the description of the findings relating to evidence.

6.3.2 Variable quantity and quality of evidence

The quantity of evidence, deemed appropriate to be considered for discussion of the guideline review questions, became a talking point at many guideline group meetings. The quantity of evidence accepted during the data sifting process varied according to the type of review question (Appendix viii). Many thousands of publications and other types of evidence were screened and sifted, firstly by using computer searches and then by title and abstract. Those deemed appropriate were ordered for full text appraisal. The publications were reviewed against eligibility criteria and then accepted or rejected as support for the guideline recommendations. For addressing questions of effectiveness of

medications, generally there was a higher percentage of publications accepted than for review questions concerning diagnostic procedures, preventative measures or psychological therapies. Tables 6.4 and 6.5 illustrate this difference.

Table 6.4: Percentage of publications accepted after full text appraisal for questions concerning the effectiveness of drug interventions

Review Question	Publications accepted	Publications rejected	Percentage accepted
What is the effectiveness of adjunctive therapies for the treatment of neovascular AMD? (RQ13)	18	59	23.4
What is the effectiveness of different frequencies of administration for anti-angiogenic regimens for the treatment of neovascular AMD? (RQ18) and What is the effectiveness of different anti-angiogenic therapies for the treatment of neovascular AMD? (RQ12)	36	53	40.5

Sources: NICE AMD Guideline, Appendix E: Evidence Tables, (2018) and NICE AMD Guideline, Appendix F: Excluded studies, (2018)

Table 6.5: Percentage of publications accepted after full text appraisal for questions concerning diagnosis, preventative measures or psychological therapies

Review Question	Publications accepted	Publications rejected	Percentage accepted
What risk factors increase the likelihood of a person developing AMD or progressing to late AMD? (RQ2)	35	246	12.5
What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD? (RQ4)	17	160	9.5
Frequency of monitoring questions (RQ19-22 – see Appendix viii for full questions)	0	21	0
What strategies and tools are useful for monitoring and self-monitoring for people with AMD? What strategies and tools are useful for monitoring and self-monitoring for people with neovascular AMD? (RQ23)	10	44	18.5

Sources: NICE AMD Guideline, Appendix E: Evidence Tables, (2018) and NICE AMD Guideline, Appendix F: Excluded studies, (2018)

As a reason for this difference, one NICE team member suggested that, where there was a proprietary interest in a drug, high-quality RCTs would be available since these are required to gain a marketing authorisation. Other reasons for this discrepancy included data available, but not published, which precluded its inclusion in the guideline evidence base. For example, there is a large database for a certain diagnostic tool for macular degeneration, which is held by a commercial company. Individual doctors and hospitals have access to their own data, but the company do not publish the aggregate data.

Early on in fieldwork, noted in the Research Reflections Diary is: *"Lack of evidence on which to base recommendations is astounding".* (Reflections Diary, 6 Apr 16). This comment reflects the surprise at the many thousands of articles and other types of evidence which were reviewed and rejected for inclusion as evidence for the guideline. The surprise at the paucity of evidence for some review questions was mirrored by members of the guideline group who had expected a larger evidence base: "…*so, are we actually looking at enough material to make a decision here?"* (Interview 8), was typical of the comments made by group members.

Review questions considered by the guideline group earlier in the guideline development were diagnostic or strategic in nature. Drug treatment intervention questions, where more evidence might be expected, came later in the development cycle. This might explain the early research fieldwork diary entry concerning the perceived lack of evidence available to support the formulation of guideline recommendations. However, the apparent lack of evidence, even for treatment effectiveness questions, continued to worry many of the group:

> *"….the quantitative data's not that robust. You do things to three decimal places and all that kind of thing and* [it's] *how people then interpret those differences and understand them."*
>
> [Interview 16]

Noted, again in the Research Reflections Diary, is the effect on group members of the perceived lack of evidence: "it *worries and annoys them and makes their task difficult but, at the same time, unites them*" (Reflections Diary, 12 Jul 16). However, there were other views. Group members who had had previous experience working on other guidelines did not find the sparse evidence base for diagnostic and strategic-type questions surprising; it was in line with other guidelines. Furthermore, for this guideline, there was, they noted:

> "…..*a large number of RCTs"* and *"we feel like we had pretty good evidence there and you're normally lucky if you get something that lives up to those standards."*
>
> [Interview 20]

The quality of evidence for this guideline followed a similar pattern to the quantity of evidence. Higher-quality evidence was more often associated with larger RCTs for drug treatments and regimes. Diagnostic and strategic studies were usually small, addressed discrete variables and had qualitative outcomes. This lack of quality in the evidence was another issue of concern to group members. This is illustrated by two quotes from interviews with participants:

> "*.....in terms of the presentation of evidence that we've had, there doesn't seem to be anything that's particularly strong evidence. .....you know, it's all sort of, moderate to low quality."*
>
> [Interview 7]

> *"I think, depending again on the particular bit of evidence that we've been looking at, it's shocking in some respects that there isn't more that is of a better quality."*
>
> [Interview 11]

Some participants felt that the application of quality parameters was important to obtain robust evidence to support guideline recommendations; indeed, that was what NICE was commissioned to do. Those who had had previous guideline development experience were, again, less surprised about the variable quality of the evidence. Despite desiring and understanding the need to provide as high quality an evidence base as possible, they cited a similar pattern in other guidelines.

It is difficult to compare across guidelines as this is a single case study, despite NICE team members suggesting similarities in the quantity and quality of evidence with other guidelines. However, the findings indicate that the quantity and quality of the evidence base were a major concern to guideline group members in that they were not receiving as full and robust a picture as they would like in order to feel confident when making guideline recommendations.

6.3.3 Availability and acceptability of evidence

The evidence for a guideline arises from multiple sources but not all is acceptable for inclusion as part of the supporting evidence base. Excluded data is that which is

unpublished, published only as conference proceedings or opinion pieces, and promotional material. There is also another circumstance when data is excluded and that is when data on the relevant disease topic is amalgamated with data on other diseases. An example of this occurred for this guideline. Review Question 9 (Appendix viii) concerned the effectiveness of support strategies for patients with visual impairment and AMD and this included low vision services as an "intervention". Many of the studies concerning low vision support have, as the study population, those with visual impairment due to many causes, not just due to AMD. Extracting the data pertinent only to AMD is not possible and these studies were excluded from the evidence base despite being relevant. One group member commented on this:

> *"What I think is difficult is that a lot of this is tied because it has to be about AMD. So, there are lots of studies out there that might show that doing certain things is helpful. The studies have looked at* ***whole*** *populations of people with poor vision or what support you have in poor vision needs but they aren't going to be included in this because they're not purely AMD."*
>
> [Interview 17]

For each review question, the information imparted to the guideline group as a basis for their discussion and deliberations, included information on why studies were rejected for inclusion. Whilst too numerous to detail by each review question, two examples are given below (Table 6.6), one from drug intervention review questions and the other from strategic support review questions. As the number of studies rejected is high, for each review question type, only some of the reasons for rejection are highlighted.

Table 6.6: Reasons for rejections of publications

Review Question Type	Reason for Rejection
Drug Intervention	Excluded on outcome: *no comparison data*
	Excluded on study type: *abstract*
	Excluded on target group: *did not meet vision threshold*
	Excluded on study type: *pending data*
	Excluded on disease condition studied: *diabetic macular oedema, not AMD*
	Excluded on outcome: *extremes in visual acuity (very good or very poor) of the fellow eye (FE) influence vision of the study eye*
	Excluded on target group: *not defined for study population*
Strategic Support	Excluded on study type: *not RCT*
	Excluded on study type: *case control study*
	Excluded on study type: *case series*
	Excluded on study type: *non-randomised*
	Excluded on study type: *qualitative study*
	Excluded on evidence: *different types of intervention (no control)*
	Excluded on language: *full text in German*
	Excluded on target group*: mixed low vision population*
	Excluded on evidence: *no new evidence in a meta-analysis*

Source: Adapted from NICE AMD Guideline, Appendix F: Excluded studies, (2018)

The reasons for rejection were very varied and were similar for all review questions. There did not appear to be any particular pattern for different types of review questions except that for diagnostic, strategic and support type review questions, there were many study design exclusions. This reflected the extensive variety of study designs to investigate these types of questions, many of which had qualitative elements or were case

studies. It also reflected the hierarchy applied to the evidence search that privileges designs higher in the hierarchy.

Other types of data are termed (by the researcher of this study) as "missing" from the evidence database. These are categorised into three types of data: data that is not accessible but relevant, data that is relevant and becomes accessible but was not uncovered by literature searches and data that individual members of the guideline group consider "missing" or would like to see more of as an aid to making guideline decisions.

Data that is relevant but not accessible includes data such as that held by commercial companies which is accessible only to individual doctors and hospitals. Such data often pertain to diagnostic tests that are read centrally by one particular commercial company. It is not published as aggregate data and is, therefore, unavailable as evidence for the guideline.

Data that becomes accessible but was not uncovered as part of the initial literature searches includes articles "in press" that are published during the course of guideline development. Another example of this type of data in this study is data in the Medisoft Ophthalmology electronic medical record system (Medisoft, 2017) which is used by over 150 hospitals in the UK. It allows the recording of patients' clinical visits, observations and tests permitting clinicians and allied health professionals to monitor progression of disease over time in their own patients. One group member rued the unavailability of real-time data, such as that provided in the Medisoft database, feeling that real-time data would add to that provided by strictly monitored clinical trials:

> *"....we haven't particularly drilled down on that in terms of, you know, what treatment regimes are being used in the* ***real*** *world. How many people in the real world actually are treated to plan ... You should include it* [Medisoft data] *because it does mirror what happens, I think, a lot in the real world."*
>
> [Interview 18]

Members of the GDEG, who had access to their own Medisoft data, made this available to NICE. This, then, was usually unavailable data becoming accessible for guideline development purposes.

One question posed to guideline group members during interview was what evidence they considered to be missing and what sort of evidence they believed would add to the body of evidence supporting the guideline recommendations. A number of responses indicated that there was a belief that more patient-experience data would be valuable. Data "missing" was that concerning how patients felt about their treatments, studies investigating patients' understanding and expectations of the treatment process and data examining best-support strategies. This, they believed, would be qualitative in nature and aligns with views on the lack of qualitative evidence accepted. This is from a group member discussing their thoughts on missing data, particularly psychological therapies and treatments considered to have impact for patients:

> *"I think a lot of the evidence that we have for things like psychosocial therapies and those sorts of things are more anecdotal than scientifically measurable…..I think it does give us the drive to say: well actually we do need more evidence and we can say, well this is something we really feel should be included and should make a difference and should be considered in this group. We don't have enough evidence to base our decisions on so we would like some research to be done from this. So, it gives us the opportunity to highlight a need. A lot of what is delivered in clinic day to day is social support, psychological support, emotional support. They're very hard things to measure, very hard things to prove that you are making a difference but, from what the patients tell you, you know that it makes a tremendous difference to them. But we don't have anything* [evidence] *to prove that…."*
>
> [Interview 8]

Others thought valuable data to be included, or at least to be part of the search strategy, would be basic sciences data, such as physiological, pharmacological or mechanistic study data, that underpin clinical trial protocols. For this they considered: *"essential prior knowledge is missing"* (Interview 5). Further comments concerning "missing" evidence aligned with the lack of evidence found for many review questions, especially data on service provision and monitoring strategies.

6.3.4 Health economics data

Decisions about values of treatment and their costs is a core responsibility of NICE. Economic evaluation is an integral part of clinical guideline development although recommendations are not made on cost alone. The benefits to health of the interventions are expressed in terms of Quality-Adjusted Life Years (QALYs), despite some concerns about restrictive assumptions underpinning this economic approach (Birch & Gafni, 2002). The cost-effectiveness analyses estimate differences in costs and differences in outcomes between interventions in terms of QALYs. There is then a threshold of £/QALY applied which determines the likelihood of any intervention being recommended or not. Although this is not absolute, it is a major factor in determining cost-effectiveness (Appleby et al., 2007).

In this guideline development, the economic evaluation took a prominent position in evaluation of macular degeneration management with a complex model developed specifically to address the controversial problem of macular degeneration treatments. The model used the best clinical evidence available but, also, there was much input from GDEG members (mainly from the clinical experts and those with a health economics background) about model assumptions. What was evident from observing the meetings when the model was being discussed, was that many members of the GDEG had limited training in, or an understanding of, health economics. The input, therefore, was from a narrow set of people. However, both the NICE Technical Team as well as the GDEG contained members with health economics expertise. This expertise was appreciated by group members:

> *"I think they're excellent, I really do. I think they grip the issues and I think they're very good at articulating them very clearly to a non-health economics specialist audience."*
>
> [Interview 14]

Observation of the presentation of health economics data to the guideline group led to a reflection that: *"Health economics data is very complicated and understood by few. This then becomes a case of the whole group being led by the nose by a few people"* (Reflections Diary, 6 Dec 16).

One participant commented in interview on how they expected more interaction between group members for health economics discussions and that there was a lack of relevant expertise or understanding of the subject:

> *"..they're* [group members] *very much happy to let you lead and to learn from what you're saying and listen to what you're saying. I had anticipated it would be a little bit more vocal and people would be just jumping in and chipping in and that wasn't generally the case."*
>
> [Interview 21]

Another reflection concerning discussions of the model, noted*: "Sometimes, those who do understand, clarify points for the others. This leads to personal interpretation being "forced" on others"* (Reflections Diary 6 Dec 16). This indicates the variable understanding of different guideline group members and also how individual interpretation of information can influence and drive group understanding.

The economics model underwent a number of iterations as more data became available during the evaluation. Each time, the GDEG was asked for verification of new assumptions about the model with a similar pattern of input from the same GDEG members. Direct access to the model for research purposes was not permitted because of the inclusion of commercially sensitive information. However, it was clear from observing the discussions at committee meetings that there was a very positive reception to the value of the model and that the millions of scenarios produced by the model would add favourably to the evidence base for the guideline. Group members cited the model and its outputs as something of which they were proud:

> "*I've taken a particular interest in this on this one, deliberately, because it just really matters. I feel we have significantly pushed the field on. We've answered the series of questions in front of us in a more robust and comprehensive way than anyone's got close to before……. it is an unusual feeling to get to the end of it and feel quite proud of the work technically."*
>
> [Interview 20]

6.3.5 The application of a strict hierarchy

The stated view of NICE for this guideline was that all types of evidence should be considered as having equal value. However, assessment of the quality of studies included in the evidence base shows that a strict hierarchy for study design was applied. RCTs were at the apex of the hierarchy with less attention and value placed on other types of studies. This was clear both from the downgrading of the quality rating of studies when the study design was not a RCT and from interview responses of participants to being asked about what value they assigned to different study designs. Many respondents pointed to RCTs as being of higher value than other types of study design:

> *"I think there's a very, very steep progression in terms of quality after that* [after RCTs at the top], *you know, we move down from RCTs to cohort studies and then right at the bottom we've got some narrative reviews".*
>
> [Interview 2]

> "*The best is the RCT and there's no creditable argument against that."*
>
> [Interview 1]

Views of what constitutes "good" evidence and what evidence is necessary for guideline recommendations appeared to differ depending on whether the group member had a scientific or clinical background. In this case, systematic reviews and meta-analyses of data were privileged and they would look to RCTs as a favoured design before data obtained via different study designs.

The application of an evidence hierarchy also became clear whilst observing the presentation of data at guideline group meetings: quantitative data was preferred above all other types of data. Qualitative data was used scarcely and, amongst some group members, a reductionist view prevailed that qualitative data is only useful if it can be made quantitative. The following quote from an interview with a participant illustrates this point:

> *"....it's very hard to make guidelines on the basis of qualitative anecdotes. Normally the role of qualitative* [data] *is to generate research questions which you then answer by doing a quantitative study."*
>
> [Interview 5]

There was a concern, however, that RCT-type quantitative evidence was given too much credence:

> *"There's always a bit of a worry for me around quantitative data that appears to, sort of, overly infer a sense of accuracy which doesn't exist."*
>
> [Interview 16]

Others did see merit in evidence lying further down the hierarchy, such as qualitative evidence. This was seen as providing complementary information and was especially important for questions around patient experience:

> *"I think it's* [qualitative data] *an important source of information and it can often highlight and shine a light on things that you can't get from purely quantitative analysis."*
>
> [Interview 22]

> *"....if you are trying find out what patients think and feel as they go through the treatment pathway, I think qualitative evidence is really good evidence."*
>
> [Interview 1]

Expert opinion appears at the bottom of the hierarchy of evidence but, in this guideline, occupied a prominent role. As such, it emerged from data analysis as a strong theme and is, therefore, accorded its own section.

6.3.6 Expert opinion as evidence

All members of a GDEG, whether clinicians with years of experience or patients with the disease, are considered to be experts with equal status who bring their relevant knowledge to the benefit of the guideline. The findings from the data analysis of this case study concerning the use of these experts can be distilled into a number of overarching points.

Firstly, expert opinion *is* valued as a source of evidence. For example:

> *"I'd find it obviously **colossally** difficult to provide guidance on **any** number of the other questions we've looked at in this guideline which have no robust evidence base at all. We're **entirely** reliant on the expertise of the people who deal with it day by day."*
>
> [Interview 20]

It is needed as a substitute when evidence is sparse but, even where evidence is plentiful, it adds personal experience of the disease or treating individual patients that population studies cannot provide. Here one group member comments that a guideline is not just the scientific evidence available; it is a combination of that and the knowledge of the experts present:

> *"…there's going to be a guideline written and it's got to be based on the knowledge of people around the table **and** any sort of evidence that's out there to inform that."*
>
> [Interview 7]

Another group member demonstrates a similar recognition that expert opinion is an integral part of the whole evidence base:

> *"Obviously, the recommendations are very contextual and it involves a lot more areas of expertise than just the evidence."*
>
> [Interview 22]

Secondly, patient expert opinion is especially valued as adding to the understanding of the disease and to ensure patient concerns are addressed in the guideline. For example:

> *"……*[patients] *will give us the perspective, the qualitative perspective of the patient experience."*
>
> [Interview 1]

> *"…you need to have them because they're very important. They have, not only an experiential point of view of their own narratives, but they have ability to reflect*

back to the professionals, the practicality of, and the difficulties that some of the recommendations may lead to."

[Interview 6]

Thirdly, expert opinion needs to be balanced. The following quotes are from two group members about the weight that expert opinion is afforded and the impact on the guideline outcome:

"*The impact on the guideline comes back to the limitations of which clinician you have round the table and how many ophthalmologists you have. That to me is a massive limitation. If it's left to expert opinion, that's what you're left with and the experts in the room then really, really matter."*

[Interview 15]

"…if there's something contentious, usually there's an expert and people respect that expert's view, so there's going to be no argument over what they say."

[Interview 4]

The concern around balance of expert opinion was mainly directed towards clinical experts, this group having only one expert clinician present until at least halfway through the development period. This was an unintended consequence of numerous conflicts of interest for ophthalmology clinicians that precluded service on the group. An imbalance in clinicians in the group was seen as a possible source of bias, "*the maverick nature of expert opinion"* (Interview 15), as one group member termed it, and a representation of practice in one area of the country only. There was also the view that if two or more clinicians had opposing views, this would be difficult to represent in the guideline and may lead to conflict within the group.

This leads to the final overarching point that managing experts giving their opinions during the guideline process is difficult and the perceived value of experts may be different from their actual value. On occasions, irritations showed but these were often due to a frustration at the lack of scientific evidence or a misunderstanding of the process.

For example, from an interview with a group member who felt confusion at the role of expert opinion:

> *"I've heard it said by NICE team members that you round the table are there to give your expert opinion, but then… we don't want it."*
>
> [Interview 15]

A final illustration of the difficult task of managing expert opinion and its value to the process comes from another group member:

> *"….we need that expert opinion when it comes to evidence-free zones or even evidence-poor zones. When it comes to the stuff that is well-evidenced, yeah, actually adding expert opinion on top of that tends to be more of an irritant."*
>
> [Interview 20]

The management of expert group members during their deliberations and decision making is detailed in 6.4.1: Roles adopted and 6.4.4: Group dynamics and decision making.

This part of the chapter has reviewed the evidence landscape of the macular degeneration guideline development. The next part of the chapter describes findings related to how the guideline group functioned, the roles played within the group and how they interact in their consideration of evidence for the formation of guideline recommendations.

6.4 Part 3: Group functioning and interactions

One lens within the conceptual framework (Chapter 3) focused on group functioning and interactions, which are especially important in understanding the social processes of guideline development. This study found multiple factors affecting the group functioning and an effort was made to separate individual and group factors during analysis. This proved difficult because many individual factors play into group interactions and many group-based factors influence individual perceptions or actions so they cannot be neatly

divided into two distinct categories. Thus, the themes emerging from the data are not strictly categorised, although where either individual or group factors were more influential, this is highlighted. The first section details the roles adopted by group members. Then status hierarchies within the group are described. This is followed by the process of the conversion of evidence to guideline recommendations and group dynamics and decision making. The final two sections detail the emotions engendered by participation in the guideline development process and trust as an emergent theme.

6.4.1 Roles adopted

The macular degeneration GDEG included all professional roles recommended by the NICE process. The professional background of the participants indicated their formal role on, and contribution to, the guideline group. This was demonstrated in observing the type of contributions made during guideline group meetings and in responses to interview questions about what they felt their presumed guideline group role to be. Thus, clinical questions were most often deflected to those with clinical roles. Similarly, questions concerning health economics were answered by NICE health economists or the members of the GDEG with health economics training. Questions concerning care strategies and patient experience were contributed to by many, although the patients and those representing patient interests had greater input.

The chair was the most important role on the GDEG. The chair guides the group in terms of task and process making sure their work is collaborative and there is a balanced contribution from all. Chairs are selected for their experience in chairing and this is their main role, although they will have some topic knowledge too. A member of the group concurs:

> *"I think that if you've got a good chair, it shouldn't make a difference whether they're an expert in that field, or not, because the chair is about managing the group and making sure things are conducted appropriately."*
>
> [Interview 9]

Another view concerning the chairing role:

"The role of chair is really to try and get all views heard, as you do in a magistrate's court, and then facilitate the whole committee coming to a right answer. They should try very hard not to be directive but one of the things is letting people talk because of allowing people to be heard. People need to be seen to be heard as well and those are two different things"

[Interview 10]

The NICE team manage the guideline process overall but it is the chair with the primary facilitation and management role at guideline group meetings. No training is given by NICE in chairing and the consensus from participants is that recruitment of chairs should focus on ability to lead groups and facilitate discussions rather than on topic expertise. The following quotes from participant interviews concern how they feel s/he fulfilled the facilitation role:

"……s/he's done good work in jollying things along and keeping the group together".

[Interview 20]

"S/he doesn't have that thing that some chairs do: they have to be in charge all the time, sit there and stamp over stuff… s/he does let conversations just flow and s/he will interject and ask questions just to keep it and everything going."

[Interview 18]

"Their attitude is not wanting to get in there and say: "no you're wrong", which I think is a good thing. It has allowed us to be more collegiate but s/he seems a bit too mild-mannered."

[Interview 15]

The role of the patient member is important to balance the service provision view with that of the service user. Patient inclusion within the guideline group was seen as strongly positive:

*"…it has been my experience that the patient and public involvement representatives we have contribute **most** value to the guideline."*

[Interview 3]

"…so they're there to represent patients' views, views as users of the NHS. So, they can add lots because, one: they've experienced the service and have an idea about how the service is delivered, what it's like to be on the receiving end of that, and two: they've experienced the conditions, so they know how the condition can affect you and what an impact it has on your life. So, yeah, I think, they bring a lot from that point of view."

[Interview 18]

The NTT had individual technical roles, such as clinical technical analyst and health economics technical analyst but, taken together, the NICE team played a support role. They were providers (and seekers) of evidence, administrators and managers of the whole process. The core NTT included in this case boundary also acted as a conduit, transferring information and questions to the wider NICE organisation.

A number of other roles, important to the guideline process, emerged from the data. These were not guideline group roles, as defined by NICE, but roles defined by case respondents or through analysis of group observations. There was the role of "arbiter", defined by case respondents. The role referred to the power to decide, or give judgement on, various issues. This applied mainly to the chair but also, on occasions, to other members of the guideline group and to NICE as an organisation. For example, the chair would decide when discussion would cease and who should contribute; core GDEG members, usually clinical experts, would give clinical judgements and decide whether assumptions made were valid; NICE team members, such as an associate director, would make judgements about wording of recommendations or the process in general.

Another role was that of "broker", defined in analysis of group observations as an intermediary in translating complicated data into more understandable information. This role applied to a number of individuals depending on the type of data being discussed. Thus, clinicians would act as brokers to explain disease pathology or the intricacies of

different treatments. Indeed, one clinical expert gave two presentations to the rest of the team about the pathology of macular degeneration. Brokerage was also recognisable during statistical discussions with health economists simplifying the evidence for those with little statistical training.

Finally, there was the role termed "clarification-seeker" defined in analysis of group observations. One group member illustrated this:

> *"I know that yeah, it doesn't matter, it actually doesn't matter if you ask a stupid question. When you're in a group, it's that's rescuer* [thing], *isn't it? If you sort of preamble something with …"help me out", you know that, if somebody's crying for help, they'll help you and* [it]*'ll help others*."
>
> [Interview 7]

This role, usually carried out by a patient member, involved asking for clarification or simplification of an issue. The difference between this role and that of "broker" is that the "clarification-seeker" looks for an explanation of an issue for themselves but also recognises that others may benefit.

6.4.2 Status hierarchies

There was a wealth of professional knowledge and expertise in the guideline group. Information elicited at interview indicated that the majority of GDEG and NICE team members had undertaken tertiary education and taken professional exams and had many years of experience in the specific guideline topic. The process of appointing GDEG members takes into account the draft scope so that participants are tailored to that specific guideline. NICE is clear about the equal standing of GDEG members valuing their individual expertise and experience. Observing the group at work, however, hierarchies amongst participants were displayed. These were demonstrated explicitly by deference to certain individuals during evidence discussions or when writing recommendations, or, were commented upon by participants during interview. For instance, one group member describes their view of some group participants who are not directly involved in care of patients with AMD:

"I think there's some who are overshadowed by a lot of professionals because they work in the field, they have more knowledge and expertise."

[Interview 19]

The following is from a group member who suggests that challenging clinical experts is difficult if one is not from the same clinical area:

"…having an ophthalmologist say this is what we do, this is not important or this is important, I am thinking, actually, no, I disagree with that but my view is not as strong as another ophthalmologist who could say the same thing."

[Interview 9]

Other manifestations of hierarchies operating were more implicit, demonstrated by occasional breakdowns of dialogue and rescinding of discussion contributions when contradicted by someone at a presumed higher level in the "status hierarchy". There was also uneven participation that reflected professional hierarchies for the type of questions discussed. The most obvious hierarchy was the clinical hierarchy: at the top were the clinical experts who would usually be the first to answer (or be asked to answer) all types of clinical questions, then nurses and allied health professionals, then others on the fringes of clinical work, such as the commissioner of services, and finally lay persons. Other hierarchies could be identified where deference to presumed superior knowledge was demonstrated. For example, those without health economics training deferred to those with training and, since statistics are an important part of health economics, there was an assumed superior knowledge of statistical data that was not always demonstrated in practice. This deference was often commented upon by respondents, for example:

"I think, possibly, the ability to interpret the evidence is an issue and I feel that for myself. I'm reliant on other people accepting that the evidence [is] *saying that it means what it says it means. I don't have the ability to do that. I'm not a statistician so, I find that difficult to challenge. I guess that's why there are lots of us but it does mean that I am ceding judgement to other people in lots of cases."*

[Interview 14]

Another hierarchy involved the NICE team and knowledge of the NICE process. Occasionally noted was a managerial reporting relationship between individuals and this influenced their interactions and contributions. For example, the following explains the influence of line management on how evidence was presented to the guideline group:

> *I think, getting stuff done in time is a big pressure. The influence on this is from line management. How we deal with that pressure comes from the line management. So, one approach* [presenting all evidence] *is safe but possibly means more work than necessary. One approach* [extract the most useful evidence and present less to the group] *is more risky but would mean less work. If any of those risks blew up in your face then you're set back. ….it's difficult, so, your line manager guides you through that".*
>
> [NTT member]

However, the NICE team in the group generally belonged to different reporting lines and the hierarchy appeared to be based on knowledge of the NICE process and experience in guideline development.

Whilst hierarchies based on professions were evident, social hierarchies in this group were notable more by their absence than their presence. When asked to provide one word to describe the group, many offered words such as "*collegial*", "*harmonious*" or "*friendly*". There were also comments on the confidence felt in the group to offer an individual point of view that would be listened to, regardless of who voiced these:

> *"….there may have been one point, again, where, perhaps, s/he and I had different views but, I still felt confident enough to say what I thought."*
>
> [Interview 11]

From the same interview, illustrating the lack of a social hierarchy:

> *"…my view is that they are only ordinary people with a specialism. At the end of the day, the doctors are only humans and so, I suppose, I became a bit desensitised to a them-and-us kind of culture. I recognise their intellect, I recognise their dedication to their jobs and the hardship that they must have had in gaining their*

qualifications, but they are only human beings and I feel I'm on an equal footing with all of them."

[Interview 11]

6.4.3 The conversion of evidence to recommendations

Draft recommendations are produced during GDEG meetings. The wording of the recommendation is entered electronically by a NICE team member and projected onto a screen so all (GDEG and NTT members) can contribute to its revision. The words and phrases are revised until consensus is reached that the wording reflects both the supporting evidence and what the group wish to convey as guidance. The draft recommendation is then conveyed to the Editing Team who ensure that the language used aligns with NICE standards for writing style and has clarity for the different audiences who access guidelines.

The process of the transformation of evidence to recommendations for this guideline development was described as *"problematic"* (Group member) and concerns about this process could be separated into four key themes.

The first theme concerned the initial process of forming individual guideline recommendations. The chair asks the GDEG to propose wording for the recommendation. It is an open invitation for someone to start the process but this caused some consternation for members of the group:

"I think that's when it gets quite tricky because then no one is coming up with a sentence. I find phrasing things very difficult. I think we all seem to be very good at talking through the evidence and then, there's that moment when you have to say what you are actually going to recommend. That's when it seems to be very difficult and everyone goes a bit quiet."

[GDEG member]

Usually someone volunteered to provide initial wording for the recommendation (except on one occasion when the chair asked a specific group member to start the process) and once the initial sentence was formed, all contributed to revise it until consensus on the

wording was reached. An example of how the recommendation might evolve from the initial wording is given below[10]:

> 1st wording: *"Health professionals should recognise the difficulty some people have with self-monitoring and provide appropriate encouragement and support."*
>
> 2nd wording: *"Healthcare professionals should recognise some people lack confidence with self-monitoring and offer appropriate encouragement and support."*
>
> 3rd wording: *"Offer appropriate encouragement and support to people who lack confidence to self-monitor."*

From observation of the process, the writing down of the recommendations was beset by a number of issues. One of these is the lack of accepted evidence and the low quality of some of the available evidence. This meant that, frequently, strong recommendations could not be made and the group found difficulty in wording a draft recommendation to reflect the guidance they wanted to provide. On occasions, there was no evidence to support *any* recommendation. In cases of insufficient evidence, research recommendations may be made to inform future decision making about filling current gaps in the research. For this guideline, twenty-one research recommendations were made.

The second theme concerned the limited nature of the language allowed by NICE in writing recommendations. This is detailed in Chapter 5 which sets out the generic NICE guideline process. In essence, certain verbs are used to convey guidance and the verbs reflect the strength of a recommendation. An entry in the Research Reflections Diary ponders on this situation:

> *"Use of linguistic tools in the way the recommendations are written to sign-post the meaning/intention, is interesting. Why has this come about? It is probably good to have standardised wording for all guidelines but it is limiting and everyone has to understand the "language" if this approach is to work. Do they?"*
>
> [Reflections Diary, 6 Dec 16]

[10] Note: this is not a verbatim example due to issues of confidentiality

Many of the group expressed concerns about this in interview. They felt that the vocabulary was too limited and that the use of certain phrases may suggest a course of action to the patient that was not intended. Further, that certain verbs may not convey the urgency of a course of action. Two examples of this recurrent finding are given as illustrations of the concern felt by group members:

> *"I think it makes it difficult because the phrases that you're not allowed to use, because they're not NICE-speak, seem to be the ones that we would all naturally choose to use. So that makes it difficult…..I think it's fine then when someone tells you what it should be but I think it just seems a bit alien. They never seem to be the phrases you would naturally choose".*
>
> [Interview 17]

> *"So, there is an awful lot of constraining of what we're allowed to say and not allowed to say"*
>
> [Interview 15]

The third theme was centred on the editing process for recommendations and how the edited version was then re-presented to the GDEG for approval. There were often weeks between the first version of the recommendation and its return from the Editing Team. Occasionally a member of the Editing Team would be present at the meeting where the revised version of the recommendation was discussed, but this was not always the case. The edited recommendation would be displayed at the guideline group meeting and the GDEG asked to agree to the changes. Whilst the evidence pertaining to the recommendation could easily be called up electronically, the original discussion was often not recollectable to the members of the group. One participant reflected on this:

> *"Recommendations. It feels like a complete free-for-all at times, you know. Everybody just pitches in with what they would like to say and then somehow it is edited down. The re-editing moments of those recommendations are really interesting in that they come back to us after going through NICE. The people at NICE criticise whether the language is good enough. It comes back and we approve it but, of course, that's two or three meetings afterwards and you no longer have the evidence in front of you so those subtleties of wording then actually make a massive difference."*
>
> [Interview 15]

The fourth theme concerned how differing interpretation of evidence could influence the shape of the recommendations made. This was linked with the participants' different views of the value of the various types of evidence. The example given concerns the differences in interpretation of the quality and content of qualitative data by different group members. Some qualitative evidence, addressing the various barriers and facilitators to patient attendance at hospital appointments, was presented to the guideline group. The evidence included data concerning intolerance to the treatments for macular degeneration given by injection into the eye. There was disagreement between group members about the level of pain from these injections. Interpretation of this qualitative data plus experience of the injections (giving and receiving) led some members of the group to insist that the draft recommendation should include offering support to patients with regard to treatment injections. On asking one group member during an *ad hoc* interview about the stance they took, they said:

> *"….my interpretation of the* [qualitative] *study was that intolerance to treatment was pain on injection and, as I have experienced that too, I wanted to give support to future patients and add something to the rec*[ommendation]*."*
>
> [*Ad hoc* interview 7]

6.4.4 Group dynamics and decision making

A number of findings emerged concerning the changes in the dynamics of the group and how these impacted decision making. Changes in group composition, detailed above in 6.2.3, did affect group functioning. The group often took time to adjust to new members. An example is where a new group member with evidence presentation responsibilities joined the group. Thus, this individual was important to the group in ensuring that evidence was presented with clarity. The group took time to adapt to the new style of presentation and personality of the new team member:

> *"It's very hard work to under* [stand], *it's not their fault, I mean what s/he says, the content of their presentation is brilliant but, my God, it's a struggle to hear her/him. I don't know if I'm going deaf, actually, I'll have to go and get my hearing tested, but, no, s/he's very quiet."*
>
> [Interview 14]

Some of the changes in group structure were seen as positive, for example, addition of another clinical expert, and some less positive, for example, the move from experienced NICE health economist to a junior health economist. In spite of constant changes in personnel, the group appeared to function well. There was generally cohesion and collaboration in interactions which was underpinned by open communication. Early on in the history of the group, one participant notes:

> *I don't think there's any disrespect between anybody on that group and I think everybody gets on pretty well. I mean we're still, it's that norming, storming, forming thing, isn't it with teams and we're still getting to know each other but there isn't anybody there that I don't feel you couldn't approach and start a conversation with."*
>
> [Interview 7]

Two others also commented on how the group worked together to complete the task:

> *"I think that it* [group functioning] *is remarkably good (laughs). We are a very varied group of people from very different backgrounds but that work together well."*
>
> [Interview 8]

> *"I think it's* [group functioning] *been quite effective really. I think people speak up and participate when their area of expertise is discussed."*
>
> [Interview 9]

One event temporarily halted the guideline proceedings but, even though construed to be negative, did not adversely impact the functioning of this group. For the first day of a two-day guideline group meeting, attendance by the GDEG did not reach a quorum. There were different reasons for individuals being absent. Some had informed the project manager in advance but others had reasons that necessitated late withdrawal from the meeting. Those present expressed irritation and annoyance with those absent, *"It affects the morale of the group. I wouldn't say "divisive" but…."* (Group member). No decisions could be made while the group was not quorate so the group members present discussed guideline questions without coming to any consensus and finished the meeting early. The following day, when the GDEG was quorate again, there was no in-depth discussion of

non-attendance or participant responsibilities and when it *was* mentioned, it was accompanied by humour. On hearing there was a Christmas market at the time of the next meeting, one participant commented, *"Can we ask people not to turn up again so we can go to the market?"* (Group member). The humour diffused the situation and there appeared to be minimal negative impact on the group functioning during the second day of the meeting, nor subsequently.

There were also fluctuations in group dynamics with respect to responsibility taken for contributions and decisions. This varied according to the type of question being discussed. Whilst decisions were made by consensus, where questions were purely of one type, for example, clinical questions or health economics question, those with the relevant expertise led the group deliberations. The decision making observed was a negotiated process leading to consensus. Informal consensus methods are usual in NICE decision making with opportunity to turn to formal methods if necessary (NICE, 2014, updated 2017). This was not necessary for this guideline and the view of participants was summed up by the following quote from an interview with a group member:

> *"…there's always sort of a downside to the committee making decisions* ***by*** *committee, isn't there? But I think, given that that's what it is, I think it works OK really. I think everybody's views are taken into account and I think it works as well as it could do."*
>
> [Interview 14]

The most important individual influence on the group interactions and on decision making was that of the chair. This was endorsed by the participants:

> *"I suspect that, in some cases, it might be difficult finding people who are appropriately skilled as expert in the subject and appropriately skilled as a chair but I think that role is so vital."*
>
> [Interview 13]

> *"I often come down on the side of having a good chair rather than having a clinician; somebody who keeps order and understands process and that's really what you want a chair to be there for, to keep everything going and keep everything together."*
>
> [Interview 15]

The chair for this group was experienced in chairing different types of groups and committees; this was evident in the way s/he managed the group to work collaboratively to reach a consensus. For instance, on one occasion where the facilitators and barriers to patient attendance at clinics were being discussed, one of the guideline group showed concern that other members of the group were not taking their viewpoint seriously. The chair intervened and allowed extra time for the group member to express their views fully. The chair also returned to the issue at the end of the day's meeting to check that the group member was happy with the outcome of the discussion and that s/he agreed with the consensus view.

Mostly, interactions between individuals in the core guideline group were constructive and productive. Only rarely was there any conflict. The conflict, when present, was often due differences in an understanding of the data and how the data reflected experiences of the disease. However, the conflict did not tend to impact the overall task of producing a guideline due to enough time being allowed to resolve such conflict. For example, on one occasion, there was a discussion about adverse events in the studies being appraised. The events were classified as "non-significant" and were largely dismissed by the clinicians and those with statistical training. However, one of the members of the group was concerned by the apparent dismissal of these adverse events and pointed out that, although the adverse event rate was small and "*non-significant*" (Group member), it did matter to individual patients with those side-effects. Time was allowed, by the chair, for a debate about statistical versus clinical significance and how even "non-significant" data can be important to patients.

On occasions, coalitions were seen to form supporting one particular viewpoint. An example is in the differing viewpoints relating to evidence in populations versus individual patient management and experience. There were two coalitions: NICE health economists and one GDEG member with service commissioning experience represented one coalition who understood and supported evidence pertaining to population health. The other coalition, comprising some clinicians and allied health professionals, wanted to see more personalised evidence, which took into account multi-morbidity and variation in practice. As with other interactions within this group, there was a determined focus on

resolving issues with minimal conflict. However, the lack of overt conflict, led to one group member to question whether this collegiality was always better than conflict:

> *"There's no energy, the energy isn't that vibrant, it's not a very energetic group to my mind. It's just a bunch of well-mannered, nice people who get on, you know, who are quite happy…..It's an interesting observation: at what point of the group dynamic, at what point of that process do you get to before that team really works as a team and says the sort of stuff that you want them to say. You know the inspirational stuff, the creative energy."*
>
> [Interview 15]

6.4.5 Emotions engendered by participation

The data analysis revealed many emotions engendered by the guideline process. There were both negative and positive emotions: "*belonging*", "*optimism*", "*fun",* "*respect",* on the one hand, and "*resentment*", "*boredom*", "*anger*" on the other. These were the emotions cited by respondents in interview (on being asked how they felt about participation in the process) as well as those observed being enacted during guideline group meetings. An example from each situation is given below. In each case, there is consideration of how the emotion felt to participants as well as how it impacted the functioning of the group.

One member of the guideline group was observed being provocative in meetings by asking difficult questions and suggesting that others' opinions were purely anecdotal and they should not be included in the deliberations. Others noted his behaviour too:

> *"…. And sometimes I think s/he's toying with it. I just think s/he's being a bit mischievous."*
>
> [Interview 7]

The particular group member professed that s/he was *"bored"*, and this was driving their challenging behaviour in the meetings. Perhaps key to their behaviour was their mode of recruitment in that s/he was approached to become a member of the Committee rather than seeking out recruitment themselves. S/he said of this:

"….they had to bend my arm really coz it's not the sort of thing I would naturally gravitate towards."

[Interview 6]

The initial reluctance to participate culminated in boredom which affected their behaviour within the group and ultimately had a mildly disruptive effect on group functioning by occasionally delaying proceedings.

The second example concerns an interaction between two group members, over two meetings. The discussion at the meetings concerned the barriers and facilitators to patients in attending appointments and in their uptake of treatment. Much of the evidence discussed was qualitative research of patient experience. At the first meeting, one member was observed to be quite disengaged, often having side conversations, but the other was animated and contributed much to the discussion. At the subsequent meeting, there was a revisiting of the same review question and this included a discussion of transport for patients. During this discussion, the interaction between the two group members became rather sarcastic and unpleasant. The frustration felt by one of the group members seemed to affect subsequent contributions and interactions with the rest of the participants during this one meeting. Endeavours were made by the chair and other group members to bring this individual back into the group. The Observation Fieldwork notes of that incident noted that there were: *"some efforts by the chair and others to mitigate their concerns"* (Observation Fieldwork notes, 13 Jul 16). On questioning this individual at a later date about the incident, the response was that they felt *"disrespected"* (*Ad hoc* interview 6). This illustrates how interactions of two individuals can engender some negative emotions which can potentially affect the functioning of the whole group.

6.4.6 Emergent trust

Trust, defined here as a belief in the reliability, ability or truth in someone or something, emerged as an inductive theme. This was based on the numerous times respondents in interview used the word "*trust*" when describing various scenarios and how they felt about them and on observation analysis of how group members interacted.

There were two main areas where trust emerged as a theme. The first concerns trust in the NICE guideline process. The following, taken from different interviews, all illustrate trust in the guideline process with respect to the ability and reliability of NICE technical staff to search for and select appropriate evidence:

> *"I take them at their word that they've looked through the appropriate stuff in the first place and weeded it out to the stage that they're then prepared to share with us. So, I don't have any qualms with that part of the process."*
>
> [Interview 11]

> "*But we do rely very much on that sifting process because, you know, out of those three thousand, two hundred studies, we end up with seventeen studies, for example. Who's to know that one of the good studies hasn't been picked out in the sifting so we have to take the word of our NICE internal team to trust that they've done a good sift and they've not thrown out some of the good studies that we really needed to have seen."*
>
> [Interview 10]

> *"…in terms of the statistical side of it, people are looking at it and grading it, that's where their expertise comes in and….. as a novice, you look and you think I might be seeing that but, for some reason, this is trusted. It's brought to you and it's trusted and you've got to trust people, haven't you?"*
>
> [Interview 7]

Many GDEG members were inexperienced in statistics, in health economics and in the NICE methodology and there was a conviction that the GDEG was being led through the guideline development process with the right tools, in the right way to achieve the desired outcome.

There was one instance where there was a loss of trust in the guideline process. This is described more fully below in section 6.5.1 as it relates to the macular degeneration treatment issue (previously outlined in section 6.2.2), part of the external environmental influences. In essence, there was a change in the guideline process which did not fit with the GDEG members' expectations of what would happen. A change was made to the wording of a draft guideline recommendation without the endorsement of the group. This

caused some anger that there was a lack of transparency in actions taken outside of the group by NICE. Noted in the Reflections Diary was: "*There was certainly loss of trust of NICE (not the NTT) and the process*". (Reflections Diary, 6 Sep 16).

The second area where trust emerged as a theme was in how the individuals of the guideline group appeared to trust each other in their efforts to complete the task. This was despite different personal agendas or motivations for being a participant. The belief was in the desire of each other to overcome their differences and deal with any interpersonal conflict. This was, for example, manifest in the type of words used by participants to describe the group and the process: "*respectful*", "*harmonious*", "*task-focused*". Their descriptions of the group were consistent with each other and across the development period, so it was not thought that participants were just presenting a picture of group cohesion to the researcher.

The following was from one group member giving feedback on the guideline development process as a whole. Here, s/he talked of the collaborative and respectful environment produced by the members of the group:

> *"I think yeah the collaborative aspect is good, it's, there's something cumulative about this as opposed to just the individual members contributing so you go away feeling like, feeling better that when you arrive because you have not just gone through the agenda but you have interacted with your colleagues. Each meeting it builds and that I think is positive, because obviously the hard work will be not just sifting the data but bringing together a useful product at the end. I think, if you have built up into a respect, a respecting environment, then, that will produce good results."*
>
> [Interview 6]

A further illustration of how group members were prepared to put aside differences and work together is the following from a group member relating their view of how s/he felt the group functioned:

> *"I'm overwhelmed by how committed they* [the GDG as a whole] *are to try and get to a really good outcome, to produce a really good product though I think I'm surprised. I had some anxieties that there may be a couple of people on the*

committee who just have a certain way about them which might cause a little bit of disruption in the way they operate. I was expecting one or two characters who might be like that but actually I was so surprised there isn't anyone there who was like that. I think everyone, so far, has been prepared to compromise on things…."

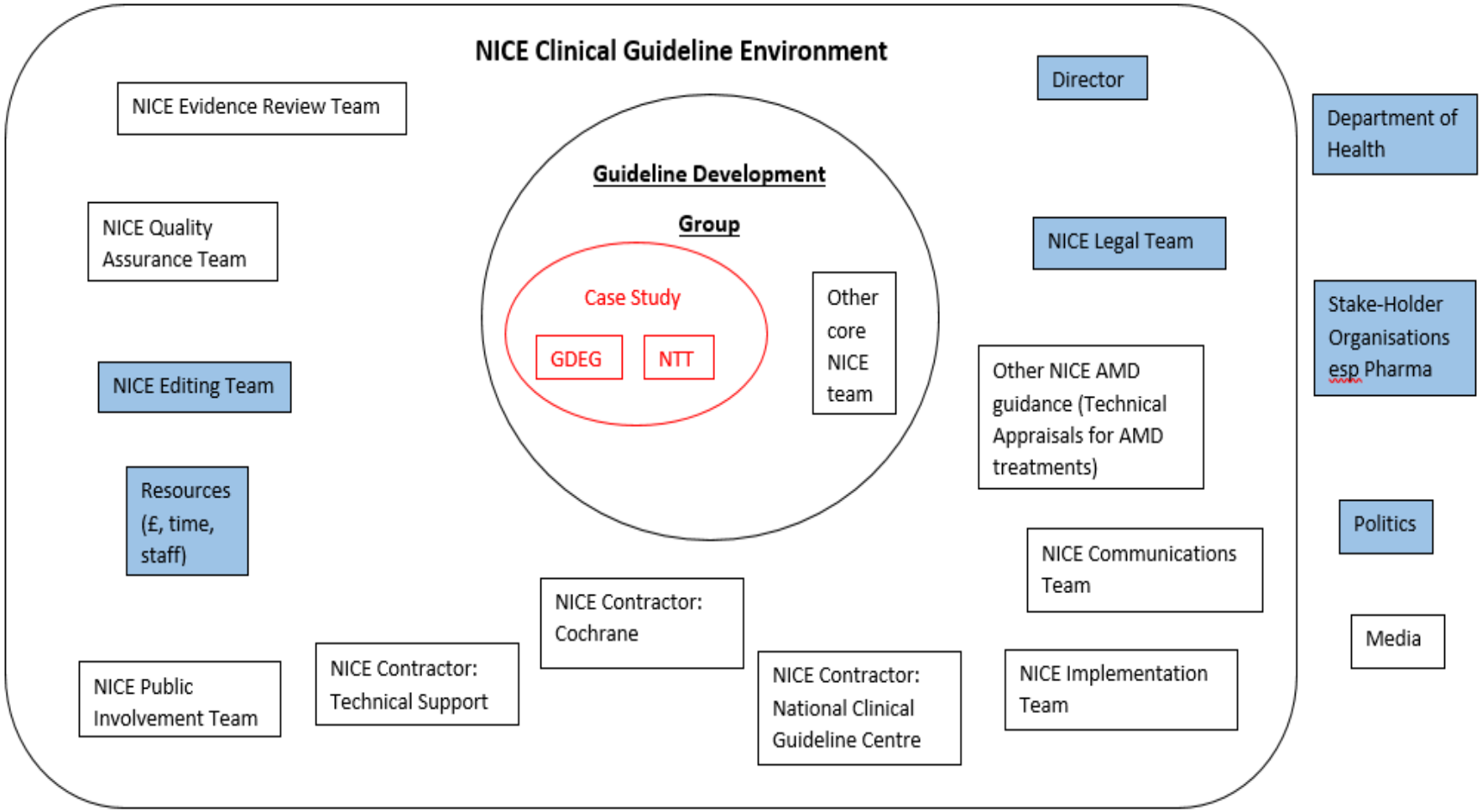
[Interview 10]

Part 3 has described the findings relating to the functioning of the guideline development group. The final part of this chapter turns now to findings concerning the influences on the guideline group from the wider environment within which it operates.

6.5 Part 4: Broader network influences

The generic broad environment in which NICE operates was reviewed earlier in this thesis (see Chapter 5). In Figure 6.4, that generic depiction has been revised to show this specific guideline group within its broader environment. Figure 6.4, like the previous iteration in Figure 5.2, includes the physical bodies, teams and organisations affecting the guideline's development. It also includes wider abstract concepts, for example, "politics", that have proved influential in the development of this guideline. The network elements seen to have the most influence in this case are highlighted by "block-filled" boxes. The remainder of this part of the findings describes these main influences on the development of the macular degeneration guideline. Firstly, there is a description of political and legal influences on the guideline development. This includes the issue of macular degeneration treatments. Then resource influences are detailed. The next section shows how there is adherence to processual rules in the guideline process and the final part describes the influence of various external stakeholders.

Figure 6.4: The broader network around the guideline development group



6.5.1 The political/legal environment and macular degeneration treatments

The political/legal environment, in which the guideline development took place, was both contextually influential and had a direct impact on the development process itself. There was a recognition within the macular degeneration group that a wider political network may impact how the group operated:

> *"I mean NICE does not exist in isolation, they're part of a society and NICE is paid for by the taxpayer …so there is a political drive, there is an economic drive, there is a capitalistic influence."*
>
> [Interview 6]

However, for this guideline, one particular issue demonstrated how politics and legal/regulatory frameworks can play into guideline development. The issue concerned a specific treatment approach for macular degeneration – regular injections of anti-angiogenic agents into a diseased eye. In essence, despite widespread clinical (off-label) use, the most cost-effective agent did not have a licence for use in macular degeneration in the UK. Furthermore, arguments about the funding for such macular degeneration treatments had been played out in the media and in academic, medical journals (BBC, 2015; Cohen, 2015b, 2015c) prior to the start of the development process and one of the guideline group participants had been involved in this.

As NICE have to abide by legalities, the guideline group was instructed initially that they could not make a recommendation for its specific use. This limited the scope of the guideline (previously described in Part 1, 6.2.2). It also impacted the guideline development process.

The direct impact of this issue on the development process was seen more than two thirds of the way through the process when the group was instructed by the Director of the Centre for Guidelines to now consider evidence for the use of the off-label drug. The Director's guidance gave the group more flexibility in their considerations although it still fell short of allowing the group to overtly recommend the treatment. This was a matter of concern to the group as

they felt it unclear what would happen if they *did* decide to recommend that treatment and that what they suggested may be changed anyway. This from group members:

> *"Why the change, bearing in mind legal issues; is this empowerment rather than* [top] *down regulation?"*
>
> [*Ad hoc* interview 5]

> *"...because if they could, they would have made recommendations that said everyone should be offered bevacizumab and they weren't in a position to do that and so, I think, it irritated the committee ever so slightly that that it* [the guidance to now consider bevacizumab] *happened at the end. I think the* ***wiser*** *members of the committee saw through it immediately as, say what you like about this, NICE are going to cross it out and put what they think there anyway. So the committee's hands were tied to a degree that they couldn't say what they really wanted to and I think they'd probably rather have said nothing in a way."*
>
> [Interview 20]

The guideline group considered the evidence for bevacizumab, along with the evidence for other similar anti-angiogenic therapies, and a statement was included in the draft guideline that "all" such treatments had been proved to be safe and effective and can be offered to patients with certain visual acuity. The draft guideline underwent the editing process with input from the NICE Legal Team. This process changed the wording agreed by the guideline group and the draft guideline was readied for consultation. The new wording was not returned to the GDEG for approval. This angered some of the members of the guideline group and conflict between the GDEG and NICE was averted only after the intervention of the Director of the Centre for Guidelines and a rewording of the recommendation. In the published guideline, NICE note that the bevacizumab may be prescribed, but the prescription will be off-label (see Appendix ix). Also, in the notes to the guideline recommendations, clinicians are reminded that they should be mindful of the rules concerning such prescriptions and, thus, the responsibility is transferred to them. This issue did result in one member of the guideline group to suggest that such external influences can run counter to the philosophy of guidelines:

"*I mean that* [the issue and the way it was dealt with] *obviously provides context within which the guidelines are clearly* ***not*** *evidence-based are they?"*

[*Ad hoc* interview 20]

The final quote in this section is illustrative of the feelings of many of the group about how external influences may affect the guideline development process. It links the influence of the external environment with the specific anti-angiogenic treatment issue:

"*…you're very aware of what is happening outside, especially with the Avastin thing being there, and it does make it more difficult, shall we say, that you know you're acting in a sphere where you can't quite say what you want to do."*

[Interview 17]

6.5.2 Resource influences

Resource availability emerged as influential on the progress and completion of the guideline. This was from one group member on being asked about resources for the guideline task:

"I try not to really consider cost or, you know, resource in terms of space or people because what we're wanting to do is to develop the best guidelines we can. But, obviously, we are constrained by resources."

[Interview 9]

Time was noted by participants in interview as one resource critical to the completion of the guideline and in short supply because of the guideline's wide range and scope. Two group members illustrated this when responding to a question about the challenging parts of the guideline process and resource availability:

"So, yeah, there's definitely a time resource and human resource pressure."

[Interview 2]

"I think the challenge is the amount of work we have to do in the time space."

[Interview 19]

Additional time for discussion was required to solve the treatment issue described above, as well as the delay introduced as a result of the 2017 UK General Election.

Other resource issues impacted the guideline group's task with respect to sufficient availability of NICE personnel with relevant expertise. This mainly concerned the health economics part of the guideline:

*"Time is an issue and, well, it's **all** resource really and the level of methodological expertise available to us is limited."*

[Interview 20]

Part of the work, which included a complicated modelling exercise, had to be contracted out to external parties. This culminated in an extension to the timeline that added further constraints concerning the workload of NICE personnel and requiring additional time for guideline group members to attend extra meetings.

6.5.3 Adherence to processual rules

The NICE manual for the guideline process is now two hundred and thirty-eight pages long and none of the GDEG professed to have read the whole manual. Therefore, the NICE team, as owners of the process, led the experts through it at every stage. Views of GDEG members on the process varied from "*robust"*, "*brilliant*" and "*neutral*" to "*cumbersome*" and "*rigid*".

Whilst many GDEG members accepted much of the process, particular elements were highlighted as being problematic. One was the lack of input to the scope of the guideline. The scope is set prior to the recruitment of most members of the GDEG; only the chair and one other expert is consulted. Some felt that not being present when scope was decided meant a lack of understanding about how the scope was arrived at. There were

complaints about constraining boundaries for certain review questions and a lack of involvement at an important stage of the guideline process:

> *"The one thing that I'm slightly mystified about, if I'm perfectly honest, is the scoping that went on for the guideline committee. It seems strange that you come in on something that's already been kind of scoped."*
>
> [Interview 8]

Another example of the constraining influence of processual rules is that any proposed recommendation cannot have a service provision consequence because of cost implications to health service providers. This, on occasion, frustrated the group members:

> *"…all the trials point to monthly treatment being the most effective so I was quite concerned about the recommendation of three-monthly bevacizumab* [which would be cheaper] *and that, I guess, that came from the analysts rather than the committee. I felt at that point, well, it was left unresolved and, in some ways, the opinions of the committee were being superseded by the approach by NICE"*
>
> [Interview 18]

The NICE team acted as monitors of the process but they were also seen as a support with deep knowledge of how best to succeed in the guideline task. Particular members of the wider NICE team were looked to for this support, for example, the technical advisor who is nominally the leader of the NTT. This person was deferred to many times by group members with respect to the NICE "rules". One respondent commented on the role of the advisor:

> *"S/he gives clear guidance on due process and stuff like that. People like* [the technical advisor] *is very good at encapsulating discussion and terminating discussion with a positive conclusion."*
>
> [Interview 5]

One of the guideline group, new to guideline development and NICE processes, had undertaken research previously and had written a number of papers. S/he felt the NICE process was quite prescriptive in the way of writing and presenting evidence.

"I am getting used to the process of how you structure a sentence compared to my previous research writing. It's quite different but, again, it's kind of, process-driven. You just have a certain way to write certain things."

[Interview 12]

The adherence to the NICE way of writing, mostly related to recommendation wording, was monitored particularly by an associate director who would give advice on what would be acceptable and what would be rejected by the NICE Editing Team.

There were mixed views about the guideline process and whether having process "rules" mattered. Some members of the group thought the guideline process was prescriptive and controlling, for example:

"They're so process-driven, aren't they, that you wonder if they want, if they perceive the people around the room are just little robots commissioned for the process".

[Interview 15]

However, others felt that having a standard process in place ensured uniformity and transparency across guidelines:

"I think that's a real strength that when someone picks up a guideline, they know exactly the process it's gone through and it's completely explicit."

[Interview 13]

"….it's obviously such a prescriptive process, because there are certain things that you seem to have to do in a certain way. It has to be done so that you can compare across guidelines."

[Interview 17]

6.5.4 Stakeholder influences

Stakeholders, as defined by NICE, are those with an interest in a specific guideline and who are involved in the consultation process. Stakeholders, in this thesis, are also defined as those whose activities underpin the guideline, such as researchers and their companies who provide evidence, or other organisations to whom guideline work is outsourced. Stakeholders can also be those organisations to which participants in the process belong or are linked to.

NICE is clear that "Committee members do not represent their organisation(s)" (NICE, 2014, updated 2017:41). On asking participants of the GDEG whom they represent whilst participating in the guideline development process, all concurred that they represent themselves and their own views, although they remained aligned to the organisations to which they belong. This from one group member:

> *"Inevitably, having been involved in* [organisation] *for nearly ten years, it's part of my work make-up. I'd like to think that I'm there with my* [profession] *hat on and I think that probably is easy to do."*
>
> [GDEG member]

The influence of the organisations to which GDEG members belonged was also evident in the motivations of individuals to participate (see 6.2.4). Five of the thirteen expert group members were asked by their organisations to apply to participate in this guideline. One group member commented on the influences to participate, or not, in the guideline development process:

> *"So how do people get to the table; there'll all be different influences on that. The big influence there is the way in which NICE doesn't fund* [pay] *the guideline committee."*
>
> [Interview 13]

NTT members represented NICE and not themselves. They were influenced strongly by their parent organisation with respect to the NICE methodology and the processual way

of working. However, they did occasionally express views about the NICE process and the influences from stakeholders:

> *"We say what topics we're going to cover and what we're not going to cover and this is done in a kind of communion with the stakeholders. So, you know, the people who have vested interests say they want us to cover this."*
>
> [NTT member]

Stakeholder influence on the guideline process seemed especially strong from the pharmaceutical industry. The influence of their marketing authorisation ownership of anti-angiogenic drug treatments on this particular guideline has already been described, but their influence was seen in other ways too. Many of the publications selected as evidence were a result of drug trials and other studies financed by pharmaceutical companies; these are heavily weighted towards commercial interests and many of the large RCT drug trials came from this source. Studies undertaken by pharmaceutical companies often involve clinicians as investigators. One direct effect of this is that those clinicians are then excluded from serving on a guideline group due to potential conflicts of interest. Pharmaceutical companies were also key contributors providing comments on the draft guideline. The influence of pharma was not well-received by many on the guideline group. For instance:

> *"…..there's huge external pressures to over treat from pharmaceutical companies."*
>
> [Interview 5]

> *"……there were two ophthalmologists recruited initially and one person had to resign and they have struggled, they've interviewed several but conflicts of interest is a major problem in the field."*
>
> [Interview 4]

There were views, however, that perhaps the role of the pharmaceutical industry in guidelines is seen in too negative a light:

"In fact I think probably they might be an extent to which the pharmaceutical industry is over-demonised but I don't know. I mean, I'm not a great conspiracy theorist, but I know that people are deeply suspicious and I think there is deep suspicion amongst some people in NICE, not everybody, but ***some*** *people in NICE are deeply suspicious of the pharmaceutical industry".*

[Interview 14]

The final illustration of how the case participants viewed the influence of stakeholders on NICE comes from one interviewee on being asked to comment on whom they perceived as being significant external stakeholders in guideline development:

"NICE can be told what they can and can't do because NICE doesn't pick and choose what guidelines they're going to write; they get told by the Department of Health. Even though NICE is independent, there can always be a steer of what NICE does through that channel I guess."

[Interview 21]

Various stakeholders, therefore, were perceived as having influence, in different ways, on NICE and the guideline process.

6.6 Summary

This chapter has set out the main findings of this case study. The structure has paralleled the conceptual framework with sections germane to the use of evidence, group functioning and interactions, and identification of the main influences from the broader network surrounding the case study boundaries. There is also a section at the beginning setting out information about the specific guideline topic and the characteristics of the group.

The findings have shown that the evidence on which this guideline is based is variable in quantity and quality. On some occasions, the lack of evidence frustrated the participants and led to difficulties in framing guideline recommendations. Several types of evidence were considered for inclusion in the supporting evidence but a strict hierarchy operated

to assess the quality of the evidence. However, expert opinion within the group was relied upon frequently. Health economics evidence assumed a high degree of importance. The process of converting evidence to guideline recommendations seemed problematic.

Guideline development is a multi-factorial, social process. The guideline group for this guideline was multi-disciplinary and the patient viewpoint was well represented. Motivations for joining the group were varied. Some were participating for altruistic reasons, others for education, and yet others for recognition amongst peers or to counteract perceived pharmaceutical industry involvement in guidelines. The perceptions of what guidelines are, and to whom they are addressed, were equally varied. They were perceived as advice for clinicians and other health professionals, recommendations on which funding decisions are based and information for patients and carers.

Guideline group functioning was affected by changes in the composition of the group, status hierarchies in play as a result of the different professions represented in the group, the varying emotions engendered in participating, and the role of trust. However, any negative effects on group functioning were usually temporary and, overall, the group interacted positively in addressing their task. The professional roles played by individuals were clear and other roles, such as "arbiter" and clarification-seeker", emerged as important to the smooth running of the group. The key role to ensure seamless progression of the guideline process was that of the chair. The NTT members also played a facilitatory role, as well as being "monitors" of the NICE process.

The key findings concerning external network influences were that they set the context for guideline development and had a direct effect on the guideline development process. The macular degeneration treatments issue was one such influence. This issue dominated parts of the process and led to conflict within the guideline group. There were other external factors that were seen to be influential. One was the strict adherence to NICE processual rules and, another, the influence of various stakeholders on the process.

Having set out the findings, the next chapter turns to a discussion of these in relation to existing literature on the clinical guideline process.

Chapter 7: Discussion

7.1 Introduction

The previous chapter presented findings from this case study of the guideline development process. This chapter discusses these findings, (summarised in Table 7.1), and their relevance, with respect to the wider body of guideline literature. A new integrative framework is presented at the end of the chapter that brings together the principal findings. There is a discussion of the key elements of this framework and some reflections on its development.

Table 7.1: Key findings

1: Guidelines draw on a mixed evidence landscape.

The quantity and quality of evidence used as support for the guideline recommendations is variable and depends on the nature of the review question. An evidence hierarchy (with RCTs at the apex) is still evident. Expert opinion (at the bottom of the hierarchy) is influential, especially when the availability of evidence is low; in these conditions, in effect, the hierarchy is turned upside down.

2. Guideline development is a multi-factorial, social process.

The guideline process involves the interaction of a diverse group of players. Factors such as roles adopted, status hierarchies, changes to the composition and dynamics of the group, and emergent trust can all affect the functioning of the group.

3. Guideline development takes place within the context of a broad network of actors and external factors.

The guideline development group constitutes a network which operates within a wider network. The external environment acts as a contextual influence and can also provide specific challenges that constrain and shape the guideline process.

Whilst other factors do play a role in the guideline development process, the significance of the evidence cannot be underplayed as the main support for guideline recommendations. However, the evidence landscape presents a mixed picture: the supporting evidence base is of variable quantity and quality and there is a reliance on expert opinion where evidence is scarce. Further, although many types of evidence are considered, there is a strong adherence to an evidence hierarchy which impacts assessment of its quality.

The study findings have shown that guideline development is a process underpinned by social interaction. This is evident in the way the core guideline group debates, discusses and interprets the evidence on which recommendations are based. Multiple factors affect the interactions of the group, for example, the composition of the group, the roles adopted by group members and emergent states such as trust.

External factors are influential in the process. Guideline development operates within a broader network of actors and stakeholders and, while there may be some positive influences from this broader network, they also have the potential to disrupt the guideline process.

7.2 Examination of key findings with respect to the literature

In line with the key findings, the discussion is set out under three main headings. Firstly, there is a section concerning the evidence landscape of guideline development. Then, there is a discussion of the findings that point towards a multi-factorial, social guideline development process. Finally, external influences on the guideline process are discussed.

The evidence landscape in guideline development

The nature and utility of evidence for clinical guidelines continues to be a subject of debate (see for example: Oxman et al., 2006; Steel et al., 2014; Carroll, 2017). Evidence remains, however, a fundamental building block of guidelines and its significance to the guideline process is reflected in the proposed integrative framework, discussed later in this chapter, where evidence is both an input to the process as well as an enabling or disruptive factor. This section discusses the study findings in relation to the research aim

of understanding how evidence is perceived and used within the guideline process. The type of evidence that enters the NICE process, the assumptions on which selection of evidence is based and how the core guideline group perceives this evidence is reviewed. Also discussed is how evidence availability and acceptability can act as an enabling or disruptive influence.

There is a concerted effort by NICE to gather data from many sources and of many types, appropriate to each review question, in order to present the "best-available" evidence to the guideline group for formulating guideline recommendations (Hill et al., 2011:752). The types of data gathered and appraised are not limited only to peer-reviewed scientific research. Other data may be included in the search strategy including, health economics data, basic sciences data (sciences such as anatomy, physiology, and biochemistry which are foundational to medicine), and grey literature (NICE, 2014 updated 2017). However, the large amount of data now available causes concern in terms of how it can be managed effectively (Greenhalgh et al., 2014). Further, the high volume of guidelines themselves are seen as counter-productive in the quest to practise evidence-based medicine (Swinglehurst, 2005; Greenhalgh et al., 2014; Upshur, 2014).

Grey literature (for example, unpublished data, conference abstracts, policy documents, book chapters), is viewed by some as having more importance than it has previously been afforded in health policy arenas and have advocated its inclusion in systematic reviews (Benzies et al., 2008; Higgins & Green, 2011). The focus on grey literature is due, in part, to publication bias: large studies with positive treatment effects are more likely to be published and included in systematic reviews and meta-analyses (Song et al., 2010; Goldacre, 2016). When a systematic review is conducted, inclusion of these studies only, can lead to an artificially high treatment effect compared with reviews including smaller studies from the grey literature (Hopewell et al., 2007b). There is also a concern about publication lag where studies can take years to be published. This means that relevant literature may be omitted as evidence, a gap that can be filled by grey literature (Pappas & Williams, 2011).

There was a comprehensive search for relevant data for the macular degeneration guideline. Thousands of publications were screened initially but grey literature was notable by its absence in the results of searches, having been filtered out at the primary search stage. However, it was included (on the request of the GDEG) during the development process, for example, the Medisoft data on disease progression available only to individual clinicians. Thus, despite increasing interest in it and the apparent acceptability of it to NICE, its inclusion as part of the guideline's supporting evidence remained mostly elusive in this study.

Evaluative judgements are made during the selection stage about the "weight" of the evidence: its quality and relevance to questions being asked (Gough, 2007). The selected evidence is synthesised using a range of techniques, such as systematic review, so that a summary of all the evidence may be developed for the expert group to then appraise (Liberati et al., 2009; Higgins & Green, 2011). In this study, of the many thousands of publications screened, only a small proportion was part of the supporting evidence base presented to the guideline group and used to support the final guideline recommendations. This is in line with observations of how scant evidence bases presented for guidelines development may be (Woolf et al., 1999; Goergen et al., 2009; O'Hare et al., 2009; Paul et al., 2009; Speijers et al., 2010; Marciano et al., 2014). However, the data reported by these authors originates from different therapeutic areas and is for guidelines developed under different health systems, using different methodologies, and includes a mix of national and regional guidelines.

In the macular degeneration case study, for review questions relating to treatment interventions, the number of publications accepted to those screened was higher than those for questions concerning diagnosis, preventative measures or psychological therapies (see Tables 6.4 and 6.5). Reasons for rejection (Table 6.6) were varied and similar for both intervention questions and diagnostic questions. However, there were more exclusions due to study design type for the diagnostic category. Furthermore, in the latter category, where observation and cohort studies were more common, a rating of "low" quality was more likely to be ascribed during quality appraisal. Treatment intervention questions are usually associated with larger, randomised-controlled drug studies, often

sponsored by commercial pharmaceutical firms (Perlis et al., 2005; Every-Palmer et al., 2014; Djulbegovich & Guyatt, 2017). The privileging of RCTs as evidence in this case study suggests continued adherence to assumptions about what constitutes the "best" evidence, that is, randomised-controlled trials and accepted methods, such as systematic review, to synthesise such research (Campbell Collaboration, 2017; Cochrane Collaboration, 2017). It also points to rigid assessment of evidence quality in NICE guideline development using hierarchies based on study design. Since NICE follows EBM principles with regards to the robustness of evidence, this is not unexpected although Michael Rawlins, the then chairman of NICE, in his 2008 Harveian oration, stressed the need for many forms of evidence to aid decision making in guideline development. He called for a replacement of hierarchies of evidence with a more diverse approach encompassing different sources of evidence and an acknowledgement of the role of judgement in assessing evidence (Rawlins, 2008). The continued adherence to rigid hierarchies of evidence is also counter to other calls for a broadening of the evidence base to take account of context as well as efficacy, with inclusion of studies with multiple methodologies such as mixed methods and qualitative studies (Noyes et al., 2010; Shaw et al., 2014).

Contextual and experiential perspectives in clinical guidelines are said to be provided for by patient representation on guideline groups (Boivin et al., 2010), and by the inclusion of qualitative studies which seek out views of patients and service users (for example, see Tan et al., 2009; Carroll, 2017). Qualitative research was part of the evidence base for certain review questions. These questions were ones exploring patient experience of treatment and management, such as the barriers and facilitators to appointment attendance and uptake of treatment. However, overall, qualitative research was under-represented in the presented evidence base for the macular degeneration guideline, mirroring other studies (Tan et al., 2009; How et al., 2015). Tan and colleagues (2009) reviewed 49 NICE guidelines published between 2002 and 2007, and less than half (47%) included qualitative studies as a basis for guideline recommendations. Qualitative research was thought useful by many of the macular degeneration expert participants, especially where disease and service-user experience were central to the review question. However, there was a reductionist view too, held mainly by those in the guideline group with formal

scientific training, that qualitative research was not valuable unless it could be reduced to something measurable. The "low" quality ratings (in line with the prevailing assumptions about evidence) given to the few qualitative studies included, were seen as endorsement of this view and of the value of qualitative evidence in general. However, despite little qualitative evidence being included in the macular degeneration evidence base, NICE has made a formal commitment to including such experiential evidence. For example, it has added a framework for quality assessment of such studies to the NICE methodology, been attributed as placing patient values and experience at the centre of its guidance (Kelson, 2005; Rawlins, 2008; Kelly et al., 2009), and set up a patient involvement unit and a Citizen's Council to increase patient and service user input to guidance.

Evidence, which is judged to be robust and supportive of benefits that outweigh any harms, enables the formulation of "strong" recommendations. Strong recommendations are those "that the Committee believes that the vast majority of practitioners or commissioners and people using services would choose a particular intervention if they considered the evidence in the same way as the Committee" (NICE, 2014, updated 2017:167). The wording of the recommendations reflects the strength of the recommendation made. For example, the AMD Guideline, (2018), Section 1.5, concerns Pharmacological Management of AMD. This section encompasses RQs 12 and 18 (see Appendix viii) and includes an "offer" statement as guidance with regard to anti-angiogenic therapies. The strength of the recommendation reflects the evidence, mainly RCTs and graded high quality, associated with these review questions.

For many review questions, there was often an adjudged lack of evidence which precluded the formation of a strong recommendation. The lack of evidence often acted as a factor which disrupted the process, for example, more time was required for the acquisition of more evidence or for further discussion of the currently available evidence. The scant evidence for some review questions was reflected in the high number (21) of Research Recommendations made when the guideline group felt no useful guidance could be supported. In many situations, but especially where evidence was sparse, the judgement and experience of the experts of the guideline group were turned to as a source of evidence. For example, the use of low vision services for patients with macular

degeneration was not supported by evidence in these specific patients since it was amalgamated with evidence from patients with low vision due to all causes (see 6.3.3). During the guideline group discussion about this, the patient members and the low vision expert of the group were seen to contribute most. The final published guideline recommendation was to "consider referring people with AMD causing visual impairment to low-vision services" (NICE AMD Guideline Recommendations 1.6, 2018) The use of the verb "consider" indicates a recommendation of lower strength than if the verb "offer" is used.

The term "expert opinion" is often used in relation to experiential evidence and judgement for guideline recommendations, although it is not transparent exactly what this means (Ponce et al., 2017). NICE does not recognise "expert opinion" in the process manual. Rather, it uses the term "colloquial evidence" to represent expert testimony, evidence from groups of service users or stakeholders, GDEG experience and judgement (NICE, 2014, updated 2017:75). The use of expert opinion is inescapable since evidence on a majority of issues is said to be always incomplete in some way, either because relevant research has not been undertaken or is unacceptable for reasons of quality, (Sniderman & Furberg, 2009). The inclusion of expert opinion in many hierarchies of evidence, albeit usually sitting at the bottom of the hierarchy (Guyatt et al., 1995; Howick, 2011), suggests that it could be a source of evidence although its inclusion as evidence is said to decrease the trustworthiness of the guideline (Murad, 2017). Others disagree that expert opinion should be included in evidence hierarchies that are based on study design. Oxman and colleagues (2006) caution that expert opinion is not a study design and is more than evidence alone, encompassing judgement and interpretation of facts. The appropriate use of expert opinion should include transparent identification of the evidence underlying this expert opinion (Oxman et al., 2006; Ponce et al., 2017).

Many have argued that guidelines should reflect all types of knowledge (Rawlins, 2008; Zuiderent-Jerak et al., 2012). However, the reliance on one type or another appeared, in this study, to depend on evidence availability. The lack of evidence for many review questions in this guideline led to a reliance on the experience, opinion and judgement of the expert participants. Some authors have indicated the increasing use of expert opinion

in guideline development with calls for the use of an expert opinion quality checklist, similar to the checklists employed for quantitative data (Sharma et al., 2015). The frequent use of expert opinion in this study suggests that its place as an evidence source may still be under-acknowledged in guideline development. These findings add to the body of literature questioning the validity of existing evidence hierarchies for *all* situations (Vandenbroucke, 2008; Osimani, 2014; Blunt, 2015).

Interpretation of evidence is, according to the formal NICE processes, "at the heart of the work of the Committee" (NICE, 2014, updated 2017:162). This is reflected in the multiple publications describing the work of NICE and guideline developers worldwide (Hill et al., 2011; IOM, 2011; Legido-Quigley et al., 2012). What is less well documented is how individual guideline group members' perceptions of what "good" evidence constitutes, plays into that interpretation. This is important since interpretation of evidence drives the formulation of recommendations. The findings demonstrated that the perception of evidence differed among guideline group members. Those trained in science/medicine fully endorsed study designs at the top of the evidence hierarchy. This was despite understanding some of the disadvantages of RCTs, such as not representing individual patients with co-morbid conditions (Shekelle et al., 2012; Hughes et al., 2013). They also were inclined to place less value on designs further down the hierarchy. Those with disease experience placed value on studies that related to patients and disease experience and occasionally questioned why more such evidence could not be included. These findings suggest that the EBM notion of what "good" evidence is, was not a common understanding across group members. This occasionally affected the drafting of recommendations where perceptions and interpretation of evidence, and its consequent acceptability to support recommendations, caused disagreements during group discussions. For example, there was a discussion around the perception of pain from injections of anti-angiogenic medication into the eye. There was little high-quality evidence (although some qualitative evidence was available) supporting the views of the patient members of the guideline group that the injections were painful. The lack of any high-quality evidence in this regard, caused the clinical experts to suggest that the experience of these individuals could not be proved. The final guideline recommendations (NICE AMD Guideline Recommendations 1.2.4 and 1.2.5, 2018) did not include specific

reference to possible pain on injection but did advise that peer support should be promoted for patients especially those beginning a course of injections. Thus, in accord with the view: "the adequacy of evidence is a matter of judgement" (Tunis, 2007:w501), assumptions about evidence and the interpretation of it, are linked. Further, in the guideline scenario, the differing perceptions of evidence can influence group functioning and, ultimately, the outcome of the guideline process in the shaping of the guideline recommendations.

This study of guideline development reveals a mixed evidence landscape. There is a strong adherence to the principles of EBM and evidence hierarchies in the selection of evidence but differing perceptions of the value of evidence. The process for evidence appraisal was in accordance with the NICE methodology. Many thousands of articles and many types of evidence were screened during the literature searching. This accords with the claim that guidelines should reflect many types of knowledge (Rawlins, 2008; Zuiderent-Jerak et al., 2012) although there was a high rate of rejection of evidence during the screening process for this guideline. Where formal evidence was sparse, the study revealed a reliance on expert opinion. When evidence was plentiful and of high quality, according to the NICE process, it acted as an enabling factor for the formulation of guideline recommendations. Differing interpretation of the evidence and experiences of the disease affected the drafting of the guideline recommendations. Conversely, evidence may disrupt the process too. It can slow the process down if conflict about its interpretation occurs or the outcome may be that a weak, or no, recommendation is made.

This section has discussed findings related to what Eccles and colleagues (2012), term the "technical" part of guideline development. This concerns evidence gathering and appraisal and how evidence is perceived and used throughout the process. The next section moves on to how guideline development may be viewed as a social process.

Guideline development: a multi-factorial, social process

A number of empirical studies, highlighted previously in this thesis, have investigated some of the social processes of guideline development (Pagliari & Grimshaw, 2002; Moreira et al., 2006; Atkins et al., 2013; Richter Sundberg et al., 2017). However, how

guideline groups debate evidence and form guidelines has yet to be fully illuminated and observational studies reporting on the whole process are lacking (Hopthrow et al., 2011; Atkins et al., 2013). This study provides a novel perspective in, not only, observing these specific processes, but also, considering influences on this process from the wider group of stakeholders and actors.

The fact that social factors influence the guideline process is not unexpected as a group of people with diverse opinions and backgrounds is brought together to interact, give opinions and debate issues to complete the task. Despite these social processes being under-represented in the empirical literature, they are recognised as separate from technical aspects of guideline development. Eccles and colleagues (2012) describe guideline development as having a technical element (evidence gathering and review) and a social process (interpretation of the evidence and the forming of guideline recommendations). They argue that disruption of either part can influence the validity of the recommendations. This is reflected in the proposed integrative framework, detailed later in this chapter, where changes to inputs, or the presence of enabling or disruptive factors, modifies the flow of the guideline process and influences the nature of guideline recommendations (although this case study does not assess or comment on the validity of the recommendations).

Firstly, the effect of the diverse nature of a group can have both positive and negative effects. Recent reviews of the current state of research into group diversity suggest that educationally-related diversity has a positive effect on group performance when the task is complex and that diversity is positive for decision making, but negative for group cohesion (Guillaime et al., 2017; Güver & Motschnig, 2017). More specifically, the development of guidelines by multi-disciplinary groups is generally viewed as a positive feature in the literature. A range of views from different professions and different therapeutic specialities is said to guard against extreme opinions because participants who hail from diverse areas have a modifying effect on others (Hutchings & Raine, 2006; Eccles et al., 2012; Kunz et al., 2013). The findings of this study concur with this strand of literature. A number of the clinical members of the guideline expert group were macular degeneration specialists but other participants came from other ophthalmological

backgrounds and brought a slightly different viewpoint. For example, there were two primary care GPs. The GPs both had a special interest in ophthalmology and took the lead in treating such patients in their practices as well as contributing to various ophthalmological public bodies. They encouraged the guideline group to take a more holistic view of patient care encompassing the social aspects of having an eye disease which limited vision. Despite differences, such as these, it should be pointed out that the group is still essentially from the same therapeutic area.

Another finding endorsing the stance that having diversity in groups modifies extreme views is seen in the effect on the group of having only one hospital clinical expert for a number of meetings. This expert described themselves in interview as *"having a certain view"* which was not necessarily in line with mainstream ophthalmology. S/he took the lead constantly in answering questions, whether clinical or not, and was deferred to by others in the group. The clinical expert was aware of the over-reliance on their views and considered this as a failure of due process. This changed when another hospital clinical expert joined the team. From then on, there was usually a discussion between the experts if they disagreed with each other. They usually aimed to resolve differences between each other before they proffered a joint view to the group. From this, it could be construed that having more than one, and more than one type, of hospital clinical expert on the guideline group is beneficial, if not essential, for garnering different opinions and modifying extreme views.

Pagliari and colleagues' (2001) review paper highlighted some of the key psychosocial influences in guideline development. Their paper was written in response to the authors' doubts that guideline reliability and validity are due *only* to evidence and that people and organisational issues may also play a part. Others echo this, saying that discourse and argument should be recognised as key to the construction of health policy rather than it being based solely on evidence (Russell et al., 2008). Furthermore, with respect to forming guideline recommendations, human judgement has a key role (Raine et al., 2004; Atkins et al., 2013). Pagliari and colleagues (2001) cite the key psychosocial influences on the guideline development process as conformity to the perceived behavioural norm, obedience to authoritative views, compliance with majority opinion, status influencing

decisions and persuasion. Although this research was not set up to study specific *psycho*social processes, a number of findings were congruent with the points made by Pagliari and colleagues (2001). Observation of the group discussions revealed how some group members deferred to others with perceived high expertise and declined to offer their own views in the face of this presumed authoritative opinion. This, perhaps, reflected having only one hospital clinical expert in the group initially. Some individuals were perceived to have high status within the expert group due to extensive experience and knowledge and this led to others being persuaded to follow their direction.

The acceptance of contribution to discussions, meaning that a particular view is endorsed by the others in the group, also tended to be dependent on perceived status in the group. This finding concurs with Pagliari and Grimshaw's (2002) empirical study, one of few such studies on the social processes of guideline development. Their study demonstrated that contribution to debates was strongly aligned with professional role and status, with expert hospital consultants being afforded higher status than allied health professionals. However, their study did not specify exactly the type of review questions that were considered by the guideline group. It was not clear whether there were any questions that would have benefited from, for example, a patient's disease-specific experience. In this research, a number of review questions explored patient-specific experiences, such as probing what information patients and their carers find useful and the barriers and facilitators to appointment attendance by patients. While perceived status based on professional role and experience was evident, the findings of this study also suggest that contribution is linked to the type of review questions being discussed. Where the question concerned a clinical intervention, supported by complicated statistical data, clinical experts and health economists tended to be those with the highest level of contribution; where disease experience was important, there were more contributions from the patient members of the group.

The literature points to the outcome of guideline development being influenced by the composition of the guideline group which affects relative contributions to decision making, endorsement of certain interventions and procedures, and a wider range of views given in multi-disciplinary groups (Pagliari and Grimshaw, 2002; Hutchings & Raine,

2006; Eccles et al., 2012; Oliver et al., 2015; Richter Sundberg et al., 2017). The effect of the composition changing *during* the guideline development period has not been studied. Pagliari and Grimshaw (2002) do comment on the changing composition of the guideline group they observed, but do not discuss the effects of this on group functioning. In this case study, changes in the composition of the core group were many and occurred in both the GDEG and in the NTT. This occurred at different time points during the guideline development period. It is claimed that group instability, such as that caused by constant membership changes, necessitates adjustments to newcomers and a period of socialisation of the new group member. This, in turn, means acceptance of newcomer contributions is less likely (Rink & Ellemers, 2013). However, this effect was not demonstrated in the macular degeneration guideline development: newcomers appeared to be integrated and accepted into the group quickly. For example, a junior NICE health economist joined the group late but was key to the health economics data modelling exercise. S/he was relied upon by the GDEG in explaining the model in detail and both their expertise and contribution were mentioned by GDEG members during interview.

Patient and public involvement in guideline development and implementation is considered beneficial (Schünemann et al., 2006; Krahn & Naglie, 2008; Boivin et al., 2009). Reasons for consumer involvement include alignment of recommendations with patients' needs, incorporation of patients' values and experiences, and improvement of outcomes for patients by, for example, promoting value-based patient decision making (Boivin et al. 2009; Légaré et al., 2011). Barriers to patient and public involvement in clinical guideline development appear to be a difficulty in recruitment of consumers to participate, a limited understanding of scientific data and differing perspectives between clinical experts and patients (Légaré et al,. 2011). This is in line with attitudes to public involvement in science in general (Boaz et al., 2016). However, some of these barriers can be mitigated by offering training and support for such participants (Légaré et al., 2011). The attitudes of interviewees in this research to the inclusion of patients in the macular degeneration guideline group were very positive. Their disease experiences and familiarity with the services provided were valued by both the GDEG and the NTT. The patient representatives were confident in contributing to questions, especially when these were of a psychological or experiential nature. However, for questions concerning

medical treatments and interventions, they contributed less and, in line with previous literature (Légaré et al., 2011), felt a gap in their scientific knowledge despite the training they had received from NICE.

This case study demonstrated acceptance and value in patients participating as part of the main guideline development group. This is counter to the view of consumer participation in guideline development as tokenistic (van de Bovenkamp & Trappenburg, 2009). Some have suggested a more effective method of involvement is via parallel consumer workshops which feed opinions into the main development group (Tong et al., 2012). The results seen in this research, while positive towards consumer involvement, apply only to one disease area and one guideline group; as such it is not possible to generalise on the value of consumer involvement. However, it does add support to the call for more research into how best to involve consumers in development and implementation of clinical guidelines (Boivin et al., 2010; Légaré et al., 2011).

Both professional roles and group roles were enacted during this study. Certain roles could be aligned with the role clusters of Driskell and colleagues' (2017) TRIAD model, a recent model which combines the many existing role taxonomies. For, example, the technical advisor was recognisable as the "task motivator", driving the group forward in addressing and completing tasks. The NICE project manager and others of the NICE Technical Team acted as "teamwork support" and "task completers". The chair of the guideline group is the "leader" and this role was significant for managing time and the overall task, as well as for facilitating group interactions in discussions and decision making. The TRIAD model is structured into three behavioural dimensions that underlie group task behaviour: dominance (activities of control and direction), sociability (how relationships are maintained) and task orientation (towards task completion). The model relates behaviours to roles and, the authors suggest, it could have utility in defining core roles for the optimal composition of a group (Driskell et al., 2017).

As one of the major aims of this research was to elucidate the social processes of guideline development, observation of the chairing role was of particular interest. This is because, with respect to managing social group interactions and moderating discussions, the

chairing role has been highlighted as a key role in the guideline development group (Oliver et al., 2015). The TRIAD model maps the "leader" of a group to a profile of high dominance, moderate sociability and high task orientation (Driskell et al., 2017). However, in this study, with data gleaned from interviews and from observation, this is not the profile that either the group members would produce for this individual nor how the chair would characterise themselves. Group members felt s/he was good at encouraging all to contribute and was a likeable character (high sociability), was not directive enough on many occasions (low dominance) but was excellent at keeping the group focused on the task (high task orientation). The chair considered themselves "high" in all three domains. This does not, of course, suggest that the chair in the macular degeneration group was ineffective, especially since their characteristics were not independently rated. However, it could point to the influence of context and task type where a different behavioural approach is deemed necessary depending on the situation. The effect of contextual factors and task type on performance is, the authors comment, a direction for further research (Driskell et al., 2017). The model does, nevertheless, offer a further perspective into roles played within a group and is one way to consider roles within the guideline group.

Group roles (as opposed to functional or professional roles which are set at the beginning of group work) tend to emerge during the life of the group (Belbin, 2010), often as a consequence of communicative interaction (Lehmann-Willenbrock et al., 2016). One clear role emerging from the macular degeneration guideline group is that which is termed "clarification-seeker". The role holder seeks descriptive information and clarification of particular problems both for themselves and to help others. The definition of clarification-seeker here is similar to the TRIAD model's "problem solver" and/or the "social" role (Driskell et al., 2017). Drawing from the organisational citizenship behaviour literature, this is considered a "helping behaviour", and one which is intended to aid other group members or the whole group (Organ et al., 2006; Sparrowe et al., 2006). The role of "clarification-seeker" was held by one of the patient representatives who believed that others, like themselves, found clarification of sometimes complicated science, beneficial to the group. A number of individual personality traits are related to helping behaviours in teams (Chiaburu et al., 2011). One of these is extroversion, high mean levels of which

are positively associated, via co-operative group norms, with individual helping behaviours (Gonzalez-Mule et al., 2014). Simply put, in a co-operative group, a helping behaviour in an individual with an extrovert personality, is accepted and valued. This study supports this observation since the patient representative in this group did have an outgoing personality (commented on by others in interview) and the collaborative atmosphere that usually prevailed at group meetings, enabled the clarification behaviour. Returning to the earlier discussion concerning the value added by consumer involvement in guideline development, the "clarification-seeker" role may be another worthwhile role for consumers in the guideline development group.

The formation of recommendations within a guideline group follows from the group's consideration of the relevant evidence. Various factors such as differences in interpretation of evidence, status within the group, and professional experience can affect the process (Pagliari & Grimshaw, 2002; Raine et al., 2004; Hutchings & Raine, 2006; Atkins et al., 2013). However, there has been little research previously which documents exactly how recommendations are formed by guideline groups and what tensions exist in this process. The findings of this study demonstrate that evidence is not easily transformed into recommendations by the guideline group. Key tensions observed were the lack of available or acceptable evidence on which to base guideline recommendations, disagreement as to what the evidence means and how it should be used, the prescribed vocabulary for the recommendation text, and the subsequent NICE editing process. The strict rules concerning vocabulary caused much irritation to the expert group, often directed at the NICE technical staff, as proxy authors of the rules. Thus, these findings concur with previous authors but also contribute to the literature in demonstrating how the prescriptive rules of guideline development can be a source of conflict.

Conflict in groups and the influencing and mitigating factors on this are well-documented in the literature (Jehn & Mannix, 2001; de Dreu & Weingart, 2003; de Wit et al., 2012; Hjerto & Kuvaas, 2017), with trust seen as a key moderator of both individual-level and intra-group conflict (Simons & Peterson, 2000; de Jong & Elfring, 2010; Lau et al., 2010; Salas et al., 2015). Trust, defined in this thesis as a belief in the reliability, ability or truth in someone or something, was a feature of group functioning that emerged in this research.

Trust took different forms: there was trust of each other in that task focus would assume more importance than any personal conflict and trust in the process that it would enable task completion. It is unclear, however, whether trust was key in preventing or moderating conflict. Nevertheless, it appeared to be a factor in maintaining the cohesion and collaboration of the group. This observation is supported by the way participants described the trust they felt and in words, such as "*harmonious*" that they ascribed to the group's functioning. No studies, thus far, have investigated the role of trust in guideline groups. However, this study demonstrates that trust is present; its influence and role as a mitigating factor in conflict are possible avenues for further research.

The previous sections have discussed the evidence landscape and group functioning in this study. However, guideline development is also part of a wider healthcare environment and, as such, the core guideline group is open to various external influences. The next section discusses the influences seen to be significant in the macular degeneration guideline.

Network influences on guideline development

NICE, is a government funded but a quasi-independent body (Le Grand, 1999; Legido-Quigley et al., 2012). It does not operate in isolation but sits within the broader practice and policy setting of the UK health system with multiple links to other health and government organisations. Thus, the external environment, and changes to it, are part of the context of guideline development. These external influences, on the guideline group do not appear to have been reported in the empirical literature previously. An aim of this study was to explore the major influences on the macular degeneration guideline group, including those external to the core group. Discussion of the influence of the external environment is in two parts: firstly, how guideline development can be characterised as a network and secondly, discussion of the key external network influences on the macular degeneration guideline development process.

Guideline development: a network within a network

The situation of NICE with respect to other health service bodies and health policy organisations is consistent with O'Toole's (1997) notion of a network. That is, a structure

with multiple organisations and actors which are interlinked but with ties that extend beyond formal linkages. It also accords with Ostrom and colleagues' (1961) concept of polycentricity in public policy arenas. NICE operates within a network of inter-related health and government bodies, many of them acting independently, or quasi-independently, but working on co-operative projects with central mechanisms for issue resolution. Individual guideline groups also are networks of actors with interconnected relationships. In essence, NICE guideline groups are networks within networks.

The rationale for viewing guideline development as a network is threefold. Firstly, the actors of guideline development exist in networks such as social, professional and knowledge networks and participants are subject to network influences (Rangachari, 2009; Armstrong & Kendall, 2010; Cunningham et al., 2012). Secondly, quasi-independent or seemingly autonomous bodies are not totally self-determining; they influence, and are influenced by, connecting parts. Thirdly, with a focus on evidence-based healthcare being provided in an interconnected system of people, policy and politics, (Best & Holmes, 2010), we should understand the networks and decision making involved in making any healthcare policy, including guidelines. Indeed, some feel that a network lens is beneficial in elucidating the role of networks in improving medical care and services (Cunningham et al., 2012).

Where to situate the guideline groups, or NICE as a guideline body, with regard to the vast network literature is difficult since guidelines fall somewhere between policy and practice. The lack of previous work on networks in guideline development points, perhaps, to the difficulty of categorising the guideline environment as any particular type of network. Some have argued that network traditions, for example, in public administration, political science and sociology, should be more closely aligned theoretically and methodologically to facilitate research (Berry et al., 2004); this might help with the placement of guideline networks in the body of network literature. Isett and colleagues (2011) identify three main foci of network research: policy, collaborative and governance networks. Policy networks aid public decision making, collaborative networks combine for the delivery of services and governance networks include policy making and delivery of services. Guidelines could be feasibly aligned with this definition of governance

networks since the product of guideline development is a document that influences both strategy and service provision.

Guideline group participants from medical backgrounds belong to professional bodies, associated with specific therapeutic areas and many participants work in, or in conjunction with hospitals, said to be exemplars of professional networks (Rangachari, 2009). Thus, health professional networks, consisting of one category of participant and holding the views, beliefs and interests of that group (Rhodes & Marsh, 1992; West et al., 1999; West & Barron, 2005; Cunningham et al., 2012) are recognisable in the guideline environment, although the guideline group experts in this study claimed to represent only themselves and not their professional organisations.

Characterising the guideline environment as a particular form of network was not an aim of this research. However, Raab and Kenis' (2009) suggestion of two different forms (mandated and natural) of networks accords with the study findings. They describe a mandated network as one which is consciously formed and task focused. In this scenario, the formal recruitment of GDEG members, a prescribed set of processes used to aid completion of the task, formal linkages with organisations, such as Cochrane, who provide services to the guideline group, are features resonant of a mandated network. A natural network emerges as a result of actor relationships, seen here as the multiple relationships between group members that developed over the course of the task and relationships between group members and external providers (such as the Cochrane organisation or other contractors of services). Furthermore, the formation of these linkages accords with relational features of interpersonal, social and inter-unit networks (Brass et al., 2004; Wasserman & Faust, 1994; Chambers et al., 2012).

Mandell and Keast (2009) see the labels of "policy networks" or "governance networks" as too wide and prefer to use the level of horizontal integration in defining networks. The different levels are co-operation, co-ordination and collaboration (Brown & Keast, 2003; Keast et al., 2007). The critical characteristics of collaboration in networks are interdependence among related organisations and participants and a focus on process as well as task completion (Mandell and Keast, 2009). Trust, too, is required for

collaboration in networks in order to effectively manage complex problems (Lecy et al., 2014). This characterisation of collaborative networks aligns with the findings of this study where high levels of integration and collaboration were seen between guideline group members and between the group and related organisations. It is also reflected in participants' description of the macular degeneration guideline process as "*collaborative*", *harmonious*" and "*collegial*". Furthermore, trust emerged as a feature of how the guideline group functioned, although trust between the group and its linked organisations was not explored as part of this thesis.

Decision making in networks as opposed to that within hierarchical and linear structures, requires a different set of leadership skills (Provan & Kenis, 2008; McGuire & Agranoff, 2011). This is especially true in collaborative networks where responsibility placed solely in one individual is rare. In collaborative networks, there is not a traditional leader, rather there are key members who have the ability to induce agreement of participants (Agranoff, 2006). These Mandell & Keast, (2009), term "process catalysts". This resonates with the findings of this study: there are members of the NTT who monitor adherence to the process and timelines, members of the expert group who are key in guiding discussions and a chair who manages contributions from group members and guarantees consensus is reached.

The collaborative nature of the guideline "network" suggests horizontal integration and decision making. However, vertical, hierarchical input was also observed in this research. This was sometimes evident within the core guideline group amongst the NICE Technical Team members where the technical advisor tended to be the final decision-maker on technical issues and in the interactions of the core guideline group with NICE management staff. Conceptually, hierarchical decision making involves regular, sequential steps with a clear start and end point, and an overt leader (de Bruijn & ten Heuvelhof, 2018). Collaborative decision making includes understanding that participants have an equal say and finding ways to agree on how the task is accomplished (Mandell & Keast, 2009). Observation of the process of drafting guideline recommendations indicated a mix of collaborative and hierarchical decision making. The guideline group would come to agreement (via the "process catalysts") about each

recommendation. The draft recommendations would then be edited and reformatted by the NICE Editing Team and an associate director according to NICE processes and legal advice. This, then, accords with the presence of a leading actor at the top of the hierarchy, recognised as having all the information and power, who leads other actors in the decision-making process (de Bruijn & ten Heuvelhof, 2008). Observation of how decisions are made about guideline recommendation content and format, suggests there is a hybrid network/hierarchical model of decision making. Claims that, in public organisations, "lateral network connections seem to overlay the hierarchy rather act as a replacement for them" (Agranoff, 2006:57) seems to be borne out by the findings of this study.

Key external influences on the guideline process

Influences on the guideline process, external to the core development group, are described poorly in the literature. One of the aims of this research was to characterise these. The findings and proposed integrative framework reflect the influential role that external factors can have in the guideline process. External influences appear both as input to the process and as enabling or disruptive factors during the development period. The following section highlights those influences seen to be key in this case study.

One external influence on the recruitment of people to the expert group was conflicts of interest. The presence of these has concerned the medical profession for two decades or more (Neuman et al., 2011; Eccles et al., 2012). The areas of concern have been the relationship of clinicians with the pharmaceutical industry, the use of industry ghost writers for publications and, more recently, conflicts of interest in clinical guideline development (Moynihan, 2008; Ross et al., 2008; Okike et al., 2009; Shaneyfelt &Centor, 2009; Chimonas et al., 2011; Lenzer, 2013).

A number of studies have demonstrated how prevalent conflicts of interest are in guideline development. Choudry and colleagues (2002), detailed possible conflicts of interest for more than 85% of 192 guideline authors from 44 guidelines. The conflicts of interest arose because of some kind of relationship of the guideline authors with the pharmaceutical industry. More recently, Kung and colleagues (2012) screened, at random,

130 guidelines for compliance with 18 of 25 Institute of Medicine standards for guidelines (IOM, 2011). One of these standards concerned the declaration of interests of guideline authors. Few guidelines (less than 50%) detailed any information on conflicts of interest and, where information was included, financial conflicts of interest were evident for more than 70% of guideline group chairs.

Conflicting interests in guidelines may be financial - receipt of endowments, consultancies, gifts, direct payment for advocacy of products in guidelines (Eccles et al., 2012) or intellectual - academic activities creating the potential for an attachment to a specific point of view that could affect an individual's judgement (Guyatt et al., 2010; Akl et al., 2014). Guideline developers use various quality instruments and processes to mitigate against the presence of conflicts in expert advisors (AGREE, 2003). NICE has been particularly proactive in this area and has a code of practice for managing conflicts of interest (NICE Policy on Conflicts of Interest, 2014 and see section 5.3).

In this study, 49 declarations of interest were made by 12 members out of 14 (this includes the clinical expert who left the group) on the GDEG panel. (NICE, Macular Degeneration Guideline, Appendix A: Committee membership lists and declarations of interest, 2018). Managing conflicts of interest during the guideline development period was not problematic; it was recruitment of the expert group before development started that was more difficult. The appointment of clinical experts was particularly challenging: more than 30 clinical experts were interviewed (personal communication by a guideline group member, 2016) but only two experts were deemed sufficiently free of conflicts of interest to serve as a GDEG member. By the time of the third meeting, one of these experts had also withdrawn from the GDEG citing "personal circumstances" as a reason for withdrawal (NICE AMD Guideline Meeting 2 Minutes, 2018), which affected the operation of the group until a replacement was eventually recruited. Thus, this study further supports concerns about the impact of conflicts of interest on recruitment of topic experts for guideline groups.

The size of the task for the guideline group gives an indication of resources that will be required to complete the task. This is indicated by the scope of the guideline which defines

the range of questions to be answered, the populations to be included and the economic perspectives to be used. There were some constant resources, such as NICE processual rules, which provided structure. These were strictly adhered to, occasionally leading to accusations by expert members of the guideline group of process rigidity; however, having such rules appears to ensure that NICE methodology remains an exemplar of guideline development (Legido-Quigley et al., 2012). Other resources, such as technical expertise and time, were added as required. Time pressure was evident in this case study: the synthesis of the evidence for certain review questions was contracted out to the associated National Clinical Guideline Centre. There was also an extension of the timeline for this guideline due to the high number of review questions to be answered and the extensive health economics modelling undertaken. Stress, due to time pressure, with a subsequent negative effect on group performance, might have been expected (Kerr & Tindall, 2004; de Paola & Gioia, 2016). However, an increase in task focus with the imposition of deadlines, has also been noted (Karau & Kelly, 1992). The impact of time on performance was difficult to assess in this study. Members of the NICE Technical Team, who had the main responsibility for delivery of the guideline, did express concern, both within group meetings and in interview, at time constraints imposed on the macular degeneration guideline development. This was not the case for GDEG members of the group but, perhaps, less responsibility for task completion and the lack of any hierarchical management of the expert group, led to this view.

Whilst there is little emphasis in the guideline literature on the effect of external factors on the guideline process, they affected it in a number of ways. In this study, the external environment influenced the scope and focus of the guideline before the process started and it presented challenges during the process. The one external factor that was dominant in this specific case was the anti-angiogenic treatment issue. The issue has been described in detail elsewhere in Chapter 6 and Appendix ix. The issue affected scope of the guideline, the specific disease topic and had already been a contentious issue involving at least one core group member. It also proved to be a disruptive factor and caused conflict during the process.

Licensing constraints for the use of bevacizumab in macular degeneration were in place prior to the start of the guideline process. This led NICE to instruct the group to refrain from referring to this particular drug in recommendations. This instruction was included in the scope of the guideline. Discussion of evidence concerning anti-angiogenic treatments included research, funded by the National Institute for Health Research, which demonstrated the safety and efficacy of bevacizumab for treating macular degeneration. Also discussed was the regularity with which the drug is used by clinicians in the UK, outside of its usual licence. This led to the core guideline group drafting a recommendation which endorsed its use along with other anti-angiogenic agents. This draft recommendation was changed by the Editing and Legal teams within NICE just prior to the draft guideline being published, without endorsement of the expert group. Some members of the GDEG felt anger at what they saw as a lack of transparency for this part of the guideline process. An intervention by senior NICE personnel and a revision of the draft recommendation resolved this particular disagreement. The subject of pharmaceutical licensing constraints and the effect on patient choice in macular degeneration, plus how regulatory/legal frameworks can force the direction of clinical practice, remain subjects for much commentary (Cohen, 2017; Hambleton, 2017).

External factors can be influential to the guideline process, at the start of the process as well as during it. An example of their influence in the macular degeneration guideline at the start of guideline development was the difficulty in recruitment of experts and the subsequent availability of clinical experts to participate in the process. External factors may also present challenges, having the potential to upset the process, during the guideline development period. An example is the issue of the licensing constraints with regard to anti-angiogenic therapies. Identification of possible external challenges, before and during guideline development, may be a practical course of action to mitigate similar confrontation.

7.3 A guideline development integrative framework

An integrative framework of the process has been developed to capture the interplay of factors influential to the guideline development process. It is presented schematically and described in this section.

This research has shown that guideline recommendations are not based solely on the evidence gathered and appraised. There are existing conceptual frameworks, such as the Promoting Action on Research Implementation in Health Services (PARiHS) framework (Kitson et al., 1998; Rycroft-Malone et al., 2013), which describe the factors affecting how research flows into practice. However, none similarly scrutinise the guideline development process itself: how research evidence is transformed into guideline recommendations and the factors affecting this process. The proposed framework aims to address this gap by providing a more comprehensive and structured way to examine the guideline development process.

Before describing the framework, some definitions of the key terms contained within it are provided. Then, there is a visual depiction of the framework and a description of the main components. Empirical examples from this case study are provided to illustrate the interplay of the various factors and how changes in some of these can influence the guideline process and the recommendations produced.

Definitions of key framework terms

Ostrom (2005, 2011) makes a distinction between frameworks and theories although the terms are often used interchangeably by different disciplines. Ostrom's distinction resonated with this research and it has been used in developing the proposed integrative framework. For Ostrom (2005, 2011), frameworks identify general elements/variables of the subject being described, and the relationships between them, for organisational analysis and diagnostic and prescriptive inquiry. The way that these elements/variables interact results in process differences. Further, the elements/variables aid researchers in generating questions for inquiry. Theories are more specific than frameworks and permit specific questions to be derived from each element and to make general assumptions about how they interact. Theories allow assumptions necessary to predict outcomes or elucidate processes of a particular phenomenon. Others have added further insights into what a theory is: Whetten (1989), for example, highlights four building blocks of theory: the factors, (the what); relationships of the factors, (the how); justification of the choice of factors, (the why); boundary states (the who, where, when). Corley and Gioia (2011),

in their review of the current literature on what constitutes a theoretical contribution, highlight the need for originality and utility.

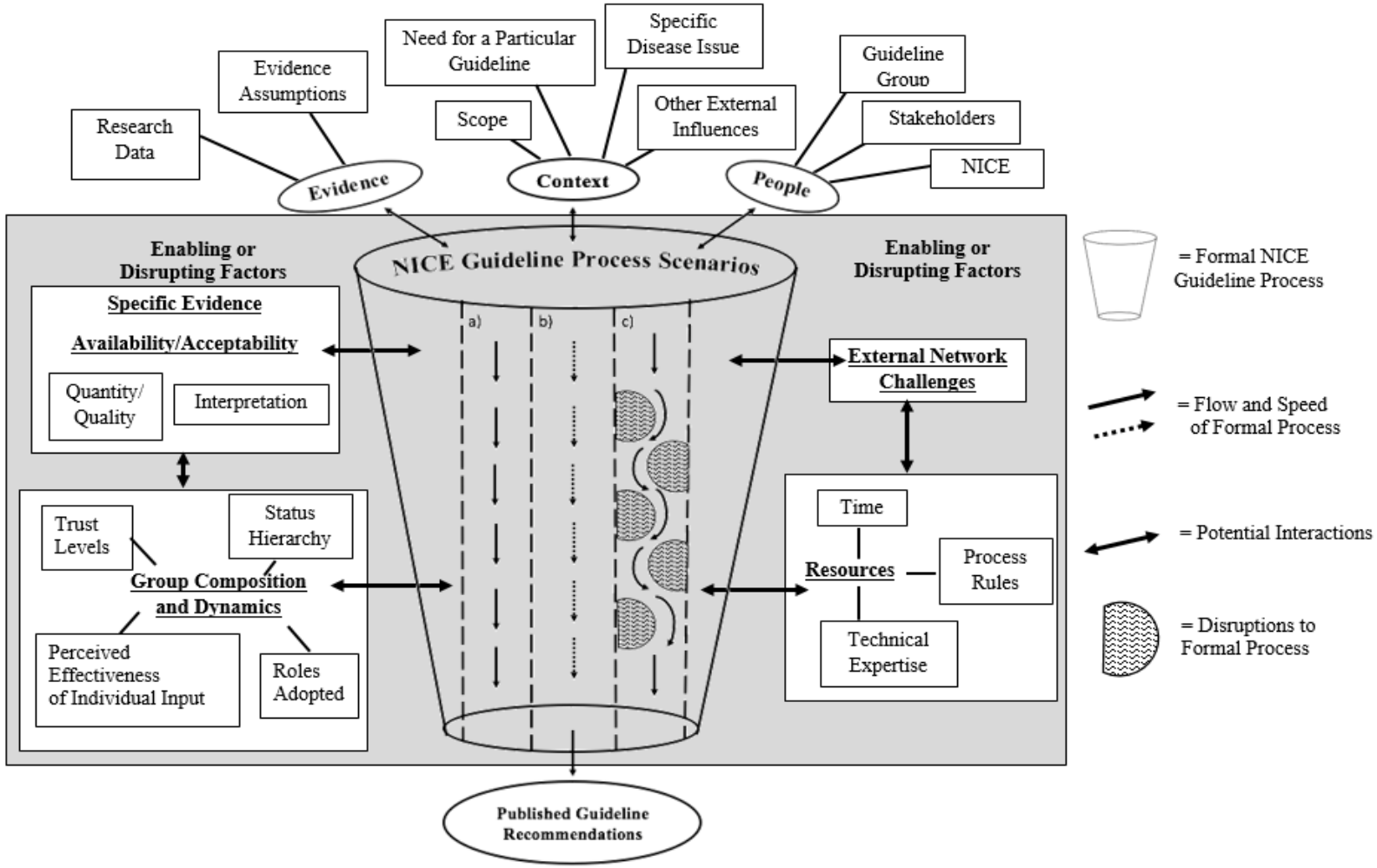
Following Ostrom's definition (2005, 2011), this integrative framework is concerned with representing the elements/variables of the guideline process as well as identification of some of the relationships between the components. The framework is a map of the factors revealed by the findings of this research, with a description of some of the relationships between factors. As such, it is congruent with Whetten's (1989) "what" and "how" building blocks of theory. It also fulfils the originality criterion of what constitutes a theoretical contribution (Kilduff, 2006; Corley & Gioia, 2011) since the guideline process factors have not been integrated previously in this way.

Feeding into the framework are various factors or bodies of information required for the guideline process to proceed. These are termed *inputs. Inputs* may be contextual, for example, the political environment at the time of guideline development or the scope and the specific disease topic addressed by the guideline. The *inputs* enter the formal NICE *guideline process* which is described in detail in Chapter 5. The *guideline process* culminates in the *outputs* which are the guideline recommendations. It should be highlighted here that *outputs* relate to individual guideline recommendations and not the whole guideline. This is because guideline recommendations align with the review questions considered by the guideline group. Using guideline recommendations as the *outputs* in the framework enables provision of specific examples where changes in factors have influenced the *outputs*.

Depiction of a Guideline Development Process Integrative Framework

Figure 7.1 depicts the framework and indicates the individual components as well as how changes to these influences the process; illustrative examples are provided from study findings.

Figure 7.1: A guideline development process integrative framework



The framework can be divided into the formal NICE *guideline process* (depicted as the central cone in Figure 7.1) and other framework parts. These parts can be clustered into the *inputs* (Evidence, Context, People), *enabling or disruptive factors* (Specific evidence availability/acceptability, Group composition and dynamics, External network challenges, Resources) and the *outputs* (Guideline recommendations). There is a flow through the process indicated by Columns a), b) and c). Once the process begins, it may be affected by a number of *enabling or disruptive factors* which can modify the process, for example, by slowing it down or affecting the type of guideline recommendations made as an *output.* The final *outputs* are influenced by both the nature of the *inputs* and by the existence, or emergence, of *enabling or disruptive factors*. The next section describes the components of the framework. As there is a general flow from *inputs - process - outputs*, the sections below are aligned with this flow. *Enabling/disruptive factors* are described after the *guideline process* section but prior to the *outputs* section.

Description of the elements of the integrative framework

Inputs

A number of inputs emerged as key to the guideline process. Firstly, the evidence supporting the guideline recommendations. The types of research data and assumptions about evidence emerged as key inputs to the formal process. As discussed earlier in this chapter, the strength of recommendations depended, in part, on the assessment of the quality of the evidence. The quality ascribed to evidence reflected its place in the evidence hierarchy including individuals' assumptions about what constitutes high-quality evidence. High quality labels were applied more often to randomised controlled studies at the apex of the hierarchy than to observational or qualitative studies at lower levels in the hierarchy.

A second input is the people engaged directly in the guideline process as well as those indirectly involved. So, the Guideline Development Expert Group (GDEG) plus the NICE Technical Team (NTT) is central to the process. Described in Chapter 5, other core NICE staff, aside from the NTT, are involved in the development of one guideline. The GDEG and the NTT plus these other core staff comprise the Guideline Group depicted in Figure 7.1. There are individuals, such as the Director of the Centre for Guidelines, and teams in

the organisation that have an input to the process but are not part of the core guideline group. For example, (see Figure 5.2, Chapter 5), there is the Editing Team, the Publishing Team and the Public Involvement Team. These and other NICE teams have some input to individual guidelines. Finally, there are "stakeholders": these are defined (by NICE) as individuals or organisations having a specific interest in the guideline topic and they are registered by NICE to participate in the guideline consultation process.

The context within which the guideline is developed is also an input. That is, the characteristics of the environment in which the work is being carried out which can influence outcome (Pawson & Tilley, 1997; Ritchie & Lewis, 2003; Dopson & Fitzgerald, 2005). The significant contextual factors found in this study are the need for a particular guideline, the scope the guideline is to cover, specific disease issues, and other external environment influences. The need for the guideline encompasses how the topic is chosen and for what reason. Guideline topics are ranked according to national priorities and other healthcare frameworks but who prioritises topics, and why, is part of the context of individual guidelines. Context also includes the scope of the guideline since this varies and the broader range of the scope may impact resource availability. The guideline followed for this research had a wide-ranging scope covering both diagnosis and management of macular degeneration and had, therefore, many review questions to be addressed. This indicated that time and other resources could be pressured as the process proceeded. Specific disease issues are included in the context input too since contentious issues, played out before the start of guideline development, may affect the process. The issue around anti-angiogenic treatments for macular degeneration, which featured in the media prior to the start of the guideline's development, is an example. Finally, there is what is occurring in the general external environment as this too may impede development progress. For this guideline development, for example, a General Election, called at short notice, in June 2017, put the process into "purdah". The whole process was put on hold due to political uncertainty and was delayed until the election was completed.

The framework inputs are not static entities set at the start of the process; some may evolve during the process. A number of situations in this study demonstrated this dynamic nature. An example is where the guideline group membership changed (on more than one

occasion) during the formal process. Another example is where new evidence was sought and included in the group's appraisal and debate. This situation occurred when the guideline group indicated that it would be beneficial to include Medisoft data, which monitors disease progression over time in individual patients. Individual expert members provided this data to the group which then became part of the supporting evidence base Thus, a linear progression from inputs into the formal process should not always be assumed. What occurs during the process can influence and alter various inputs (hence two-way arrows in the diagram).

Scenarios of the guideline process

Column (a) in the framework depicts the aspirational guideline development process. The inputs interlink effectively, the development of the guideline proceeds without disturbance and a recommendation can be made. If the evidence is robust, the guideline group functions effectively and the context is stable, the guideline recommendations produced are more likely to be "strong" than if there is misalignment of these elements. Enabling factors will smooth the process and may optimise the time taken to draft the guideline recommendations. An example where an enabling factor facilitated the process is in the availability of technical expertise. Health economics modelling had to be undertaken since the requisite evidence was not available from empirical research. The NICE Technical Team assigned to the guideline group contained two senior health economists, one of whom who had deep experience in modelling. External health economics contractors were also available to the team. The availability of such expertise meant the modelling did not have to be contracted out wholly to an external organisation and time was saved with the work undertaken internally.

Column (b) illustrates a slowing down of the process. This may be input dependent or due to disruptive factors. An illustrative example is where evidence was not available or accessible to the guideline group. Empirical data assessing the impact of low vision aids often uses a population with low or no vision due to a variety of diseases. Macular degeneration patients with low vision often form a majority of these target study populations but patients with low vision from other causes are included. Such data was discussed for Review Question 9 (Appendix viii), which concerned the effectiveness of

support strategies for patients with visual impairment and this encompassed low vision services as an "intervention". It was not possible to extract data specific to macular degeneration patients and it was decided by the guideline group to exclude this data from the evidence base. The effect was a disruption of the process whilst the debate was on-going concerning how, then, this question could be approached. It also affected the outcome in that the recommendation without that specific data was not a "strong" recommendation. The situation also warranted a research recommendation made by the group to discover the impact of optimising low vision services specifically for macular degeneration patients.

Column (c) illustrates a perturbation of the process when disruptive factors come into play. An obvious example in this study which caused a disturbance of the process was the contentious issue concerning macular degeneration treatment with anti-angiogenic treatments. This has been discussed at length elsewhere in this thesis so will not be repeated here other than to point to how such disruptions can derail the process. Here, the issue, and the management of it, led to the unusual step of the draft guideline having to be withdrawn and the relevant recommendation amended. It also led to anger in certain GDEG members who then questioned the transparency of the NICE process.

In Figure 7.1, the different scenarios are separated by a "permeable" line. This is to indicate that different scenarios may occur during one guideline development period for different review questions or, even, the same review question.

Enabling or disruptive factors

Inputs enter the NICE formal guideline process where they can be subject to enabling or disruptive factors which can modify the process in some way. Four main enabling or disruptive factors emerged from the data. There was the availability of resources, those most often impacting the process being time and technical expertise. Another factor was the way the group functioned. Included here was the trust that emerged from interactions within the group, how the process rules were operationalised and facilitated, the perceived effectiveness of contributions to discussions, and how the perceived status of individuals affected their input and the operation of the group. The availability and acceptability of

the evidence, being assessed as high or low, influenced the strength of recommendation made. Then, there were certain external network challenges which influenced the outputs. The presence of disruptive factors appeared to slow down or disturb the process while enabling factors enhanced the speed or smoothness of it. Whilst the distinction between enabling and disruptive factors in this study was made in retrospect by considering their effect on the process, it may also be possible that the distinction could be made in principle. So, for example, having technical expertise always available and no time constraints would be enabling whereas having little technical expertise available and added time pressures would be disruptive to the process. There may be interplay between the enabling and disruptive factors. Connections between them, and between them and the process, are shown in the framework diagram as an illustration to indicate possible interactions, for example, external network challenges arising during the guideline process may impact resources. The impact of the General Election, as described above, is an example of where two enabling/disruptive factors may be linked.

Outputs

The outputs are the guideline recommendations that result from the guideline process. The guideline group uses structured review questions (Appendix viii) to formulate recommendations and more than one recommendation may be made per review question. For example, RQ 12 and 18 relate to the use of anti-angiogenic therapies for macular degeneration. There are different anti-angiogenic therapies for the disease and the guideline group formulated 11 recommendations for these two review questions (AMD Guideline, 2018). For the macular degeneration guideline, as a whole, there are 56 separate pieces of guidance from 25 review questions (AMD Guideline, 2018). In the final published guideline, a number of recommendations are subsumed under one heading, for example, the recommendations pertinent to RQs 4, 5, 16 and 24, (see Appendix viii) appear under the "Diagnosis and Referral" section of the published guideline.

Reflections on the integrative framework

The proposed framework organises the key findings of this research and maps the wide range of factors influencing the guideline process. Some of the factors, for example, external network factors, have not been highlighted previously as important to the process,

so, framing the guideline process in this way adds further insight into the facets of guideline development. As the literature review of this thesis has indicated, an examination of guideline development can be informed by various theories and concepts. Some are directly related, such as the empirical literature on guidelines, or are more tangential, such as literature pertaining to small group processes or social psychology. An integrative framework is a way to bring all this together and is a key contribution of this research.

The framework describes the components that were integral to, or had some effect on, the macular degeneration guideline process. It was not possible to elucidate all the relationships between components nor the relative influence of inputs and enabling/disruptive factors in affecting outputs. Further, it was not possible to state whether one poorly functioning component could be overcome by another well-functioning one or by another extraneous factor not demonstrated in this research. In short, it is difficult to claim causal relationships between the different components.

On reflection, another potential issue is in the labelling of the components in the framework. The choice of one label over another may lead a reader in a direction that is not intended or the choice of one phrase may preclude use of another. For example, "facilitation" does not feature as a separately labelled factor in Group Composition and Dynamics in the framework. However, good facilitation was observed to be impactful in the guideline process. It is "included", albeit without overt statement, in the sub-components "Effectiveness of Input" and "Roles Adopted". Thus, labelling matters in the interpretation of the framework.

The framework has been developed from only one case study. The factors identified and any linkages between components may exist for this case but not for others. Criticism may also, perhaps, be levelled that having data from multiple cases would add to the validity of the framework. However, this should not detract from the richness of observation detailed in this single study.

Ostrom (2007) warned of creating frameworks as "panaceas" when they have multiple variables since it is unlikely that solutions may be found to complex problems with many variables. This framework *does* have multiple components underpinned by multiple concepts/theories, but, it is not proposed to provide solutions, rather, it is intended to identify factors with potential to impact the process. Its relevance is a further understanding of the guideline process with special focus on the social processes of guideline development, previously under-represented in the literature. The framework also has practical implications; these are discussed as part of the final chapter of this thesis where the contributions of this research are examined.

7.4 Summary

Firstly, this chapter discussed the key findings of this case study with respect to the guideline literature. It then moved on to describe a new integrative framework for the guideline process which illustrates the key factors involved.

What emerges from the case study is that guideline development concerns more than just the supporting evidence. Guideline development is a social process, the outcome of interactions dependent on such influences as group diversity, group dynamics and emergent states such as trust. The social processes of guideline development are one area that has received little attention so far and this research adds to that corpus of literature.

Evidence *is* fundamental as a supporting base for guidelines although there is a mixed picture of what evidence is available or acceptable and how it is used. In the case study guideline, a strict hierarchy of evidence was adhered to; this led to little supporting evidence being available to support the formulation of some of the recommendations. In these cases, there was a reliance on expert opinion and this supports views that judgement and interpretation also play a significant role in the guideline process.

Other factors appear to be important too. The guideline development environment has features of a network; it is most closely aligned with a collaborative network. By its nature, the existence of a network implies influences from the broader network linkages. The external influences on guideline development are another area that has not been paid

sufficient attention to in the literature. This study has demonstrated that external influences, whether present at the start of the guideline's development, or arising during development, can be challenging and have the potential to derail proceedings.

A new integrative framework for analysing and understanding the guideline development process has been proposed. This brings together all the factors that have been identified as key to the process in this study. It highlights that the formulation of guideline recommendations depends on more than the evidence base. Key factors also include the social interactions of the core guideline group and influences from the external environment.

Chapter 8: Conclusions

8.1 Introduction

The previous chapter discussed the key findings of this research into the guideline development process in relation to the literature. This chapter, provides an overview of the thesis and the contributions it makes to the existing literature on clinical guidelines. Firstly, there is the overview of the thesis: its aims and research questions, how these were addressed, and the key findings. It then highlights the main contributions of the thesis. This is followed by an outline of potential areas for further research and the practical implications of the findings. The chapter then reflects on the methodological approaches used in the study with a reflection on the research from the researcher's perspective. It ends with key summary points.

8.2 Thesis overview

The starting point for the research was an interest in improving understanding of the clinical guideline process. This was particularly from the point of view of the group of individuals charged with producing guideline recommendations. What happens during the guideline development process in terms of interactions between these individuals and how guideline recommendations are actually formed, was of particular interest.

Exploration of the clinical guideline literature showed that, while areas such as the methodologies of guideline development and implementation of guidelines are well-represented, research on the social processes of guideline development is more limited. There is also a paucity of research looking at factors, external to the core development group, which enable or disrupt the process. From the literature, a set of research questions emerged which encompassed the aims of unpacking the clinical guideline development process and addressing the gap in the literature.

The overarching research question is: how does the multi-actor guideline group interact and use evidence in guideline development? A multi-perspective framework has been utilised to address this question. This has been especially useful in providing a rich picture

of the whole guideline process. Aligned with this, and to investigate further the primary question, the following subsidiary questions have also been considered: how is evidence perceived, interpreted and used by the group developing a guideline; how does the group interact and what are main within-group influences; how does the broader network, surrounding the core development group, influence it or impact the process?

Guidelines are produced by a number of different organisations. Some of these are part of government apparatus and others are independent bodies with special disease interests. In the UK, the National Institute of Health and Care Excellence (NICE) is the body producing the most widely used guidelines and it is held up an exemplar of guideline development. For these reasons, NICE was selected as the research setting for this inquiry. A single case study approach, following one particular guideline process, was chosen as a useful way of illustrating all the factors impacting guideline development from the beginning of the process to the publication of the final guideline. It was also a practical choice as the researcher was familiar with the disease topic and had had experience in that particular clinical field. This reduced the time taken to learn the technicalities of the disease and aided understanding of the nuances of treatment in that therapeutic area.

A longitudinal qualitative case study (27 months) of one NICE guideline group developing an ophthalmology disease guideline was undertaken. The guideline group's formal meetings were observed for more than 120 hours. This observation was supplemented by semi-structured interviews (22 formally recorded interviews and numerous *ad hoc* interviews and communications) with core group participants, which included external expert group members and internal NICE technical staff. Also undertaken was documentary analysis of guideline documents and group meeting outputs to supplement the observation and interviews.

This thesis demonstrates that the production of guideline recommendations depends, not only on scientific evidence, but also on social interaction and the factors affecting this. Composition of the group and changes to this, the roles played in the group, professional hierarchies and emergent states, such as trust, are all key factors in the functioning of the group and the outcome of the task.

The evidence base supporting the guideline is mixed in terms of the type, quantity and quality of evidence. The quantity of evidence available, or considered acceptable, is variable and the quality often assessed as "low". Both the quantity and quality of evidence depends on the type of guideline review question being asked, with intervention-type questions most likely to be associated with more evidence judged to be of a higher quality. The evidence was subject to assessment and interpretation by the individual members of the guideline group and thus, judgement, is a key part of how evidence is assessed and appraised. Expert opinion played a significant part, both in interpretation of evidence and in the formulation of guideline recommendations. It was relied upon frequently, especially where availability of evidence was judged to be low. This was in spite of a strict adherence to an evidence hierarchy where expert opinion appears at the bottom of the pyramid.

A guideline development group can be characterised as a network within a network. The group itself consisted of multiple individuals who were linked to professions or organisations. NICE too (within which the group "exists") is part of a network of actors including the Department of Health in England and various stakeholders with interests, in this case, in the ophthalmology field. There were influences from this wider network that played an important part in the outcome of this guideline and during its development process. External factors can both set the context for the guideline and have specific impacts during the process. Their influence can potentially derail or delay the process and, as such, are currently under-acknowledged in the guideline process.

These key findings provide insight into the guideline process, in particular, into how the guideline group interacts and uses evidence. The research raises questions about the evidence base supporting guidelines, such as the continued strict application of the evidence hierarchy in applying quality ratings to evidence, and how much expert opinion is used in the process. It also highlights how the composition and the management of the guideline group is important to how the group interacts and functions and how much external factors play a role in guideline development. The insights from this research are now discussed in terms of the contributions they make to the guidelines literature.

8.3 Research contributions

This research makes a number of contributions to the clinical guidelines literature by contributing to our knowledge of the whole guideline process. In particular, insights have been gained into the social processes of guideline development, and the influence of factors external to the core development group. It builds on and expands previous work which has highlighted the social underpinning of guideline development. It does this by, not only endorsing the view that the social processes are an integral part of guideline development, but also illustrating that there are other influential factors, apart from the evidence, which impact the group's functioning. The case study observed the development of a guideline in the ophthalmology therapeutic area which has not been studied in this way previously. Furthermore, the macular degeneration diagnosis and management guideline, is the first of its type for this increasingly prominent disease area. Thus, this research provides insights into some of the challenges faced when developing guidelines in this therapeutic area.

A key theoretical contribution is the mapping of the whole process in an integrative framework. The components of the process are set out in the framework as well as factors that may enable or disrupt it. These include inputs such as the evidence and the people involved and contextual factors such as the specific disease topic and the scope of the guideline. Factors with the potential to enable or disrupt the process are also part of the framework along with the outputs, the guideline recommendations, which are influenced by the inputs and the processual factors. The framework resonates with the view that evidence is only one part of guideline development and social factors play as important a role in guideline development as the technical aspects of the process. Furthermore, the case study demonstrates the impact of factors and issues outwith the core guideline group and these are highlighted in the framework. Taken together, the framework can be used to identify the many aspects of the guideline process not previously considered in this holistic way.

The research provides a detailed account and analysis of the guideline stakeholder network, its composition and how the influences acting on the network affect the outcomes. The network within which guideline development takes place has not been

highlighted previously as having a significant influence on the guideline process. Utilising a network lens in the study has emphasised the importance of individuals, their organisations and how they are linked. The research, therefore, contributes methodologically to understanding how a network lens can be used to analyse the clinical guideline development process.

In conclusion, this longitudinal study has provided the first mapping in an integrative framework of the influences, both internal and external, on the guideline development process. It has resulted in a better understanding of clinical guideline development. It strengthens the existing body of knowledge concerning clinical guidelines especially with respect to the social processes underpinning guideline development and external factors that may impact the guideline process. Researchers, policy makers and practitioners should gain a wider appreciation of clinical guideline development.

This research was intended to develop academic understanding of the guideline process, however, it also has some implications for practice and has opened up avenues for further research. These are addressed next.

8.4 Practical implications and potential areas for further research.

The detailed mapping in the integrative framework should enable NICE to reflect on the guideline development process with potential implications for process improvements. This includes assessing the existence of personal or organisational linkages in the guideline network, or potentially impactful factors in the environment, that may affect guideline operations. Understanding these factors prior to the start of, or during the guideline process, may mean mitigating actions (or encouragement of enabling influences) can be taken. For example, in this study, conflicts of interest led to changes in the composition of the guideline group. There was also a frequent reliance on expert opinion for certain review questions due to the variable quality and quantity of supporting evidence. These two things meant expert opinion, for a while, was predominantly from one voice. Having a framework to refer to, setting out possible influential factors, may have meant greater consideration of the role of expert opinion with particular issues addressed early in the guideline process.

The integrative framework describes all the elements in this research that were integral to, or had some effect on, the guideline process. Elucidating all the relationships between the elements and the relative influence of inputs and enabling/disruptive factors affecting outputs was not part of this study. This, then, is an opportunity for further work to develop the framework. How the elements link and interact in certain contexts would add to the understanding of the guideline process.

The reliance on expert opinion in this study and the under-acknowledgement in the literature of its importance to guideline development, suggests further research into how much expert opinion figures in the guideline process, is warranted. Avenues to explore could include the extent to which expert opinion shapes each guideline recommendation, whose expert voice contributes the most for different review questions, and how expert opinion may best be assessed and appraised for quality, in the same way that other evidence is appraised. This may challenge the existing assumptions about evidence and the adherence to a strict evidence hierarchy but it will aid those using the guidelines to understand from where guideline recommendations arise.

One of the key roles for the guideline group was that of the chair. The chair in this study was experienced in chairing groups and this was seen to facilitate group functioning in a positive way. This has implications for the experience of chairs recruited for guideline development groups; it raises the question of whether specific disease experience or experience in chairing is more important for guideline group operations. Attention to this by NICE may improve group functioning and dynamics. Further research into the role of chairing, the characteristics and personality most suited to the role and the impact of these on group functioning is warranted. One other area where further research might be beneficial with regard to the roles adopted within guideline groups is by the use of the TRIAD model (Driskell et al., 2017). The use of the TRIAD framework may illuminate the role characteristics of such groups and the optimal behaviours of a well-functioning group.

The patient representatives were also key actors within the group. The two patient representatives in this study were from different parts of the disease spectrum which

added insights that would be unavailable if they were both at similar stages of the condition. Their contributions to the group, in terms of experience of the specific disease and patient management, were considered very valuable to the guideline process. There are views that patient and user involvement in healthcare is vital in developing services and their involvement in guideline development is also advocated. However, there is little empirical research into how, and why, patient involvement with guideline groups is beneficial and this is an avenue for further research.

By using a case study approach, this research has documented the development process for a guideline in macular degeneration in rich detail. Using a similar approach, and the integrative framework, across guidelines in the same therapeutic area, or for guidelines in different therapeutic areas, would deepen the overall understanding of the social processes of guideline development. Further use of the integrative framework across different guidelines would validate its use in guideline development, both from a research and practice perspective.

Trust, an inductive finding in this study, was seen to play a role in group functioning. As trust in guideline groups has not previously been explored, specific research in this area would further illuminate the process with respect to how trust arises, how it influences group dynamics and functioning and the factors that promote or discourage it.

The chapter continues with two sections detailing reflections on this research. Firstly there are methodological reflections on the study approach and then a personal reflection on the research process.

8.5 Methodological reflections

The approach taken of a qualitative case study, underpinned by a social constructionist philosophical viewpoint, was a choice that reflected the desire to study a social phenomenon and produce richly detailed narrative. This was to *understand* the guideline process and the influences on it, not just to describe elements of it as previously seen in the literature. A detailed analysis of the methodological choices for this inquiry has been

provided in Chapter 4; this section reflects on the operationalisation of these choices, the practical issues encountered and learnings for further research.

Gaining access to the research setting and to the participants of the macular degeneration guideline group was relatively straightforward. One research expectation was that the use of data gathered would also be without issue. Individual participants gave consent to their data being used in this thesis but the researcher was not allowed to divulge what NICE considered confidential information from the group meeting discussions. This was data not in the public domain. Therefore, evidence presented to the group in a different format than that published could not be used nor could verbatim conversations between participants during group meetings. Whilst understanding the need for NICE to protect the confidentiality of the expert participants, this was frustrating to the researcher since, in some cases, this precluded the use of colourful, illustrative data. Whilst it is unlikely to have made a difference in this research setting, the lesson learned for further research is to explore, and be explicit about, the issue of what data can, or cannot, be used before data collection begins.

Furthermore, recordings of the proceedings of the meetings were not permitted so the data gathered was dependent on observation and note-taking by the researcher. This led to frantic scribblings of notes during early meetings in an attempt to detail *all* the meeting proceedings and events. An *a priori* conceptual interests' guide for observation in meetings (Table 4.6) was put in place after these early meetings and this proved useful to focus on particular areas of interest. Such a guide to observation would be now considered useful for future, similar research where recordings of meetings are not allowed.

In this study, the interviews formed a significant part of the overall data. Interviews were used to gather participants' views on evidence, on group functioning and about influences on the guideline process. Interviews were also an opportunity to glean opinions about events that occurred during previous guideline group meetings. The messy reality of research came to the fore in the gathering of interview data. The main practical issue was lack of time to conduct the interviews where the interview was held on the same day as the group meeting. The meetings were generally held between 0930 and 1730 with only

30 minutes for lunch. As many participants travelled on the day of the meetings, trying to conduct interviews before or after the group meetings was difficult. Occasionally this made the interviews feel slightly rushed but efforts were made to continue the interview at a later date or by phone. This caused a disjointedness in some interviews and, as they were held on different days, some time apart, it was possible the recall of respondents could have been compromised by the passage of time between meeting and interview, especially where this was lengthy.

The issue of not having sufficient time for interviews on the day of group meetings led the researcher to try and conduct interviews at the convenience of the participants. This culminated in much travel around England as the participants were in disparate geographical locations. This added to the time and expense of the research overall. However, it did allow longer interviews to be conducted with minimal time pressure.

A further expectation versus reality concerned the amount of data generated and the methods of data analysis. The expectation was that the amount of data generated would manageable in terms of the volume of data to analyse. This was true with respect to transcription of formal interviews but coding transcriptions, *ad hoc* interview notes, and all observation and reflections data resulted in a multitude of codes at the first level coding stage. This was condensed into higher level coding (and then thematic maps) by use of visual display of the codes on large boards. The creation of the coding boards took longer than expected but having the codes displayed in this way, helped with condensation of them and with the identification of themes. It is possible that using a computerised qualitative data analysis software system may have helped organise codes more efficiently, but it remains the view of the researcher that the manual analysis allowed closer contact with the data.

The treatment of macular degeneration was a contentious issue before the guideline development started. Therefore, discussion of potentially sensitive material was expected. Thus, how to address issues of participant identity in this thesis and confidentiality of data has been an on-going consideration. Furthermore, the group studied was not large and the range of demographic characteristics may make identification of participants possible.

Various measures have been used to avoid identification of participants in this thesis (see section 4.4) and it is unlikely that the illustrative quotes used in this thesis may be ascribed to any particular individual. However, identification of individuals could be possible for whether they belong to the expert group or the NICE technical team as, on occasions, it was appropriate to illustrate a particular "voice" from one or other of these two groups. Sometimes, the data was commercially sensitive pharmaceutical economic data. On these occasions the researcher was asked to leave the room whilst the discussion took place and could not report this information. However, she was present, observing all proceedings, for the majority of time.

This research has been guided by a multi-perspective framework. This emerged from exploring relevant literatures and an interest in investigating the guideline process in the round. Viewing the process with many lenses permitted examination of both the interactions within the development group and the influences arising outwith the group. In retrospect, focusing on just one aspect of the guideline process, underpinned by less diverse theoretical foundations, may have facilitated data collection and analysis. However, the multi-perspective lens approach fitted with the aims of this research and the desire to investigate the whole process. Furthermore, the lenses used are underpinned by theories with a variety of underlying epistemologies. For example, evidence in the EBM tradition is usually viewed with a positivistic frame that assumes removal of social context from medical evidence (Goldenberg, 2006). However, it can also be viewed from an interpretivist standpoint (Upshur, 2000). The use of underpinning theories with different underlying epistemologies has allowed a more holistic view of the guideline process.

As described in Chapter 3, the mindlines concept was initially part of the conceptual framework guiding the research. Early analysis revealed that using the concept as a research lens is difficult. This is because mindlines are difficult to articulate and are not tangibly recognisable in others. The concept was moved into the background of the conceptual framework. It underpinned the other conceptual lenses as a link between the way evidence is understood, interpreted and revised as a consequence of interaction with others. On reflection, the initial choice of the mindlines lens was appropriate in that it conceptualises how different ways of knowing and evidence are blended as a consequence

of this social interaction. However, early attempts at operationalising the concept of mindlines in the data collection and analysis process did not elicit persuasive empirical data due to the difficulty of articulation of mindlines by individuals. This does point to the value of further work into how the mindlines concept may be operationalised and incorporated into guidelines research.

8.6 Personal reflections and concluding thoughts

It is important to consider reflexively how, as a researcher, one may influence one's research, to acknowledge potential bias and to reflect on the journey of developing a researcher identity. As is the tradition with personal reflections, the following is written in the first person.

For me, there were a number of areas of concern in this research. The first concerned my background as a physician and ophthalmologist. The concern was that my medical training (in a positivistic tradition) and specific ophthalmological experience could impact, not only assumptions about the evidence being used, but also the interpretation of data. Yanow (2007:114) writes that: "there is no position outside of the subject being studied from which the researcher can observe it". In other words the researcher and her subject are intertwined and, in this case, closely intertwined. However, being attuned to this allowed sensitisation to potential effects on the research process and constant questioning of the way I was interpreting what was said within meetings and to me during interviews. Being reflexive in this way encouraged consideration of points of view different from my own values and assumptions.

Also, at the beginning of the study, one clinical expert tried, on occasions, to include me, as a fellow ophthalmologist, in discussions, looking for endorsement of their point of view. This lessened as the guideline development progressed and was aided by my status as a complete observer (after Gold, 1958). I was not expected to respond and was able to sit in the background away from the discussion table. Nevertheless, the action of the clinical expert implied inclusion in the guideline group. This "inclusion" became more apparent as time progressed and relationships with the participants deepened. Throughout the data collection phase when I was with participants, I maintained that I was an

investigator of the group rather than a participant. Whilst the inclusion as part of the group was an issue for me to monitor on an on-going basis to avoid group identity and emphasis on only positive aspects of group interactions, my background and understanding did support the sharing of participants' experiences with me.

One other reflection is also linked to my background and the linear way of thinking in medicine. The multi-perspective framework used and different viewpoints sought meant a requirement for multi-level thinking. The PhD process has given me new skills of critical, multi-level thinking, enabling me to see medicine in a different light, leading to the development of a more questioning persona.

To conclude, this longitudinal, qualitative study of one guideline development process provides a richly detailed account of the way guidelines are put together by a guideline group. It shows that evidence does not smoothly translate into guideline recommendations and judgement plays a significant part in the process. Expert opinion, given in appraisal and interpretation of evidence and in forming the guideline recommendations, is relied upon heavily, especially where evidence is unavailable or deemed unacceptable. Furthermore, the guideline process is subject to many factors, both internal and external to the guideline group, which have the potential to derail, or augment, the whole process. Both expert opinion and these factors are currently under acknowledged as being influential to the guideline process.

The thesis makes contributions in a number of areas: it strengthens the body of clinical guideline literature especially concerning the social interactions involved in the process. Furthermore, the guideline development process in the ophthalmology therapeutic area has been examined for the first time. Ophthalmology is assuming greater importance in the overall healthcare provision mix due to a rising prevalence of age-related eye disease. Research in this area should aid providers and policy makers in their considerations of optimal healthcare strategies. In addition, the thesis has mapped, in an integrative framework, factors influential to the process. This indicates that guideline recommendations are not based on evidence alone; rather they are a result of an interplay of a number of internal and external factors that influence the guideline process.

Thus, this thesis offers a greater understanding of the guideline process for researchers, practitioners and policy makers alike in their critical engagement with clinical guidelines. As well as this, I have gained entry to academic conversations about a subject that has taken up much of my working life. I am grateful that I have had an opportunity to engage in these conversations and contribute to the body of knowledge in this area.

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Appendix i: Interview protocol#1

Schedule:
Introduction to aims of study; what interview involves; data handling and informed consent process; questions

Question Protocols:

Roles, Group Interactions and Clinical Mindlines:
1. Can you describe your current professional role and how do you place yourself within this GDG?
2. Can you describe any influences on your perceived GDG role?
3. How have you gained your personal knowledge of macular degeneration? (*formal/experiential*)
4. How do you personally adopt new knowledge or revise your current knowledge about macular disease? (*social interaction/tacit*)
5. What do you feel could impact, influence or change your understanding or management of macular disease? (*contextual factors*)
6. What do you think of the composition of the group?
7. How would you describe how the group interacts?
8. What are the key factors impacting how the group functions?

Some Follow-up Questions
1. Do you feel your role has changed over the course of the guideline process?
2. How has your thinking developed/practice changed over the course of the guideline process?

Evidence Use:
1. What do you consider to be evidence?
2. What would you consider to be bad/good evidence and can you give examples?
3. What do you feel are the influences on evidence selection in the guideline process?
4. Is there any emphasis on a particular type of evidence and if so, why do you think this is so?
5. What evidence do you feel is missing that might inform or improve the GL?
6. How is evidence used to make decisions about recommendations?
7. What do you think about the process of forming guideline recommendations?

External Network:
1. This is the formal NICE structure for a NICE GDG; how do you perceive this GDG fits with the formal structure? What is missing?
2. How do you see the links (*people, organisations*) functioning within this GDG?
3. How, in your opinion, are decisions made? What influences these decisions?
4. How do you relate to GDG members outside of the GDG meetings?
5. What do you see as the key influences on the group?

Is there anything else you would like to add that has not been addressed by the questions?

Triangulation Questions:

Check responses with each participant with regard to
- observations made during GDC meetings, meeting minutes contents, documentary analysis

Appendix ii: Interview protocol#2

Schedule:
Introduction to aims of study; what interview involves; data handling and informed consent process; questions

Question Protocols:

Roles and Group Interactions:
1. What is your current professional role and how do you place yourself within this GDG?
2. Can you describe any influences on your perceived GDG role?
3. What do you think of the roles played by others within the group?
4. What do you think of the composition of the group?
5. How would you describe how the group interacts?
6. What are the key factors, in your opinion, that impact how the group functions?

Some Follow-up Questions
1. Do you feel your role has changed over the course of the guideline process? How and why?
2. How has your thinking about how the group functions, changed over the course of the guideline process?

Evidence Use:
1. What do you consider to be evidence?
2. What would you consider to be bad/good evidence and can you give examples?
3. What do you feel are the influences on evidence selection in the guideline process?
4. Is there any emphasis on a particular type of evidence and if so, why do you think this is so?
5. What evidence do you feel is missing that might inform or improve the guideline?
6. How do you feel evidence is used to make decisions about recommendations?
7. What do you think about the process of forming guideline recommendations?

External Network:
1. This is the formal NICE structure for a NICE GDG; how do you perceive this GDG fits with the formal structure? What is missing that would add to the structure/functioning of this GDG?
2. How do you see the links (*people, organisations*) functioning within this GDG?
3. How, in your opinion, are decisions made? What are the influences on this from external parties/stakeholders?
4. How do you relate to GDG members outside of the GDG meetings?

Is there anything else you would like to add that has not been addressed by the questions?

Triangulation Questions:

Check responses with each participant with regard to
- observations made during GDC meetings, meeting minutes contents, documentary analysis

Appendix iii: Ethics Approval

University of St Andrews

University Teaching and Research Ethics Committee

16 September 2015
Judith Hughes
School of Management

Ethics Reference No: *Please quote this ref on all correspondence*	**MN 11756**
Project Title:	The use of evidence and decision making in the multi-actor network responsible for clinical guidelines in the UK
Researchers Name(s):	**Judith Hughes**
Supervisor(s):	**Dr Tobias Jung; Professor Sandra Nutley**

Thank you for submitting your application which was considered by the School of Management's Ethics Committee. The following documents were reviewed:

1. Ethical Application Form
2. Participant Information Sheet
3. Participant Consent Form

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' (http://www.st-andrews.ac.uk/media/UTRECguidelines%20Feb%2008.pdf) are adhered to.

Yours sincerely

Dr John Desmond
Convenor of the School Ethics Committee

cc Shona Deigman

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Appendix iv: First level coding

Derived from deductive, researcher-led codes and inductive codes, process and emotion codes, in-vivo codes

Conceptual (C) lens codes and inductive (I) codes	Description	Descriptive Codes	Process Codes	Emotion Codes	In-vivo codes
Broader Network Influences (C)	The network of individuals, groups or organisations external to the core guideline development group	Health policy Risk Political Boundaries Stakeholder interests Power Organisational influence NICE extra-GDG teams NCGCs Legal Time Resources Pharma Competing work Political agenda DoH NHS Tax-payers Purdah Technology Commissioners	Prioritising Guiding Influencing Regulating Limiting Safeguarding interests Serving different masters Modifying (GDG structure by NICE) Controlling Competing Scoping	Discomfort Anger Hostility Suspicion	“Political landscape” (NE1) “Island in the sea of politics” (NE3) “Acting in a sphere” (LN2) “Bigger forces at work” (GR1) “NICE working in a wider system” (NE3Int2) “The NICE brand” (NE6) “NICE-it-up”

		GL audience Research funding Ophth charities Media Patients			
Evidence and Knowledge (C)	The perception, the use, the interpretation of the data used as evidence for the guideline	(Guidelines ? a code) Randomised controlled trial Qualitative data Specialist knowledge Hierarchy Expert opinion Experience Evidence lack/paucity Health Economics Missing data Expertise Cost effectiveness Data search Presentation of data Variation in practice Population vs individual tension Accessibility Manipulation Robustness Bias (res, experts, publicn) Complexity Neutrality	Modelling Gaining knowledge Learning Clarifying Challenging Scrutinising Synthesising Summarising Presenting Training Analysing Setting boundaries Scoping Advocacy (of data/source/process) Justifying Interpreting Questioning (data and value of GL) Outsourcing Garnering Sifting Funnelling Screening Translating	Surprise (at lack/results) Disappointment Astonishment Frustration Pride Commitment (HE modelling) Satisfaction Feeling inadequate (in interpreting data) Suspicion Hope	“Evidence is a solution” (NE2) “Research waste” (LN3) “Evidence-free zones” (NE3Int2) “Gene-pool of evidence” (LN1) “Evidence-space” (NE5) “Piece of advice” (referring to GL) “Opportunity ot highlight a need” (SD2) “Relationship with a condition” (SD4)

		Context Anecdotal Peer review Grey literature Vocabulary/Language Availability determinants Research recs Interconnectedness (of decisions made)			
Group Functioning and Interactions (C)	Social group structure and interactions, influences and roles	Emotions Balance Communication Frustration Conflict Harmony Collegiality Arbiter Leadership Perceived roles Professional status Change Decision making Motivation Agendas Credibility Negotiation Patient representatives Kudos Engagement	Sense-checking Interacting Clarifying Simplifying Facilitating Focusing Influencing Steering Priming Taking responsibility Negotiating Planning Debating Engaging Contributing Listening Socialising Enabling Arbitration	Apologetic Respect Uncertainty Confusion (data; roles) Disbelief Anger Resentment Joviality Collegiality Friendliness Boredom Fun Optimism Comfort (to contribute) Defensiveness Including Positivity Anxiety	"A bit vanilla" (NE3) "Arguing on their behalf and representing them" (AR1) "Dispassionate professionals" (BL1) "Giving something back" (BL1; SD1) "Consensus can be wrong" (BL1) "Adapted to each other" (LN1) "Wanting to be heard" (SD3) "Able to express ourselves" (SD3)

		Group social position Personalities Tension Contribution Representation Collaboration Responsibility Ownership Perception Intuition Dominant clinical opinion Friendliness Power Consensus Opinionated Wisdom Chairing role Participation Status (prof/social) Change in personnel Commitment Inhibitory politeness Prior assumptions Different viewpoints Approached by NICE Secret club Nuanced language Topic knowledge Identity	Conflict Motivating Leading (Chair) Understanding Compromising Questioning Ceding judgement Deference Including all views Keeping order Problem-solving Arguing Mediating Provoking Sparring Conferring Discussing Providing a framework Adaptation (to GDC role) Raising profile of self Disrupting Sharing experience Translating Revising	Loneliness Annoyance Dissatisfaction Frustration Denial Cynicism Astuteness Willingness Privileged Self-doubt Belonging	

		Groupthink Rapport Honesty Expectations Participant selection Group structure Task focus Coalitions			
Process (I)	The series of steps to produce a guideline and the influences in play	Rules NICE process Adherence Constraints NICE-speak Consensus Recommendations Resources Expectations Thoroughness Slow/cumbersome Frustration Boundaries Rigidity Structured Physical space Clarity Accountability Practical Prescriptive Neutrality Standardisation	Information gathering Capturing arguments Writing recs Publishing (minutes etc) Leading (NICE) Criticising Including all views Accepting process Observing Abiding (by rules) Rubber-stamping Making order from chaos	Comfort (with process) Discomfort (with process) Threatened (patients/Drs by recs) Rewarding Reluctance (to make rec) Disinterested Concern Editing	"Brilliant process" (LN3) "Set in stone" (NE4) "A monster, elephantine process" (AR1) "They are incredibly process driven" (BL1) "Subtleties of the wording" (BL1) "Little robots" (BL1)

		Quorum Process guards Explicit Process driven GDG as a tool Evolution Intensity Credibility Insight			
Trust (I)	A belief in the reliability, or ability, of someone or something	Reliability Respect Ability Competence Dependence Constancy Consistency	Guiding Leading Ceding judgement	Misplaced Reassured	"Know what they are doing" (BL1)
Conflicts of Interest (I)	Circumstances that create a risk of influencing the outcome	Declarations of interest Financial Intellectual Pharma Anti-pharma External influences Vested interest		Sympathy	

Appendix v: Higher level coding

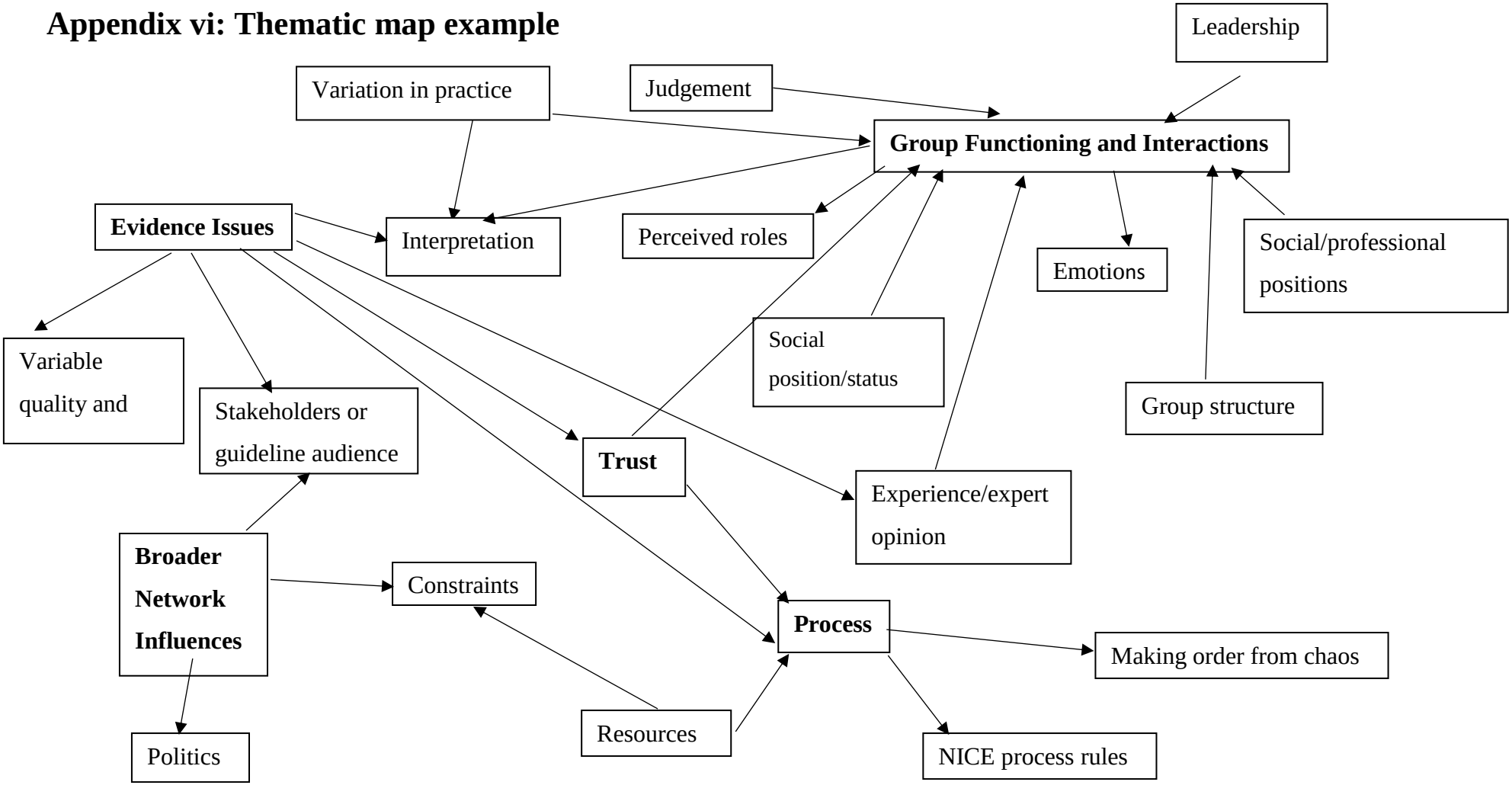
Derived from condensation of 1st level codes

Conceptual (C) lens codes and inductive (I) codes	Description	Higher Level Codes	Includes	Comments
Broader Network Influences (C)	The network of individuals, groups or organisations external to the core guideline development group	External Stakeholders or Guideline Audience NICE teams Politics Legal Resources	Interests, NHS, DoH, Pharma, Tax-payers, Commissioners, Patients, Stakeholders, NCGCs, COI (inductive code) Agendas, process, Safe-guarding interests Controlling, regulating, editing Time, £, Impact on process	Think of impact, implications, balance of the network influences
Evidence and Knowledge (C)	The perception, the use, the interpretation of the data used as evidence for the guideline	Evidence base Evidence issues Experience	RCT, Qual data, HE, CE, Modelling, Accessibility, "Gene-pool of evidence", Hierarchy, Disappointment EBM approach Complexity, Paucity, Summarising, Synthesising, Scoping, Analysing, Interpretation, Bias, Presentation, Popn vs individ tension, Variation in practice Specialist knowledge,	Guidelines ? a code

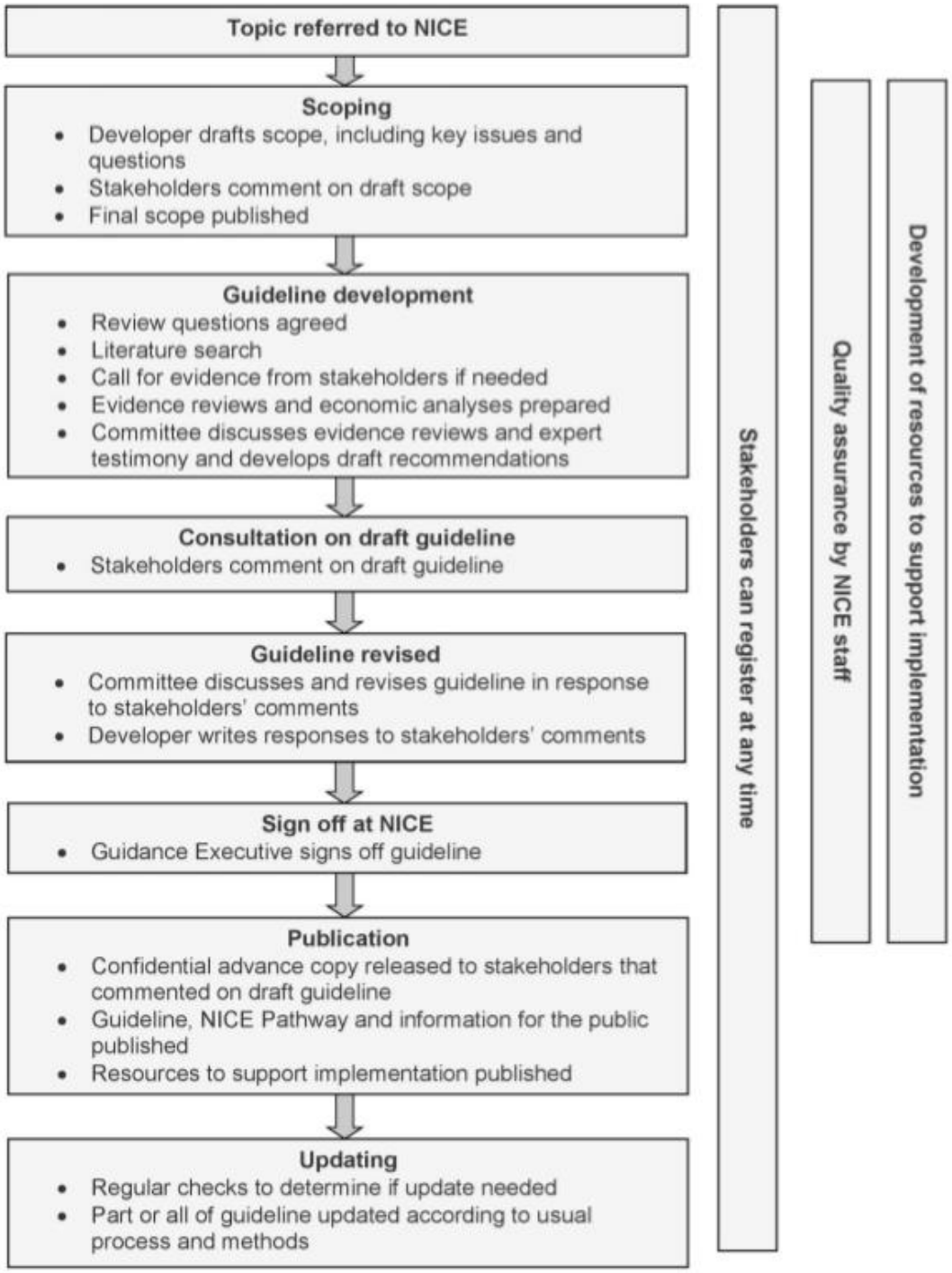
			Challenging, Scrutinising, Clarifying,	
		Expert opinion	Secret club	
		Interpretation	Questioning, Summarising, Translating, Language	Of data, of opinions given
Group Functioning and Interactions (C)	Social group structure and interactions, influences and roles	Group structure and balance	Experts, Patient members, Change in personnel, Coalitions	
		Perceived group roles (incl professional roles)	Representation, Facilitation, Steering, Leadership, Status, Credibility, Arbiter, Clarifier	
		Social position	Kudos, Identity, Power	
		Agendas and motivations	Expectations, Giving something back, Representation	
		Emotions	Anger, Collegiality, Fun, Belonging, Boredom, Respect, Resentment	
		Group interactions	Communication, Rapport, Collaboration, Contribution, Ownership, Engagement, Debating, Consensus, Negotiation,	
		Intuition and judgement		

Process (I)	The series of steps to produce a guideline and the influences in play	Rules Framework Thorough Consensus Resources "NICE-speak"	"Process-driven", Boundaries, Acceptance of rules Information gathering and sifting, Writing recommendations, "Making order from chaos", "Brilliant" "Cumbersome", Robust Constraints	
Trust (I)	A belief in the reliability, or ability, of someone or something	Reliability "Know what they are doing" Respect Competence Dependency Guiding Ceding judgement		Includes trust of NICE team, of data, of each other

Appendix vi: Thematic map example



Appendix vii: Generic NICE guideline process pathway



(NICE Manual 2014: 22)

Appendix viii: Macular degeneration guideline review questions

RQ 1: What signs and symptoms should prompt a healthcare professional to suspect AMD in people presenting to healthcare services?

RQ2: What risk factors increase the likelihood of a person developing AMD or progressing to late AMD?

RQ3: What information do people with suspected or confirmed AMD and their family members or carers find useful, and in what format (for example, written or oral), and when?

RQ4: What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD?

RQ5: How do different organisational models and referral pathways for triage, diagnosis, ongoing treatment and follow-up influence outcomes for people with suspected AMD (for example, correct diagnosis, errors in diagnosis, delays in diagnosis, process outcomes)?

RQ6: What effective classification tool should be used to classify different types of AMD?

RQ7: What is the effectiveness of strategies to reduce the risk of developing AMD in the unaffected eye or slow the progression of AMD?

RQ8: What is the effectiveness of psychological therapies for AMD?

RQ9: What is the effectiveness of support strategies for people with visual impairment and AMD (for example, re-ablement services and strategies for optimising existing visual performance)?

RQ10: What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity better than 6/12?

RQ11: What are the factors that suggest treatment should be switched or stopped for people diagnosed with neovascular AMD? What are the indicators for treatment failing and switching?

RQ12: What is the effectiveness of different anti-angiogenic therapies (including photodynamic therapy) for the treatment of neovascular AMD?

RQ13: What is the effectiveness of adjunctive therapies for the treatment of late, wet, active AMD?

RQ14: What factors indicate that treatment for neovascular AMD should be stopped?

RQ15: What is the effectiveness of switching therapies for late, wet, (neovascular) AMD if the first-choice therapy is contraindicated or had failed?

RQ16: How do different organisational models for ongoing treatment and follow up influence outcomes for people with diagnosed neovascular AMD (for example, disease progression, time to treatment, non-attendance)?

RQ17: What are the barriers and facilitators to appointment attendance and uptake of treatment for people with AMD?

RQ18: What is the effectiveness of different frequencies of administration for anti-angiogenic therapies for the treatment of neovascular AMD?

RQ19: How often should people with early AMD, intermediate AMD, or advanced geographic atrophy be reviewed?

RQ20: How often should people with early AMD, intermediate AMD, or advance geographic atrophy have their non-affected eye reviewed?

RQ21: In people with neovascular AMD who are not actively being treated, how often should they be reviewed?

RQ22: How often should people with neovascular AMD have their non-affected eye reviewed?

RQ23: What strategies and tools are useful for monitoring and self-monitoring for people with AMD? What strategies and tools are useful for monitoring and self-monitoring for people with neovascular AMD?

RQ24: How soon should people with neovascular AMD be diagnosed and treated after becoming symptomatic?

RQ25: What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity worse than 6/96?

Source: NICE AMD Guideline. Appendix C: Review Protocols (2018). https://www.nice.org.uk/guidance/ng82/evidence/appendix-c-review-protocols-pdf-4723229200.

Appendix ix: Final guideline recommendations for anti-angiogenic therapies

"Anti-angiogenic therapies:

1.5.1: Offer intravitreal anti-vascular endothelial growth factor (VEGF) treatment[1] for late AMD (wet active) for eyes with visual acuity within the range specified

1.5.2: Be aware that no clinically significant differences in effectiveness and safety between the different anti-VEGF treatments[2] have been seen in the trials considered by the guideline committee

1.5.3: In eyes with visual acuity of 6/96 or worse, consider anti-VEGF treatment for late AMD (wet active) only if a benefit in the person's overall visual function is expected

1.5.4: Be aware that anti-VEGF treatment for eyes with late AMD (wet active) and visual acuity better than 6/12 is clinically effective and may be cost effective depending on the regimen used[1, 2]

1: At the time of publication (January 2018), bevacizumab did not have a UK marketing authorisation for, and is considered by the Medicines and Healthcare products Regulatory Agency (MHRA) to be an unlicensed medication in, this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the prescribing decision. Informed consent would need to be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines, and the MHRA's guidance on the Supply of unlicensed medicinal products (specials), for further information. The guideline may inform any decision on the use of bevacizumab outside its UK marketing authorisation but does not amount to an approval of or a recommendation for such use.

2: Given the guideline committee's view that there is equivalent clinical effectiveness and safety of different anti-VEGF agents (aflibercept, bevacizumab and ranibizumab), comparable regimens will be more cost effective if the agent has lower net acquisition, administration and monitoring costs."

Source: NICE Age-Related Macular Degeneration Guideline NG82 (2018).

The wording of the final guideline encompasses **all** anti-angiogenic therapies and endorses the view of the GDG that there is equivalence in clinical efficacy and safety between the different therapies. However, it does place the responsibility for any prescription of bevacizumab with the prescriber.