Covid-19 lockdown policies: An interdisciplinary review

Dr Oliver C. Robinson
Associate Professor of Psychology
School of Human Sciences
University of Greenwich
London
SE10 9LS
Email: o.c.robinson@gre.ac.uk

Abstract

Lockdown interventions employed in response to the COVID-19 pandemic as part of a suppression strategy have been evaluated via research at biomedical, economic, and psychological levels of analysis. The aim of this article is to integrate these perspectives into an interdisciplinary biopsychosocial review. Biomedical evidence from the early months of the pandemic suggests that lockdowns were associated with a reduced viral reproductive rate, but also that less restrictive measures had a similar effect. Lockdowns were not associated with reduced mortality in any studies apart from modelling studies. Psychological research supports the proposition that lengthy lockdowns may exacerbate stressors such as social isolation that have been shown to be strong predictors of falling ill if exposed to a respiratory virus. Research at the socioeconomic level of analysis points to the possibility that deaths associated with economic harms may outweigh the deaths that lockdowns save, and that the extremely high financial cost of lockdowns may have negative implications for overall population health in terms of diminished resources for other health issues. Suggestions for future research are provided to promote an increasingly fine-grained and nuanced evaluation of these policies.

Keywords: Covid-19, lockdown, health policy, non-pharmaceutical interventions, health policy, stress, interdisciplinary

INTRODUCTION

The Covid-19 pandemic has brought about a dilemma for governments across the world: whether to enforce lockdown interventions to reduce the spread of the virus, in the knowledge that such policies contain the potential for harms as well as benefits.[12] The aim of this paper is to present a biopsychosocial analysis of lockdown measures, via a review of the biomedical, psychological and socioeconomic arguments for and against them.

Lockdown measures are interventions enacted by governments in response to a pandemic that have all of the following three features, according to the OECD:[3] (a) legally enforced mandatory restrictions on individual movement and social interaction imposed on all people living within a region, state or nation (b) the forced temporary closure of businesses, schools and hospitality venues within that same region, state or nation, and (c) legal statutes to ensure that violation of these restrictions is a criminal offence.

Within these common parameters, lockdown interventions show considerable variety.[4] They vary in duration, relation to the timeframe of a pandemic, severity of measures imposed, and penalties applied for not complying with measures. Where lockdowns are not imposed, a diverse range of other non-pharmaceutical interventions are available, for example temporary border closures, banning large gatherings, quarantining of cases, shielding the vulnerable, test-and-trace systems, mask mandates and public transport restrictions.[5] As examples of government responses that do not qualify as lockdowns, Norway and Finland implemented restrictive measures early in the pandemic such as school closures, limits on the size of gatherings and guidance to work from home, but there were no stay-at-home orders or restrictions on household mixing in these two countries.

A common portrayal of the lockdown debate is of the sceptic versus the advocate, however many health professionals have taken moderate positions in between these two sides, for example a group of 77 health professionals in the UK wrote an open letter to the

British government in September 2020 stating they although they supported the March-June lockdown, they would not support lockdown measures applied from September onwards due to the increasing risk of collateral harm attached to lengthy lockdowns.[6]

An important distinction in relation to lockdown interventions is between suppression strategies and elimination strategies.[7] Of the 180+ countries that have reported Covid-19 cases, as of January 2021, four are currently pursuing an elimination strategy. These are China, Taiwan, Australia and New Zealand. In these countries, the aim is to maintain cases of Covid-19 close to zero. The fundamentals of this approach are: (1) complete border closures to foreign nationals until herd immunity is achieved via vaccination, (2) strict quarantine for nationals returning from overseas, (3) highly developed test-and-trace systems, and (4) strict local lockdowns to contain outbreaks to contain it. In China, another mechanism at the centre of their elimination approach is mass surveillance via a governmental tracking app.[8] It is expected that the borders of these four countries may remain closed until 2022, with possible exceptions of travel corridors between the countries.[9]

An elimination strategy requires a highly developed public health system and IT infrastructure for a test-and-trace system (including most adults owning smartphones), sufficient affluence to afford the absence of tourist and business travel for up to two years, and the capacity to totally close borders. Three of the four countries taking an elimination approach are island nations with no land borders, and China, the exception to this, is using military force to maintain fully closed land borders.

The elimination strategy is not an option for emerging economies that neither have the infrastructure for such a policy nor the economic resilience to afford a full border closure for up to several years. It is also problematic for many wealthy countries for a variety of reasons. For European Union countries, closing themselves from the rest of the EU for several years is not viable given that the EU is premised on freedom of movement between member

countries. In the UK, closing the border between Northern Ireland and Ireland for a matter of years is not possible given the Good Friday Agreement. In the USA, states rather than the federal government set Covid-19 policy and there is no way of closing a state off from the rest of the USA. In sum, the elimination strategy remains an option for only a select number of countries.

The potential costs of the elimination approach will only be known after the pandemic is over.[10] Elimination can only be temporary and thus, at some point after mass vaccination, the countries who have pursed the strategy will need to open up and allow the virus to circulate. At that point, they will find out if the vaccine is sufficient for population immunity. Crucially, an elimination strategy *requires* local lockdowns to contain outbreaks. It cannot work without them. Suppression strategies, in which the virus is allowed to circulate but government measures are taken to manage and slow it, do not inherently require lockdowns. Some countries and states that are employing suppression strategies have implemented lockdowns during the Covid-19 pandemic, but others, such as South Korea, Belarus and Tanzania, have implemented a range of other less restrictive interventions instead.

The review of the evidence presented below pertains to countries and states employing suppression strategies. I consider the issue from three analytical levels: biomedical, economic and psychological. All these levels are crucial to informing a considered conclusion about whether lockdowns, in the context of suppression strategies, are efficacious and appropriate responses to the Covid-19 pandemic.

THE BIOMEDICAL LEVEL OF ANALYSIS

Research on lockdowns at the biomedical level of analysis focuses on the relationship between governmental pandemic interventions and numbers of positive tests, case reproduction number, and mortality. The principle argument for enacting lockdowns at this level of analysis is that they temporarily reduce hospital admissions and deaths, via reducing

the transmission of viruses between individuals for the period over which the intervention is applied. There is a fast-growing body of evidence that can be used to evaluate whether lockdowns achieve this objective.

Cross-country research on cases and reproduction number

Haug et al. used data on government interventions and Covid-19 cases in 79 countries from March and April 2020 to run an analysis of the relationship between different government interventions and growth in cases over time.[11] It was found that the most effective method for reducing the rate of growth in cases was small gathering cancellation, followed by school closures and border restrictions. They found that lockdowns do reduce the rate of case growth, but, like the aforementioned OECD study, they conclude that "a suitable combination (sequence and time of implementation) of a smaller package of such measures can substitute for a full lockdown in terms of effectiveness, while reducing adverse impacts on society, the economy, the humanitarian response system and the environment."[12]

Brauner et al. analysed effects of seven interventions (gatherings limited to 1000 people or less, gatherings limited to 100 people or less, gatherings limited to 10 people or less, some businesses closed, non-essential businesses closed, educational establishments closed, and stay-at-home orders) between 22nd of January and the 30th of May 2020, across 34 European countries and 7 non-European countries.[13] They found that closing educational institutions, limiting gatherings to 10 people or less, and closing face-to-face businesses reduced transmission considerably. However, they found that stay-at-home orders had a lower association with reproductive rate than the other measures.

Bendavid et al. studied COVID-19 case growth over time in subnational regions of 12 Northern Hemisphere countries between February and April: England, France, Germany, Iran, Italy, Netherlands, Spain, South Korea, Sweden, the US, Sweden and South Korea.[14]

They found that implementing non-pharmaceutic interventions was associated with significant reductions in case growth in 9 out of 10 study countries, including South Korea and Sweden (only Spain had a non-significant effect). The study found no benefit of restrictive lockdown interventions compared with the less restrictive interventions applied in Sweden and South Korea. In France, the application of lockdown was associated with higher levels of case growth rates compared with Sweden and South Korea. The study concludes that less restrictive measures generally lead to the same case growth rates as lockdowns.

Li et al. studied data from 131 countries up to June and found that a decreasing case growth rate over a period of 28 days was associated after school closures, workplace closures, banning public events and a regulation to stay at home where possible.[15] The study also found that while introducing restrictions generally led to a reduction in case growth of 3-24% after 28 days, lifting them led to increases of 11-25%.

An OECD study based on data from 130 countries from January to August found that lockdown interventions do bring the reproduction rate of a virus down.[16] They also found that measures that are less economically destructive were as effective. For example, a combination of restricting visits to care homes, a test-and-trace system, testing in care homes, recommendations for elderly to stay at home and mandatory mask wearing together drive the reproduction rate down more than a lockdown policy.

In summary, the evidence from cross-country and cross-state comparison studies is that lockdowns contribute to lowering the reproduction rate of the virus. However, the studies that have directly compared interventions have found that more moderate policies such as small gathering cancellation may be more effective than blanket lockdowns. Such evidence is further supported by within-country analyses that have looked at changes following interventions, such as an analysis of German interventions that found that banning small

gatherings was particularly effective, and that a combination of interventions in April 2020 helped to reduce the *R* rate.[17]

Cross-country research on mortality

Further research has looked at lockdowns and mortality by comparing interventions across countries. Firstly, Chaudhry et al. compared Covid-19 case numbers and mortality data across 50 countries, based on data up to 1st May 2020. They found that in these early months of the pandemic, mortality rates were associated with higher obesity, higher GDP-per-capita, and higher income inequality, but there was no association found between mortality and lockdown measures.[18]

Secondly, De Larochelambert et al., using data up to August 31st 2020 from 188 countries, found that high Covid-19 mortality was predicted by a country having higher life-expectancy, higher prevalence of chronic diseases such as cancer and heart disease, along with a high level of metabolic risk factors such as an inactive lifestyle and obesity. The stringency of government lockdown response was not associated with mortality.[19]

Thirdly, Meo et al. (2020) compared lockdown measures across 27 randomly selected countries. Prevalence and mortality were measured 15 days before, 15 days during, and 15 days after the lockdown. There was no significant decline found in prevalence or mortality at the 15 day after measurement, when compared with 15 days before or 15 days during the lockdown.[20]

In contrast, Sornette et al. analysed data from 35 countries (European and North American) found an association between the number of deaths during the 20 days following the date at which cases passed 1 death per million within a country, and the stringency of government measures 20 days before that date (to allow for the delay between infection and death).[21] Almost all the countries on the intervention census date were still in February or the first half of March and so had not yet implemented a lockdown. For example, Italy had the

earliest lockdown after China on March 9th, but this study looked at interventions being taken on March 2nd, while Ireland implemented its first lockdown on March 27th and this study looked at measures it was taking on March 22nd. Thus, this analysis is principally about the effect of interventions enacted very early in the pandemic prior to lockdowns, so can't be taken as reliable evidence in relation to lockdown policies.

In summary, a provisional conclusion from this small number of cross-country studies on government interventions mortality is that there is no association between severity of government response and Covid-19 deaths after the introduction of lockdowns.

A caution with all the above research is that the studies are based on correlational associations, and there are a range of extraneous variables that can influence how a country or state fares in terms of case and mortality numbers, including the way that such data are reported. For example, Covid-19 deaths are not defined in the same way across all countries.[22] Many of the studies described above do attempt to control for confounding variables, for example obesity and climate, but that does not preclude the possibility of others. Thus, the literature should, despite becoming increasingly consistent and clear, be treated with continued caution.

Computer modelling research

A different approach to analysing the effect of government interventions is via computer simulation of the no-intervention scenario. Flaxman et al. used this approach, looking at deaths attributable to Covid-19 across 11 European countries between February and early May.[23] They modelled the combined effect of social distancing, self-isolation of infected individuals, banning of public events, school closure and stay-at-home orders, therefore the model was not specific to lockdown. The researchers compared the actual mortality in these countries over February-May with a computer simulation of the scenario where no actions

had been taken at all. Based on that, the article concluded that the interventions taken by these nations may have reduced Covid-19 deaths by 3 million.

Several commentaries have been critical of Flaxman's study. Soltesz et al. take issue with Flaxman et al. using their findings to argue that lockdown is effective, as according to the same modelling approach, the public events ban in Sweden was as effective as lockdowns in 10 other countries at driving down infection rates.[24] Kuhbandner and Homburg in a commentary on the article presented evidence that the lockdown in the UK (one of the countries in Flaxman et al.'s study) had no effect on deaths, given the established 23-day delay from infection to death.[25] They show that growth was already declining by the time the lockdown would have influenced death rates and there was no shift at all in the downward trajectory of deaths when the lockdown would have potentially come into an effect.

An epidemiological simulation study by Hsiang et al. modelled changes in case numbers over time between February and May 2020 across six countries (China, South Korea, Iran, Italy, France and the USA) and concluded that, when compared with the computer scenario of no interventions taken, government containment interventions as a whole had reduced the growth rate of infections by a substantial and statistically significant amount.[26]

A potential limitation of all the aforementioned computer modelling studies is that they assume a continued exponential rise of the virus in the absence of interventions until all individuals are infected, but research has shown that virus case growth does not continue on a path of exponential growth; infection rates slow and decline of their own accord without any government intervention over a period of approximately 8 weeks.[27] This hypothesis was put to the test when South Dakota had a high surge of Covid-19 infections in October 2020 and subsequently implemented no lockdown or business closures. The surge peaked in mid-October and cases returned close to pre-surge levels in December, suggesting that 2 months is

an appropriate estimate of the timeframe for a virus surge to decline without the use of restrictive interventions. This fact that there is natural remission from exponential growth without intervention means that the computer simulations of deaths in the no policy scenario were likely overestimations.

In summary, the computer modelling research on combined government interventions has modelled the effect of all public health interventions versus a hypothetical scenario of no interventions taken at all, and has concluded that the interventions have been instrumental in slowing the growth of the pandemic over the early months of February to May. What they do not show is the relative merits of lockdowns versus other measures. These models have also been based on parameters about virus growth, population susceptibility and lockdown effectiveness that have been questioned by critics. The models have also assumed that lowering infection rates also lowers deaths in proportion. However, the cross-country studies suggest that this assumption is problematic. This may be because the collateral damages of lockdowns mean that while case numbers are lowered, susceptibility to serious illness and death is increased through the adoption of lockdown policies. This claim is substantiated further in the subsequent sections on economic and psychological effects.

The biomedical costs of lockdown

A limitation with all the research studies discussed above is that they give no or minimal attention to the negative effects of lockdown.[28] This is equivalent to assessing the efficacy of a drug that has potentially deadly side-effects without any mention of the side-effects.

A key concern about lockdown policies, particularly stay-at-home policies, is that they lead to a decline in uptake of other important health services. For example, lockdown in the UK led to a 70% decline in cancer referrals.[29] The drop in cancer diagnosis and treatment has led some cancer specialists to suggest that a cancer pandemic may follow the Covid-19

pandemic.[30] An analysis of excess deaths in the UK from delay in cancer treatment during the March-June lockdown suggests that from breast cancer, lung cancer, colorectal cancer, and oesophageal cancer, over a period of 5 years following the pandemic there will be approximately 3300 to 3600 additional deaths. In light of the young age of many of these individuals, the total years lost to life from this cancer surge is calculated at approximately 59,000–63,000.[31]

Another issue in terms of negative effects of extended lockdowns on physical health is the drop in exercise and activity that is evidenced in a proportion of the population.[32] Exercise has been shown to enhance immunity to disease, so when a higher proportion of the population become inactive during lockdown, it is plausible that more individuals will become susceptible to illness when exposed to Covid-19.[33]

The challenge with interpreting reduced uptake of other health services and reduced exercise during lockdowns is that the extent of such reduction in the event of no lockdown is unclear. People are likely to avoid medical appointments and going to exercise locations due to fear of a pandemic virus anyway, irrespective of lockdown injunctions. Future country comparison research on this will help to resolve this question, but until then the matter remains ambiguous.

THE PSYCHOLOGICAL LEVEL OF ANALYSIS

The psychological level of analysis considers the effects of lockdowns on thinking, emotion and behaviour, along with how these may have impacts on health outcomes. This level of understanding, so often omitted from media coverage, may be key to understanding the reasons why lockdowns do not have notable efficacy over more moderate or voluntary measures.

The first psychological argument in favour of lockdown measures is that they are what most people want, hence they have a democratic mandate. Polls in the UK showing high support for lockdown attest to this.[34,35] The psychologist Erich Fromm theorised that when people perceive an increase in disorder and danger within their community or environment, they feel an existential anxiety that breeds a desire for safety and security via paternalistic and authoritarian forms of governance.[36] A similar hypothesis has more recently been presented from studies that have found disease prevalence predicts authoritarian governance and authoritarian attitudes across countries.[37]

An example of this link between the pandemic and the popularity of authoritarianism was evidenced in the German state of Bavaria. Markus Söder, Minister President of Bavaria, implemented more draconian restrictions than other German states, such as a stay-at-home order and fines of up to €25,000 for non-compliance.[38] Söder was explicit about this approach being paternalistic – he said that "in a crisis, people often want Father to come and sort it out."[39] Söder's popularity increased exponentially as a result of his firm approach in the early months of the pandemic, far more so than other leaders in Germany.[40] However, the strict measures applied in Bavaria appear to have been less effective than the more moderate measures taken in other states; Bavaria has had the second highest Covid-19 mortality per capita of 16 German states, by the end of 2020. It has over double the mortality rate of seven of these states.

Another psychological argument presented to support lockdown is that lockdowns reduce the amount of post-traumatic stress disorder associated with bereavement and illness. For example, the UK government has justified its tiered system of mandatory enforcements by arguing that it is likely to lessen the burden from post-traumatic stress disorder, by limiting the number of those infected and who go on to suffer from severe illness.[41] The assumption here is that lockdown measures reduce symptomatic infection more than lighter

non-pharmaceutical measures. Research does not provide clear support for this assumption currently.

Contrary to the claims of the UK government that lockdowns reduce anxiety, researchers have found that anxiety and depression both increase with the duration of lockdowns and that lockdowns are a serious threat to mental health.[42] Research from China also found that anxiety levels in a population reduce from 30% to 21% when lockdowns are eased.[43] A further study using data from China in February and March found that depression was significantly higher in the lockdown group but fear was not.[44] In support of this, previous research on the effects of quarantines in prior pandemics suggest that they are related to depression that extended over a period of 3 years.[45]

Loneliness, stress and lockdown

Stay-at-home orders and rules precluding mixing with other households can lead to social isolation and loneliness, particularly in those living alone. Statistics from the UK suggest that loneliness may be a silent epidemic running alongside the pandemic.[46] Research on a US sample found that up to April there was little by way of an increase in loneliness.[47] But as 2020 progressed, the statistics have got worse. A more recent survey published in December found that a shocking 65% of US adults living under lockdown measures expressed high levels of loneliness, compared with 48% of those living without such restrictions.[48] A study from the UK found that loneliness rates in the UK increased from 10% before lockdown to 24% in lockdown.[49] More recently, an analysis of UK data from the Office of National Statistics determined that 9 million people may be suffering from loneliness now, after multiple lockdowns and further restrictions on household mixing outside of lockdown periods.[50]

In the UK, some parts of the country have been under policies that ban almost all social interaction with people outside of one's own household for over four months in total since the start of the pandemic. Corresponding to this, a recent report from the Office of National Statistics suggests that loneliness levels in the UK continued to rise all the way from March to the most recent data collected in November.[51]

A meta-analysis of studies found that social isolation, measured objectively or subjectively, increases the risk of premature death.[52] After accounting for covariates, the increased risk of death was 26% for reported loneliness, 29% for social isolation, and 32% for living alone. Other studies have found that increasing the amount of social activity experienced by individuals in nursing homes predicts a decrease in mortality.[53]

One reason that loneliness and social isolation elevate the risk of mortality is that they precipitate an endocrine stress response that impairs immune functioning and thus makes people more susceptible to disease.[54] For example, one study found that loneliness is associated with poorer antibody responses to the flu virus.[55] Similarly, Cole et al. found that in isolated or lonely participants, leukocytes showed an increased expression of genes involved in inflammation and a decreased expression of genes involved in antiviral responses.[56]

A series of experiments have been conducted by Cohen investigating the link between psychosocial factors and immune function, which are potentially relevant in regard to lockdown loneliness, unemployment and Covid-19.[57] Since the 1980s, Cohen and colleagues have studied the effects of psychosocial factors on immunity via an experimental design in which participants are exposed to a respiratory virus by nasal spray (either flu virus, coronavirus 229E or rhinovirus Types 2, 9, and 14) and then are observed for a number of days in quarantine. On average, 25% to 40% developed symptoms of the respiratory disease after exposure. Pertinently, this is a similar rate to the percentage of individuals who test

positive for Covid-19 who show symptoms.[58] Among the strongest factors that predicted showing illness in Cohen's studies after viral exposure is psychological stress. The stressful events that are most predictive of showing symptoms are chronic stressors lasting more than a month, such as loneliness and being unemployed. In a recent review of this research in relation to Covid-19, Cohen tentatively concludes that government interventions that increase social isolation and unemployment may be magnifying factors that increase susceptibility to respiratory illness.

Further negative effects of loneliness and social isolation are their impairment of restorative sleep, which leads to greater susceptibility to disease.[59] Added to this, loneliness brings about a higher risk of suicide, adding to the elevated mortality risk associated with the mass isolation that lockdown policies bring.[60]

A marker of those who develop severe symptoms of the Covid-19 disease is impaired immune functioning, specifically interferon deficiency in the blood.[61] Given that loneliness and social isolation are scientifically recognised to be as dangerous as smoking when it comes to risk of premature death, extended lockdown policies that prohibit face-to-face social interaction over many months may increase risk of mortality due to immunosuppressive effects, particularly in vulnerable populations who lack social support.[62]

As well as potentially impairing immune functioning, the loneliness and social isolation induced by lengthy lockdowns may influence behaviour after restrictions are lifted in ways that undermine any benefits gained during lockdown. There is research to suggest that people respond to the lifting of lockdowns by increasing the amount of social contact to an unusually high level, in ways that not only cancel out the benefits of lockdown but actually make the situation worse than before the lockdown. For example, the aforementioned analysis of introducing and lifting restrictions across multiple countries by Li et al. found that introducing restrictions led to a reduction in case growth of 3-24% after 28 days, while lifting

them led to increases of 11-25%.[63] In sum, after a temporary restriction of social activity is lifted, growth rates may tend to increase to a higher level than they were before the lockdown.

There may also be a further reason for irresponsible behaviour observed after lockdowns are lifted. Lockdowns work on the basis that a *pre-conventional morality*, based on the threat of punishment, must be used to enforce correct behaviour during a pandemic. Pre-conventional morality is that which is typically shown in young children; moral guidance is dictated externally by parents, guardians or teachers, and is enforced through rewards and punishments.[64] Young children's behaviour is managed in this way because they have not developed an internalised ethic of civic responsibility, which is the foundation of conventional morality.[65] To apply a pre-conventional approach to managing the pandemic therefore equates to treating adults like children. The danger of such an approach is that by engendering a parent-child arrangement of external controls and punishments, lockdowns may actively undermine the tendency of people to behave like adults and to use their own good sense.[66]

The idea that informed consent and personal responsibility should normally be at the centre of healthcare is coded in medicine as the ethic of *autonomy*.[67] The premise of upholding this ethic is that it leads to better health outcomes over the long term, despite the fact that some individuals may refuse treatment and so be harmed or die as a result of this.[68] Despite this, Western medicine is founded on the premise that giving mentally competent adults the right to refuse treatment is worth that risk.[69]

This same approach is generally taken to public health policy too. Drinking alcohol is a pertinent example: It leads to a considerable burden of illness – the World Health Organisation estimates 3 million people die every year around the world as a result of the harmful use of alcohol, so greater than the Covid-19 death toll for 2020.[70] There is no doubt

that legal prohibition of alcohol beverages brings lower numbers of alcohol-related illness, for example in Saudi Arabia where alcohol is banned, alcohol-related deaths are close to zero.[71] Yet democratic societies continue to allow people to have the choice. This is part of a general commitment to the benefits of informed choice and the long-term benefits this brings.

However, autonomy and freedom are not absolute; all modern liberal democracies combine autonomy and freedom of choice with some degree of paternalism.[72] For example, alcohol and cigarettes are allowed, but most countries ban other drugs. Freedom of speech is allowed, but defamation and slander laws put boundaries around this. Driving cars is allowed despite the high risk of harm, but seatbelts are legally obligated and drink-driving is banned. In this vein, politicians and citizens alike must evaluate how much paternalism they consider to be acceptable in the name of saving lives during a pandemic and must ensure that the general population are confident that such restrictions are temporary.[73]

THE SOCIOECONOMIC LEVEL OF ANALYSIS

Financial resources for funding medical treatments and interventions are finite. Trade-offs must be made, as money used to fight one disease means funds being unavailable to treat or prevent others.[74] A concept that is used by many countries to justify whether a treatment or intervention is worth the cost, in an environment of finite resources, is the "Quality adjusted year of life" or QALY.[75,76] One quality-adjusted life year (QALY) is one year of life in good health. Hence, when a young person dies, there is a greater loss of QALYs than when an older person dies. In the UK, the National Institute for Clinical Excellence has a metric to determine whether a treatment is cost-effective and thus should be adopted (i.e. that money is not better spent to save lives and alleviate suffering elsewhere). This metric is £20,000 to £30,000 per QALY saved.[77] Other countries set the bar at different levels, but all health services require some quantification in this regard to facilitate distribution of resources.

Miles et al. conducted an economic analysis of the costs and benefits of the March-June lockdown in the UK.[78] They analysed the potential lives saved by the March-June lockdown, on the premise that lockdowns do indeed save lives, then considered the costs of the lockdown in terms of reduced GDP. They found that in all their various calculations, the costs outweigh the benefits by at least £59 billion (2 million QALYs), and up to £547 billion (approx. 20 million QALYs). The authors conclude: "This suggests that the costs of continuing severe restrictions are so great relative to likely benefits in lives saved that a rapid easing in restrictions is now warranted."[79]

One other cost-benefit analysis conducted by Israeli researchers found that a lockdown for 200 days would cost $45,000,000 per saved death, hence that governments should consider this very high economic price when deciding on how long to implement national lockdown interventions for, given the inevitable toll on other public services and health services that are affected by reduced funds available.[80]

A multi-faceted analysis of the economic and ethical implications of measures taken by governments conducted by Reddy expresses concerns that the expenditure and resources invested in lockdowns and other non-pharmaceutical interventions are not proportionate and will, overall, decrease the aggregate population health over time.[81] For example, he makes the point that a 4.9% reduction in world GDP is predicted this year as a result of lockdowns, which is approximately US$4 trillion. If a world GPD growth of 2% is assumed as the counterfactual for 2020 (lower than recent years), then the cost of non-pharmaceutical interventions taken to combat Covid-19 would exceed US$5 trillion, which is greater than the total global annual expenditure on all other health issues prior to the crisis.

Reddy argues serious questions must be raised regarding whether lockdowns will, in fact, lower, rather than increase, overall population health over time, due to other health objectives that have lower cost and higher benefit being deprioritised. Consider the following

figures as an example: The UK has spent £280 billion on fighting Covid-19, which is considerably higher than the total spending on health and social care in a typical year in the UK, while $2.6 trillion has been spent in response to Covid-19 in the USA. Meanwhile, it has been estimated that global eradication of malaria by the year 2040 would cost approximately $120 billion. Such an initiative would potentially save 11 million lives.[82]

Another form of economic cost-benefit analysis conducted by Thomas has focused on the effect of lockdowns on decreased GDP and hence on mortality in the UK.[83,84,85] The methodology used was based on a calculation called the J-value, which considers the trade-off between safety-increasing effects and loss of income due to the costs of implementation. The essence of this approach to look at the change to years of life expectancy that a particular safety intervention brings, similar to the use of QALYs in healthcare economics. In relation to Covid-19 lockdowns, the cost is modelled as the effect on GDP. GDP is a very strong predictor of life expectancy; Thomas' J-value, based on GDP, explains 80 per cent of the variation in life expectancy across 162 nations.[86] In other words, on average, the wealthier a country is, the longer its people live.

Thomas estimated a 13% reduction in GDP for the UK over 2020 and assumed, based on previous recessions, that the country does not return to pre-pandemic levels until 2022. Both estimates appears to be accurate; in November, Reuters estimated a GDP contraction of 11.3% in 2020 (given the subsequent lockdown the contraction will be greater) and a partial recovery of 5.5% in 2021.[87] The increased impoverishment that this economic shrinkage causes will lead to the loss of 34.9 million years of life expectancy, which is the equivalent loss of 830,000 lives, given the life expectancy of the average UK citizen.[88] Even in a scenario in which the pandemic is not controlled by any lockdown, the number of lives lost to the pandemic is calculated as only a small fraction of the total lost to economic decline and

increased poverty that an extended lockdown would subsequently bring.[89] Thomas thus concludes that lockdowns are remedies that may well have costs that outweigh benefits.

A criticism of this cost-benefit approach is that GDP will be depressed in a pandemic anyway, so it is uncertain how much of the loss of GDP is down to the lockdown. Sweden, with no lockdowns implemented, is a useful comparison in this regard; its economy is predicted to shrink by 2.9% during 2020, which is one of the lowest GDP declines in Europe despite mortality rates that are about average across European states.[90] Therefore, there is growing evidence that lockdowns and forced business closures contribute to the majority of GDP loss during the pandemic.

A further key issue at the economic level of analysis pertains to the number of individuals being pushed into poverty and/or unemployment during the pandemic. The World Bank has estimated that 150 million people may be pushed into extreme poverty during the pandemic.[91] The Charity UNICEF have explicitly linked this increase in poverty to the negative effects of lockdown policies,[92] as have other researchers.[93] Peru is a case study in this regard. It implemented one of the toughest and earliest lockdowns in the world.[94] Despite the severe lockdown, as of December 2020 Peru had the fifth worst fatality rate in the world out of 218 countries.[95] Most people in Peru are in the informal economy and work in agriculture, mining and fishing. Most are paid in cash and have little or no savings, meaning that Peruvians need money weekly to feed their family.[96] Therefore, for some it may have been a matter of stay in lockdown and starve, or break lockdown to feed your family.[97] The potential for poverty, stress and malnutrition that a severe lockdown causes in countries like Peru may drive up susceptibility to illness in ways that outweigh the benefits of reduced transmission of the virus. This would at least explain Peru's contradiction between early and extreme lockdown and very high mortality.

There is a moderate correlation between GDP-per-capita and life expectancy (0.31 in developed countries, 0.47 in emerging/developing countries), and also between total health expenditure per capita and life expectancy (0.23 in developed countries and 0.51 in developing countries).[98] Thus, we should expect to see a lowering of average life expectancy associated with the declining GDP due to the Covid-19 recessions across the world, and that this will hit emerging economies hardest.

Closely related to the issue of poverty is the increase in unemployment due to business closures and stay-at-home orders that have been implemented as part of lockdown interventions. For example, 400,000 more people in the UK were unemployed in December 2020 than in December 2019, despite the furlough scheme.[99] Approximately 5 million more people in the USA were unemployed in November 2020 than in February 2020,[100] while more than 97,000 businesses permanently shut across the US during the pandemic up to September.[101] Unemployment is a high-risk factor for mortality. A meta-analysis of the relationship between unemployment and mortality found that the risk of death for unemployed persons was 63% higher than the risk of death for employed persons.[102] One explanation for this link is that unemployment has been found to lead to markers of accelerated physical ageing at the genetic level; a study found that those who are chronically unemployed shower shorter telomeres than a matched control group.[103] A further concern is that unemployment rate has a close relationship with suicide rate; Canadian data shows that a 1% increase in unemployment leads to 1-2% increase in suicide[104,105] Although suicide numbers overall are small compared with pandemic deaths, they tend to occur in younger adults and so equate to more QALYs lost.

One final consideration at the economic level of analysis is whether the approach to the pandemic taken this year is sustainable as an approach to pandemics going forward. If there were another pandemic in 5 years' time, it is an open question as to whether countries

that take a suppression strategy could afford to adopt a lockdown-based approach again. Many countries will likely still be dealing with the effects of the post-Covid recession, the weight of their increased national debt, and the deleterious effects on social cohesion and mortality that high unemployment brings.[106] It is therefore doubtful that this year's response represents an economically sustainable solution to global pandemics.[107,108]

CONCLUSIONS AND FUTURE RESEARCH DIRECTIONS

The evidence base about lockdowns is still in a nascent state as there was no precedent for these interventions prior to 2020. Currently, there is no way of stating with certainty whether lockdown damages will be greater than benefits or vice versa. Overall, the current evidence base leans towards harms outweighing benefits, but this may change if further evidence of a highly significant effect of lockdowns on mortality emerges.

Based on the biomedical evidence as it stands, the provisional conclusion is that a combination of moderate measures, such as limiting gatherings to 10 people or less and social distancing, work as effectively as lockdowns to reduce growth in case numbers, without the damages inflicted by the latter. The stay-at-home order appears to be less efficacious than expected. Furthermore, currently, there is little substantive empirical evidence that lockdowns reduce mortality despite lowering case growth rates. This may be due to immunosuppressant economic and psychological stressors that increase the risk of death in ways that offset the reduced risk of mortality brought by temporarily lower infection rates. This is supported by research showing social isolation, loneliness and unemployment lead to heightened susceptibility to coronavirus infection.[109] This must be factored into the continued policy decision-making.

Economic harms of lockdowns have been calculated via modelling the effects of depressed GDP on potential loss of life years, and through calculating the effects on lost

resourcing for health more generally. These studies, focused mainly on UK data, have mainly concluded that lockdowns may lead to more life lost than life saved.

All conclusions on lockdowns are provisional given that the literature on lockdown mortality effects will continue to develop across 2021 and there is no published research on the second wave of the virus yet. Furthermore, little is known about the effects of the timing, strictness and duration of a lockdown. Short lockdowns will have less detrimental effects on unemployment and social isolation than longer ones, so the variable of duration must be taken into account in future studies that have access to data over a longer period of time than currently published studies.

In terms of future research, studies need to investigate how cases and deaths relate to: (a) the timing of the lockdown relative to the course of the pandemic, (b) the duration and severity of the lockdown measures, and (c) whether the lockdown is implemented in an emerging economy with high levels of absolute poverty, or a developed economy where there is a relatively high level of affluence and an employment market based around service and media industries where a large proportion of individuals can work from home. Importantly, the medium- to long-term effects of lockdown policies must be examined as well as the more prevalent short-term effects, in light of the potential for rebound effects after lockdown. Furthermore, there is currently no published research on the link between lockdowns and hospitalisation rates. This is another important area to focus on going forward.

The potential collateral damages caused by lockdowns should also be the focus of further study over the coming years. The issues include social isolation, unemployment and depression, poverty and its varied negative effects on health including impaired immune functioning, as well as depleted funds for other forms of healthcare, and issues that relate to communities and families that have been damaged: domestic violence, suicide, crime and more. Future research should aim to estimate how much more of these problems lockdowns

bring compared with more moderate non-lockdown interventions (rather than just compared to a no-intervention scenario) and also how much the potential damage will differentially affect high income countries and middle-to-low income countries.

An evidence-based take on lockdowns is unlikely to reach a categorical conclusion that they do or do not work. A more likely conclusion, given the complexity of the dilemma, is that they may be beneficial at certain points in the pandemic, for example early in the process, but damaging if maintained as a policy over months or years. Whether or not the current lynchpin of lockdown strategies, the stay-at-home order, demonstrates incremental value over and above other less isolation-inducing measures, remains to be seen.

References

[1] Altman M. Smart thinking, lockdown and Covid-19: Implications for public policy. Journal of Behavioral Economics for Policy. 2020 Jun; 4:23-33.

[2] Melnick ER, Ioannidis JPA. Should governments continue lockdown to slow the spread of covid-19? BMJ. 2020; 369:1924. doi: https://doi.org/10.1136/bmj.m1924

[3] OECD (2020). Walking the tightrope: avoiding a lockdown while containing the virus. Retrieved 28/12/20 from https://www.oecd-ilibrary.org/economics/walking-the-tightrope-avoiding-a-lockdown-while-containing-the-virus_9cc22d8c-en

[4] Ibid

[5] Haug N, Geyrhofer L, Londei A. et al. Ranking the effectiveness of worldwide COVID-19 government interventions. Nat Hum Behav. 2020; 4**,** 1303–1312. https://doi.org/10.1038/s41562-020-01009-0

[6] Haynes L. GPs urge government to consider indirect COVID-19 harms in lockdown decisions. GP Online. Cited 2020 Dec 23. Available from https://www.gponline.com/gps-urge-government-consider-indirect-covid-19-harms-lockdown-decisions/article/1696300

[7] Baker MG, Wilson N, & Blakely T. Elimination could be the optimal response strategy for covid-19 and other emerging pandemic diseases.BMJ. 2020; 371, m4907. https://doi.org/10.1136/bmj.m4907 (Published 22 December 2020)

[8] Mozur P, Zhong R, Krolik A. In Coronavirus Fight, China Gives Citizens a Color Code, With Red Flags. New York Times. Retrieved 2021, Jan 6. Available from https://www.nytimes.com/2020/03/01/business/china-coronavirus-surveillance.html

[9] Mazzoni J. No US and Europe trips until 2022: Grim news as Australians face long wait for flights to tourist hotspots – but New Zealand travel bubble will open up this week. Retrieved 2021 Jan 13. Available from https://www.dailymail.co.uk/news/article-8827087/No-Europe-trips-2022-Australians-face-long-wait-flights-tourist-hotspots.html

[10] Baker MG, Wilson N, & Blakely T. Elimination could be the optimal response strategy for covid-19 and other emerging pandemic diseases. BMJ. 2020; 371, m4907. https://doi.org/10.1136/bmj.m4907 (Published 22 December 2020)

[11] Haug N, Geyrhofer L, Londei A. et al. Ranking the effectiveness of worldwide COVID-19 government interventions. Nat Hum Behav. 2020; 4**,** 1303–1312. https://doi.org/10.1038/s41562-020-01009-0

[12] ibid, p.1309

[13] Brauner J, Sören M, Mrinank S, Johnson D, Salvatier J, Gavenčiak, T et al.(2020). Inferring the effectiveness of government interventions against COVID-19. Science. 15 Dec 2020, eabd9338. DOI: 10.1126/science.abd9338

[14] Bendavid E, Oh C, Bhattacharya J, Ioannidis, JP. Assessing Mandatory Stay-at-Home and Business Closure Effects on the Spread of COVID-19. European Journal of Clinical Investigation. 2021; in press, e13484. https://doi.org/10.1111/eci.13484

[15] Li Y, Campbell H, Kulkarni D, Harpur A, Nundy M, Wang X et al. (2020). The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying

reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries. The Lancet Infectious Diseases, Volume 0, Issue 0. https://doi.org/10.1016/S1473-3099(20)30785-4

[16] OECD (2020). Walking the tightrope: avoiding a lockdown while containing the virus. Retrieved 28/12/20 from https://www.oecd-ilibrary.org/economics/walking-the-tightrope-avoiding-a-lockdown-while-containing-the-virus_9cc22d8c-en

[17] Dehning J, Zierenberg J, Spitzner P, Wibral M, Pinheiro Neto J, Wilczek M et al. Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions. Science,2020 Jul 10; 369 (6500), eabb9789. DOI: 10.1126/science.abb9789

[18] Chaudhry R, Dranitsaris G, Mubashir T, Bartoszko J, Riazi S. A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes. The Lancet. 2020; 25, 100464. https://doi.org/10.1016/j.eclinm.2020.100464

[19] De Larochelambert Q, Marc A, Antero J, Le Bourg E, Toussaint J-F. Covid-19 Mortality: A matter of vulnerability among nations facing limited margins of adaptation. Frontiers in Public Health. 2020; 8, 782. https://doi.org/10.3389/fpubh.2020.604339

[20] Meo SA, Abukhalaf AA, Alomar AA, AlMutariri F, Usmani A, Kolhnoff D. Impact of lockdown on COVID-19 prevalence and mortality during 2020 pandemic: observational analysis of 27 countries. *European Journal of Medical Research.* 2020; *25*, 56. https://doi.org/10.1186/s40001-020-00456-9

[21] Sornette D, Mearns E, Schatz M. et al. Interpreting, analysing and modelling COVID-19 mortality data. Nonlinear Dynamics. 2020; 101, 1751–1776. https://doi.org/10.1007/s11071-020-05966-z

[22] ibid.

[23] Flaxman S, Mishra S, Gandy A, Unwin J, Mellan T, Coupland H.. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature. 2020; 584**,** 257–261. https://doi.org/10.1038/s41586-020-2405-7

[24] Soltesz K, Gustafsson F, Timpka T, Jaldén J, Jidling C, Heimerson A.. The effect of interventions on COVID-19. Nature. 2020; 588, E26–E28. https://doi.org/10.1038/s41586-020-3025-y

[25] Kuhbandner C, Homburg S. Commentary: Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Frontiers in Medicine. 2020; 7, 761.

[26] Hsiang S, Allen D, Annan-Phan S, Bell K, Bolliger I, Chong T et al.The effect of large-scale anti-contagion policies on the COVID-19 pandemic. Nature. 2020; 584, 262–267. https://doi.org/10.1038/s41586-020-2404-8

[27] Ben-Israel I. The end of exponential growth: The decline in the spread of coronavirus. The Times of Israel, April 19. Cited 2020 30 Dec. Available from https://www.timesofisrael.com/the-end-of-exponential-growth-the-decline-in-the-spread-of-coronavirus/

[28] VanderWeele TJ. Challenges Estimating Total Lives Lost in COVID-19 Decisions: Consideration of Mortality Related to Unemployment, Social Isolation, and Depression. JAMA. 2020; 324(5), 445–446. doi:10.1001/jama.2020.12187

[29] Miles D, Stedman M, Heald A. "Stay at Home, Protect the National Health Service, Save Lives": A cost benefit analysis of the lockdown in the United Kingdom. Int J Clin Pract. 2020; 00:e13674. https://doi.org/10.1111/ijcp.13674

[30] Hanna T, Agganwal A, Booth C, Sullivan R.. Counting the invisible costs of covid-19: the cancer pandemic. BMJ, 2020 Nov 5.https://blogs.bmj.com/bmj/2020/11/05/counting-the-invisible-costs-of-covid-19-the-cancer-pandemic/

[31] Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. 2020; The Lancet Oncology, 21 (8), 1023 – 1034. https://doi.org/10.1016/S1470-2045(20)30388-0

[32] Active Lives Adult May 19-10 Coronavirus Report [Internet]. Sport England. Available from: https://www.sportengland.org/know-your-audience/data/active-lives

[33] Valenzuela PL, Santos-Lozano A, Lista S, Serra-Rexach JA, Emanuele E, Lucia A. Coronavirus Lockdown: Forced inactivity for the oldest old? JAMDA. 2020; 21, 988 – 989. https://doi.org/10.1016/j.jamda.2020.03.026

[34] Ibbetson C. Brits support new lockdown rules, but many think they don't go far enough [Internet]. YouGov. 2020. Available from: https://yougov.co.uk/topics/politics/articles-reports/2020/09/23/brits-support-new-lockdown-rules-many-think-they-d

[35] Smith M. Snap poll: 72% of English people back Prime Minister's plan to return to lockdown [Internet]. YouGov. 2020. Available from; https://yougov.co.uk/topics/health/articles-reports/2020/11/01/snap-poll-72-english-people-back-prime-ministers-p

[36] Fromm, E. (1941). Escape from Freedom. Routledge.

[37] Murray DR, Schaller M, Suedfeld P (2013) Pathogens and Politics: Further Evidence That Parasite Prevalence Predicts Authoritarianism. PLoS ONE 8(5): e62275. doi:10.1371/journal.pone.0062275

[38] Chae SH, Park HJ. Effectiveness of Penalties for Lockdown Violations During the COVID-19 Pandemic in Germany. American Journal of Public Health. 2020; 110, 1844_1849, https://doi.org/10.2105/AJPH.2020.305903

[39] Rujevic N. Opinion: Calls for a firm hand to fight the coronavirus are worrying. DW. 2020. Retrieved from https://www.dw.com/en/opinion-calls-for-a-firm-hand-to-fight-the-coronavirus-are-worrying/a-55686119 2020)

[40] Hockenos P. Germany Found a Strongman for Its Coronavirus Crisis. Foreign Policy. 2020. Retrieved 30/12/20 from https://foreignpolicy.com/2020/04/16/markus-soder-soeder-germany-strongman-coronavirus-crisis/

[41] HM Government Analysis of the health, economic and social effects of COVID-19 and the approach to tiering. 2020. Retrieved 30/12/20 from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/939876/Analysis_of_the_health_economic_and_social_effects_of_COVID-19_and_the_approach_to_tiering_FINAL__SofS_.pdf

[42] Fiorillo A, Sampogna G, Giallonardo V, Del Vecchio V, Luciano M, Albert, U, et al. Effects of the lockdown on the mental health of the general population during the COVID-19 pandemic in Italy: Results from the COMET collaborative network. European Psychiatry. 2020; 63(1), E87. doi:10.1192/j.eurpsy.2020.89

[43] Lu P., Li X., Lu L., Zhang Y. The psychological states of people after Wuhan eased the lockdown. 2020 Nov 12; PLoS ONE 15(11): e0241173. https://doi.org/10.1371/journal.pone.0241173

[44] Gan Y, Ma J, Wu J, Chen Y, Zhu H, Hall B J. Immediate and Delayed Psychological Effects of Province-wide Lockdown and Personal Quarantine during the COVID-19 Outbreak in China. Psychological Medicine. 2020; 13, 1- 12. https://doi.org/10.1017/S0033291720003116

[45] Brooks K, Webster R, Smith L, Woodland L, Wesseley S, Greenberg N et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The Lancet. 2020; 395, 10227, 912 - 920. https://doi.org/10.1016/S0140-6736(20)30460-8

[46] Sharpe A. The silent epidemic that has hit nine million lives as Covid rampages through UK [Internet]. Available from: https://www.mirror.co.uk/news/uk-news/silent-epidemic-hit-nine-million-23291390

[47] Luchetti M, Lee JH, Aschwanden D, Sesker A, Strickhouser JE, Terracciano A, Sutin AR. The trajectory of loneliness in response to COVID-19. American Psychologist. 2020; 75(7), 897-908. doi: 10.1037/amp0000690.

[48] Killgore WDS, Cloonan SA, Taylor EC, Lucas DA., Dailey NS. Letter to the Editor. Loneliness during the first half-year of COVID-19 Lockdowns. Psychiatry Research. 2020; 294: 113551.

[49] Mental Health Foundation (2020). Loneliness during coronavirus. Retrieved 30/12/20 from https://www.mentalhealth.org.uk/coronavirus/loneliness-during-coronavirus

[50] Sharpe (2021)

[51] Coughlan S. (2020). Lockdown loneliness reaches record levels. Retrieved 30/12/20 from https://www.bbc.co.uk/news/education-54973709

[52] Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: A meta-analytic review. Perspectives on Psychological Science. 2015;10(2), 227-237. doi:10.1177/1745691614568352

[53] Hjaltadóttir I, Hallberg IR, Ekwall AK, Nyberg P.Predicting mortality of residents at admission to nursing home: A longitudinal cohort study. 2011; BMC Health Services Research, 11, 86. https://doi.org/10.1186/1472-6963-11-86

[54] Cacioppo, J.T., & Patrick, W. Loneliness: Human Nature and the Need for Social Connection. 2008; W. W. Norton & Company.

[55] Pressman SD, Cohen S, Miller GE, Barkin A, Rabin BS, Treanor J J.Loneliness, social network size, and immune response to influenza vaccination in college freshmen. Health Psychology, 2005; 24(3), 297–306. https://doi.org/10.1037/0278-6133.24.3.297

[56] Cole SW, Capitanio JP, Chun K, Arevalo JMG, Ma J, Cacioppo JT. Myeloid differentiation in social isolation. Proceedings of the National Academy of Sciences. 2020;112 (49) 15142-15147; doi: 10.1073/pnas.1514249112

[57] Cohen S. Psychosocial Vulnerabilities to Upper Respiratory Infectious Illness: Implications for Susceptibility to Coronavirus Disease 2019 (COVID-19). Perspectives on Psychological Science. 2021;16(1):161-174. doi:10.1177/1745691620942516

[58] Peterson I, Phillips A. Three Quarters of People with SARS-CoV-2 Infection are Asymptomatic: Analysis of English Household Survey Data. Clinical Epidemiology, 2020; 12, 1039-1043. doi: 10.2147/CLEP.S276825

[59] Hawkley LC, Cacioppo JT. Loneliness and pathways to disease. Brain, Behavior and Immunity. 2003; 17, 98-105. https://doi.org/10.1016/S0889-1591(02)00073-9.

[60] McClellandH, EvansJJ, Nowland R, Ferguson E.O'Connor RC. Loneliness as a predictor of suicidal ideation and behaviour: a systematic review and meta-analysis of prospective studies. Journal of Affective Disorders, 2020; 274, 880-896. https://doi.org/10.1016/j.jad.2020.05.004.

[61] Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J, Smith N et al.Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science. 2020; 369 (6504). https://doi: 10.1126/science.abc6027

[62] VanderWeele TJ. Challenges Estimating Total Lives Lost in COVID-19 Decisions: Consideration of Mortality Related to Unemployment, Social Isolation, and Depression. JAMA. 2020; 324(5), 445–446. doi:10.1001/jama.2020.12187

[63] Li, Y. et al. The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries. The Lancet Infectious Diseases, 2020; Volume 0, Issue 0. https://doi.org/10.1016/S1473-3099(20)30785-4

I believe you have referenced this paper before? Number 15?

[64] Robinson OC. Development through Adulthood: Second Edition. Macmillan Higher Education; 2020.

[65] Armon C, Dawson TL. Developmental trajectories in moral reasoning across the life span. Journal of Moral Education. 1997; 26, 433–453.

[66] Heffer, S. The Government's attitude to risk is ludicrous – young and old, we need a cultural life. *The Telegraph.* 2020. Available from https://www.telegraph.co.uk/theatre/what-to-see/governments-attitude-risk-ludicrous-young-old-need-cultural/

[67] Beauchamp TL, Childress, JF. Principles of Biomedical Ethics. 6th Edition. Oxford: Oxford University Press; 2008.

[68] Schneider CE. The practice of autonomy: Patients, doctors and medical decisions. Oxford: Oxford University Press; 1998.

[69] Savulescu J. Golden opportunity, reasonable risk and personal responsibility for health. Journal of Medical Ethics. 2017; 44 (1), 59-61.

[70] World Health Organization Alcohol. 2018. Retrieved 23/12/20 from https://www.who.int/news-room/fact-sheets/detail/alcohol

[71] World Heath Rankings Alcohol: Death rate per 100,000. 2018. Retrieved 28/12/20 from https://www.worldlifeexpectancy.com/cause-of-death/alcohol/by-country

[72] Wiley LF, Berman ML, Blanke D. Who's your nanny?: Choice, paternalism and public health in the age of personal responsibility. The Journal of Law, Medicine & Ethics. 2013; 41: 88-91. https://doi.org/10.1111/jlme.12048 I think capitalisations are specified as not necessary after first word of title (unless place name etc).

[73] Wolff J. Lockdown life and liberty: When do emergency measures turn into dangerous government overreach? TLS [Internet]. 2020; Retrieved 28/12/20 from https://www.the-tls.co.uk/articles/lockdown-life-liberty/

[74] Thomas P, Stupples D. J-Value: A Universal Scale for Health and Safety Spending. Measurement and Control, 2020 Nov; 39(9), 273-276. doi:10.1177/0533316405049369

[75] National Institute for Health and Care Excellence (NICE). How NICE measures value for money in relation to public health interventions. 2020. Available from https://www.nice.org.uk/Media/Default/guidance/LGB10-Briefing-20150126.pdf

[76] Bertram MY, Lauer J, Johncheere K, Edejer T, Hutubessy R, Kieny MP et al. Cost–effectiveness thresholds: pros and cons. Bulletin of the World Health Organization. 2016; 94, f925-930. doi: http://dx.doi.org/10.2471/BLT.15.164418

[77] NICE (2013). How NICE measures value for money in relation to public health interventions. Retrieved 30/12/20 from https://www.nice.org.uk/Media/Default/guidance/LGB10-Briefing-20150126.pdf

[78] Miles, DK, Stedman, M, Heald, AH. "Stay at Home, Protect the National Health Service, Save Lives": A cost benefit analysis of the lockdown in the United Kingdom. Int J Clin Pract. 2020; 00:e13674, p.1. https://doi.org/10.1111/ijcp.13674

[79] ibid p.1

[80] Shlomai, A., Leshno, A., Sklan, E.H., & Leshno, M. Modeling social distancing strategies to prevent SARS-CoV2 spread in Israel- A Cost-effectiveness analysis. Value in Health. 2020; in press. https://doi.org/10.1016/j.jval.2020.09.013

[81] Reddy SG. Population health, economics and ethics in the age of COVID-19. BMJ Global Health. 2020; 5, e003259.

[82] Savulescu J, Persson I, Wilkinson D. Utilitarianism and the pandemic. Bioethics. 2020; 34, 620– 632. https://doi.org/10.1111/bioe.12771

[83] Thomas P. The length and severity of the coronavirus recession estimated from the dynamics of relaxing lockdown. Nanotechnology Perceptions. 2020; 16, 100–129. doi: 10.4024/N07TH20A.ntp.16.02

[84] Thomas P. J-value assessment of how best to combat Covid-19. Nanotechnology Perceptions. 2020; 16, 16–40. doi: 10.4024/N02TH20A.ntp.16.01

[85] Thomas P. Is the cost of another lockdown too high? The Spectator, 8th November 2020. Available from: https://www.spectator.co.uk/article/is-the-cost-of-another-lockdown-too-high-

[86] ibid

[87] Reuters. UK forecasts show 11.3% GDP contraction in 2020, rebound in 2021 [Internet]. 2020 [cited 2021 Jan 27] Available from: https://www.reuters.com/article/health-coronavirus-britain-growth/uk-forecasts-show-11-3-gdp-contraction-in-2020-rebound-in-2021-idUSS8N2HE015

[88] Thomas P. The length and severity of the coronavirus recession estimated from the dynamics of relaxing lockdown. Nanotechnology Perceptions. 2020; 16, 100–129. doi: 10.4024/N07TH20A.ntp.16.02

[89] ibid

[90] Reuters (2020). Swedish govt sees milder downturn in 2020, slower growth next year. Available from: https://uk.reuters.com/article/sweden-economy/swedish-govt-sees-milder-downturn-in-2020-slower-growth-next-year-idUKKBN28Q1VZ

[91] World Bank. *COVID-19 to Add as Many as 150 Million Extreme Poor by 2021.* Available from: https://www.worldbank.org/en/news/press-release/2020/10/07/covid-19-to-add-as-many-as-150-million-extreme-poor-by-2021

[92] UNICEF (2020). 150 million additional children plunged into poverty due to COVID-19, UNICEF, Save the Children say. Available from: https://www.unicef.org/press-releases/150-million-additional-children-plunged-poverty-due-covid-19-unicef-save-children

[93] Broadbent A, Walker D, Chalkidou K, Sullivan R, Glassman A.Lockdown is not egalitarian: the costs fall on the global poor. The Lancet. 2020; 396, 10243, 21 – 22.

[94] Hannan D. Peru has the toughest lockdown in the world and still ended up with the worst fatality rate. The Telegraph. 2020. Available from: https://www.telegraph.co.uk/news/2020/10/18/peru-has-toughest-lockdown-world-still-ended-worst-fatality/

[95] Worldometer (2020). Reported Cases and Deaths by Country, Territory, or Conveyance. Cited 2020 Dec 20. Available from: https://www.worldometers.info/coronavirus

[96] ILO (2020). More than 60 per cent of the world's employed population are in the informal economy. Retrieved 30/12/20 from https://www.ilo.org/global/about-the-ilo/newsroom/news/WCMS_627189/lang--en/index.htm

[97] Piper. The devastating consequences of coronavirus lockdowns in poor countries. 2020. Retrieved 26/12/20 from https://www.vox.com/future-perfect/2020/4/18/21212688/coronavirus-lockdowns-developing-world

[98] Biciunaite A. Economic Growth and Life Expectancy – Do Wealthier Countries Live Longer? 2020. https://blog.euromonitor.com/economic-growth-and-life-expectancy-do-wealthier-countries-live-longer/

[99] ONS (2020). Employment in the UK: December 2020. Retrieved 26/12/2020 from https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/bulletins/employmentintheuk/latest#unemployment

[100] Duffin E. Monthly number of unemployed persons in the U.S. from November 2019 to November 2020. Retrieved 30/12/20. Available from: https://www.statista.com/statistics/193280/seasonally-adjusted-monthly-number-of-unemployed-persons-in-the-usa/

[101] Sraders A, Lambert L. Nearly 100,000 establishments that temporarily shut down due to the pandemic are now out of business. Fortune, 2020 Sept 28.https://fortune.com/2020/09/28/covid-buisnesses-shut-down-closed/

[102] Roelfs DJ, Shor E, Davidson KW, Schwartz JE. Losing life and livelihood: a systematic review and meta-analysis of unemployment and all-cause mortality. Soc Sci Med. 2011 Mar;72(6):840-54. doi: 10.1016/j.socscimed.2011.01.005.

[103] Ala-Mursula L, Buxton JL, Ek E, Koiranen M, Taanila A, Blakemore AIF, et al. Long-Term Unemployment Is Associated with Short Telomeres in 31-Year-Old Men: An Observational Study in the Northern Finland Birth Cohort 1966. PLoS ONE. 2013; 8(11): e80094. https://doi.org/10.1371/journal.pone.0080094

[104] McIntyre RS, Lee Y. Projected increases in suicide in Canada as a consequence of COVID-19. Psychiatry Research. 2020; 290, 113104. https://doi.org/10.1016/j.psychres.2020.113104.

[105] Samson K, Sherry SB. Projected increases in suicide in Canada as a consequence of COVID-19 revisited. Psychiatry Research. 2020; 294, 113492. https://doi.org/10.1016/j.psychres.2020.113492

[106] World Bank. COVID-19 to Plunge Global Economy into Worst Recession since World War II [Internet]. Available from: https://www.worldbank.org/en/news/press-release/2020/06/08/covid-19-to-plunge-global-economy-into-worst-recession-since-world-war-ii

[107] Farsalinos K, Poulas K, Kouretas D, Vantarakis A, Leotsindis M,Kouvelas D et al. Improved strategies to counter the COVID-19 pandemic: Lockdowns vs. primary and community healthcare. Toxicology Reports. 2021; 8, 1-9. https://doi.org/10.1016/j.toxrep.2020.12.001.

[108] Gurdasani D, Bear L, Bogaert D, Burgess R, Busse R, Cacciola R et al. The UK needs a sustainable strategy for COVID-19. The Lancet. 2020; 396, 10265, 1800 – 1801. https://doi.org/10.1016/S0140-6736(20)32350-3

[109] Cohen S. Psychosocial vulnerabilities to upper respiratory infectious illness: Implications for susceptibility to Coronavirus Disease 2019 (COVID-19). Perspectives on Psychological Science. 2021;16(1):161-174. doi:10.1177/1745691620942516