***Title page**

A simple tool for comparing benefits and “costs” of COVID-19 exit strategies

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***Highlights**

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- As several countries begin to exit various forms of COVID-19 “lockdown,” a simple epidemiological tool – Population Attributable Risk – can help guide decisions about specific exit policy options, by quantifying the proportion of “serious” (hospitalised) COVID-19 cases likely attributable to various combinations of individual risk factors at the population level, such as age alone, versus age combined with the presence of any chronic disease/risk factor.
- Using recent COVID-19 hospitalisation data from a large hospital network, and current Scottish population age structure and risk-factor prevalences, we show that the likely impact on adult hospitalisations would be very similar (an approximate halving, compared to full lockdown exit for all adults) for the most “moderate” and yet reasonably effective options for continued lockdown: continuing to restrict the social contacts of all persons over 65, compared to all persons over 50 with any chronic disease/risk factor.
- Other considerations are therefore of critical importance to this decision, such as the equity and acceptability of these two policy options, as well their likely economic impacts.

A Simple Tool for Comparing Benefits and "Costs" of COVID-19 Lockdown Exit Strategies

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Introduction

Many countries are now struggling to identify optimal exit strategies from the COVID-19 pandemic lockdown. As with previous pandemics, responding to COVID-19 has been characterised by 'uncertainty, high potential loss, time pressure, and competing values' - all of which are a challenges to adopting an evidence based policy response.[1, 2] Weible, Nohrstedt [3] and Xu and Basu [4] have retrospectively reviewed how decisions have been made in various countries, with various degrees of success. However, watching and waiting for the optimal approach to be identified in another country is not a viable option and therefore various decision-making approaches have been advocated in the literature. These include principalism[5, 6], risk-based decision-making (RBDM)[7], experimentation[8] and analytic modelling[9-11]. Within each of these approaches data are important, including understanding the limitations of the available data when ideal data are not available.[12]

As more data about the pandemic becomes available, a variety of methods are being applied to understanding what has happened and predicting what might happen next. Stedman, Davies [13] and colleagues used trend analysis to analyse the state of the pandemic in the UK, with the intent of informing future policy actions. In the city of Honghu in Hubei, China cloud-based systems were used to monitor the pandemic.[14] Tsay, Lejarza [15] and colleagues applied more traditional infectious disease models compartmentalising: susceptible, exposed, infectious, recovered (SEIR) people in data from the USA, Germany, Italy and Spain. Li, Tang [16] and colleagues extended the SEIR model to model the impact of mass influenza vaccination and public health interventions. The computational power available today means that these types of models can be developed and run quickly. However, as Rhodes and Lancaster [10] discuss, the multitude of models can become problematic, complicating and confusing rather than supporting evidence-based decision making. Subsequently, there is a need for more easily understood and transparent models, especially when they can help decide between competing interests.[11]

We describe a traditional and remarkably simple epidemiological tool, rarely applied to infectious diseases, which can be used to quickly estimate and compare the potential main benefits and "costs" (i.e. negative consequences) of various exit strategies. That tool is Levin's Population Attributable Risk (PAR)[17] – the proportion of disease burden which is attributable to any given risk factor, such as age or the presence of one or more chronic diseases, in the case of COVID-19.

$$PAR = \frac{p(RR-1)}{1+p(RR-1)}$$

Where p is the proportion of the population exposed to the risk factor, and RR is the relative risk of the outcome related to the risk factor.

We demonstrate how this method can be easily applied to compare two exit strategies:

A. continuing lockdown for all older adults (based on two age cut-offs: 50+ and 65+);
B. continuing lockdown only for adults with one or more chronic disease risk factor/condition (CDRF), also stratified by these same age-groups, compared to continuing lockdown for all adults 20 to 49 years of age.

Methods

These calculations are applied to Scotland in May 2020 (when lockdown relaxation measures were just beginning to be considered) using data readily available at that time:

- the current Scottish population structure[18];

- recent Scottish Health Survey[19] prevalence estimates for common chronic conditions known to increase the risk of severe COVID-19 (CDRFs): "any cardiovascular disease or diabetes"; obesity; asthma or COPD (Table 2.3 of the Survey report); and
- early-pandemic (March 2020) USA age-specific rates of COVID-19 hospitalisation[20], as well as characteristics of hospitalised cases, in terms of both age and CDRF status[21].

We chose COVID-19-related hospitalisation as our outcome because hospitalisation is both serious for patients and costly to societ;y there are also fewer threats to the validity of these data than case counts/incidence rates in settings with incomplete and rapidly changing testing regimens –as is typical of many COVID-19-affected countries to date. The US COVID-19 admission rate data were collected from the large COVIDNET hospital network, with statistically stable admission rates through to April 25th. Since only relative risks will be used, these absolute population-based admission rates need not be generalisable beyond that US setting; they just need to be based on consistent admitting practices over time, by age group and risk-factor status, which is more credible inside a single set of hospitals so early in the pandemic in the USA. It is appreciated that some features of the US pandemic during this period were different from those that pertain to the subsequent few months' situation in the UK/Scotland. However, we believe that the probable continuing low cumulative incidence of COVID-19 infections in the UK (very few antibody-survey estimates have been above 10% of the general national population, through to early May[22, 23]) means that options for exiting lockdown at that time in the UK were likely to carry similar relative risks, by age and CDRF-status, to the remarkably stable age-specific admission rates over time seen in the USA COVIDNET network through to mid-April. This is especially credible because that was during a period when suitable hospital beds in most of that country were not yet filled with cases, and strong lockdown measures were not yet in place (only 32 states had even started lockdown by the end of March).[24]

Scenario A – Age-based restrictions (Table 1)
The first step in calculating PAR based solely on age is to calculate the age-specific relative risks (RR) of COVID-19 hospitalisation. These relative risks based on the COVIDNET data are shown in Table 1 (Step 1) alongside the absolute hospitalisation rates from which they were calculated.[20] Next, we tabulate the proportion of the general population (Scotland, 2011 census) in each of the age groups: p (Step 2).[18] Finally, we use the figures from the first two steps to calculate the PARs for each of the three age-groups' using the equation given above (Step 3). The resulting PARs are the proportion of hospitalisation of people aged 50-64 or over 65 years out of the total number of hospitalisations. Therefore, the PARs give an indication of the potential reduction in COVID-19 hospitalisation from of continuing lockdown for: i) those over 50; ii) those over 65. These results can be interpreted as indicating that continuing effective lockdown for only those age 65+ would theoretically reduce the total adult COVID-19 hospitalisations by 50.6% and affect the quality of life of about one in five of the Scottish population, the vast majority of whom are retired. Continuing lockdown for those over 50, on the other hand, while massively reducing adult hospitalisations by (30.6+50.6)=81.2%, would interfere with the lives of (21.0%+19.4%) = 40.4% of the entire Scottish population, of whom more than half are below age 65, with potentially significant economic effects.

Scenario B – Age- and co-morbidity-based restrictions (Table 2)
In this scenario we are estimating the population risk attributable to the combination of two risk factors; age and health, represented by the presence of one or more CDRFs. The American Geriatrics Society (AGS) has explicitly called for comorbidities to be considered in policy decision, avoiding solely age-based criteria.[25] Subsequently, the steps are slightly different. First, we estimate the relative risk (RR) of COVID-19 admission for persons with one or more CDRF, compared to the healthy population, within

each of the three age groups (Table 2, Step 1). A rapid way to approximate these RRs is to perform a case-control analysis based on CDC Atlanta's summary of the proportion of a large series of COVID-NET hospitalisations[21], in all of March 2020, who have at least one CDRF, compared to "controls" of the same age-group in the general population (from Scottish Health Survey[19]); to reduce confounding by age, use age-stratification. Note the paradoxical non-linearity of the relationship between RR and age, indicating a strong effect of co-morbidity in the youngest age-group, and also in the elderly – effectively an interaction effect. Next, we tabulate the proportion (p) of each of each adult Scottish age-group who have at least one of the following CDRFs: heart disease; COPD or asthma; diabetes; obesity; hypertension (Step 2). Some interpolation is required since the Scottish Health Survey[19] reports prevalence separately for these common (self-reported) chronic conditions. To prevent double-counting of persons with more than one condition, the estimates in Table 2 are totals of: the full age-specific prevalence of "any CVD/diabetes" added to half of each of the age-specific prevalences of the other three conditions. Better estimates can be readily derived from co-morbidity studies in primary care. As in scenario A we then calculate the analogous PARs for each of the three age-specific sub-populations' members with at least one CDRF (Step 3), modelling a policy of continuing lockdown only for that high-risk group of adults, across the three age-strata, compared to no restrictions for that sub-population. The PARs calculated in Step 3 are the proportion of admissions in each age group attributable to having one or more CDRF. Therefore, to estimate the overall population impact we need weight the PARs by the proportion of admissions from each age group. This forth step is achieved by weighting these PARs across the three age-strata, by the proportion of US COVID-NET adult admissions[20, 21] in each age group (cf. Step 3), giving the overall PARs shown in Table 2.

This analysis of scenario B tells us that restricting the activities of persons with at least one CDRF, in all three adult age-groups, should reduce the overall COVID-19 hospitalisation rate by over three-quarters (compared to no relaxation of any restrictions for any adults), but at a very high "cost" of interfering in the lives of about 30% of 20-to-49-year-olds (a very large group, demographically speaking), 55% of 50-to-64-year olds, and 64% of those age 65+ (cf. Step 4 above) – with the added concern that the two younger age groups are typically active in the labour market. Alternatively, by restricting the activity of those with CDRFs over 50, we could expect to reduce the hospitalisation rate by 57% (20.7% +36.3%), by interfering in the lives of the same proportions – 55% and 64% -- of those 50-64 and 65+ years of age, respectively. Since these persons are typically already aware of their CDRF status, their willingness to continue lockdown may be higher than for restrictions based on age alone, in order to minimise the personal risk based on their medical conditions.

Conclusion

As shown in Table 3, all five policy options are less than ideal, with only two carrying reasonable benefits, in terms of substantially reduced COVID-19 hospitalisations, without removing large numbers of people from the labour force: policies #2 and #4. There is not much to choose – in terms of epidemiologically estimated reductions in COVID-19 hospitalisations -- between restricting the activities of all persons over age 65, compared to restricting all persons over age 50 with CDRFs. However, the economic effects of the former policy would be much less than those of the latter, since the latter would affect a significant proportion of the active labour force; advocates for the elderly, on the other hand, are likely to be concerned about the "discriminatory nature" of purely age-based restrictions.[25] Policy options #1 and #3 would prevent a substantially larger proportion of future COVID-19 admissions – but only by continuing to lockdown much larger numbers of adults – almost half the entire adult population in the case of policy option #3, including many younger and middle-aged adults in the active labour force.

We recognise that there are multiple other factors that governments need to consider, when assessing the options for easing the lockdown, including indirect effects on transmission dynamics, and the varying likelihoods of being able to work from home in these different sub-populations. Yet, using only publicly available data it is possible through calculating Population Attributable Risk to gain an insight into the trade-off between protecting the public and maintaining the economy. Furthermore, compared to the mathematical models being used to model the pandemic, the arithmetic necessary to calculate Population Attributable Risk can be quickly carried out using any computer or calculator. Therefore, we believe that Population Attributable Risk is a relatively simple and transparent tool that can be used to provide useful data to quickly and easily compare the potential benefits, and crude societal "costs" (adverse consequences) of various exit policy options from the COVID-19 lockdown.

Table 1 – Calculating the population attributable risk related to age-based restrictions

	Step 1: Calculate RR		Step 2: Calculate p	Step 3: Calculate PAR
Adult age groups	Absolute Hospitalisation Rate (per 100,000)[4]	Relative risk	Percent of Scottish Population in 2020[2]	Population Attributable Risk
20*-49	22.6	1 (reference)	38.8%	Reference group (lowest adult admission rate)
50-64	69.3	3.1	21.0%	30.6%
65+	142.7	6.3	19.4%	50.6%

* Note that the COVIDNET tabulation of cumulative hospitalisation rates (per 100,000 population) for the youngest adult age group includes 18 and 19 year-olds, whereas all the other statistics used here include only those 20+ years of age; we have ignored this discrepancy, noting that COVID-19 hospitalisation rates at ages 18 and 19 are trivially small.

Table 2 – Calculating the population attributable risk related to age- and condition-based restrictions

	Step 1 – Calculate Odds Ratios as an approximation of RR			Step 2 – Calculate p	Step 3 – Calculate PAR	Step 4 – Weight the PARs relative to the whole population	
Adult age groups	Proportion of admissions[4,5]		Odds ratio	Percent of Scottish Population in 2011 with any CDRF[3]	Population Attributable Risk	Proportion of US Adult hospitalisations[4,5]	Weighted PAR
	Cases with 1+ CDRF	Controls with 0 CDRF					
20-49	85%	30%	13.2	30%	78.5%	24.9%	19.7%
50-64	85%	55%	4.6	55%	66.4%	31.3%	20.7%
65+	94%	64%	8.8	64%	83.3%	43.7%	36.3%
All 20+	90%	45%	11.0	45%	81.8%	100.0%	76.7%

Table 3 – Summary of the potential benefits (reduced COVID-19 hospitalisations) compared to the proportion of the population required to maintain lockdown for the policy options examined

Policy Scenario	Proportion of adult hospitalisations reduced	Proportion of adult population affected
A. Age-based		
1. Restrict all persons over age 50	81%	40%
2. Restrict only persons over age 65	51%	19%
B. Age- and co-Morbidity-Based		
3. Restrict adults of all ages with CDRFs	77%	45%
4. Restrict all those with CDRFs over age 50	57%	21%*
5. Restrict all those with CRDFs over age 65	36%	11%*

*These are the age-group-specific prevalences of one or more CDRFs in the most recent Scottish Health Survey, calculated as population-weight weighted averages of the prevalences in narrower age-bands

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