OPEN LETTER

REVISED Integrating economic and health evidence to inform Covid-19 policy in low- and middle- income countries [version 2; peer review: 2 approved]

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Abstract

Covid-19 requires policy makers to consider evidence on both population health and economic welfare. Over the last two decades, the field of health economics has developed a range of analytical approaches and contributed to the institutionalisation of processes to employ economic evidence in health policy. We present a discussion outlining how these approaches and processes need to be applied more widely to inform Covid-19 policy; highlighting where they may need to be adapted conceptually and methodologically, and providing examples of work to date. We focus on the evidential and policy needs of low- and middle-income countries; where there is an urgent need for evidence to navigate the policy trade-offs between health and economic well-being posed by the Covid-19 pandemic.

Keywords

Covid, health economics, cost-effectiveness

This article is included in the Coronavirus (COVID-19) collection.

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REVISED **Amendments from Version 1**

We have made edits that highlight this paper's broader relevance for future pandemics. While time has moved on, we think it remains useful going forward to map out the concepts and principles around integrating economic and epidemiological evidence. The paper however remains a viewpoint on the factors that should be generally considered in economic evaluation of pandemic responses. We have however added several new references. We have also further clarified several issues, with minor additions to the text, including: aspects of social protection, the application of the rule of rescue, the interaction between health and economic policy and the application of VSL. We have also added text on the early estimates of economic impact from other diseases and mentioned that some bore our and some did not. We clarified the value of modelling unmitigated epidemics. FInally, we note that persons with high health and economic risk the resulting choice/ behaviours are challenging to predict.

Any further responses from the reviewers can be found at the end of the article

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Introduction

Covid-19 (C19) required a 'whole society' policy response to protect health, economic and social welfare globally. Policy options were multi-sectoral and include scaling-up C19 health services, physical distancing, strengthened social protection and a wide range of additional sectoral, fiscal and macro-economic interventions[1]. Given the magnitude and breadth of impact of C19, policy action required careful consideration of trade-offs between the health, economic and social dimensions of population welfare. Understanding, not just the nature, but also the extent of these trade-offs is critical, particularly for low- and middle-income countries (LMICs), to inform policies that maximise overall population welfare during pandemics.

Health policy inevitably involves trade-offs and priority setting between and within different diseases and populations, e.g. between the young vs the old; the severely sick vs the relatively healthy (or less sick); etc. Health sectors employ a range of processes to inform this priority setting[2]. However, where formal processes for health sector priority setting exist, in the majority of cases they are designed to inform health policy decisions made at the margin; typically appraising the adoption of specific health interventions or technology (referred to as health technology assessment (HTA))[3,4]. Periodically, wider efforts are made to assess whether the range of services included in Universal Health Care (UHC) health benefit packages being delivered across the health sector is optimal[5–9].

The field of health economics has a long history of bringing together epidemiological modelling and economics to quantify the trade-offs made both within the health sector and between health and other dimensions of welfare; and supporting the use of such evidence in policy. Cost-effectiveness analysis typically assesses whether population health is maximised within the existing financial constraints (such as a budget limit on healthcare spending): acknowledging that every investment in an intervention within the health sector will mean that another intervention to improve health will be forgone – the concept of 'opportunity cost'. In priority setting, cost-effectiveness is also considered with other aspects of welfare, for example ensuring equity of health[10,11] or avoiding catastrophic health expenditures[12,13]. Health technologies, services or policy interventions are typically assessed from the perspective of the health sector, although sometimes also consider the lost productive time (productivity losses) of individuals who are sick or die prematurely is considered, known as taking a societal perspective[14].

We examine here how health economic evidence and more broadly priority setting processes to support decisions around new health technologies (pharmaceutical interventions) and public health policies need to be adapted for pandemics, focussing on eLMICs. We first explore how current approaches may needd to be adapted for C19; then we examine the empirical approaches and analytical requirements of providing integrated evidence of health, economic and social impact to health policy makers. We argue for pandemic preparedness approaches that support the rapid adaption and application of evidence informed priority setting to ensure that decisions made around pandemics remain evidence informed, transparent and accountable to the population they serve.

Broadening the assessment of health sector policy under C19

Pandemics are no different from any other health issue, in that much of the C19 response will incur 'within health sector trade-offs' and therefore it is critical to assess both the impact of overall population health and equity in C19 policy. However, the scale, speed and scope of a pandemic generate impact of exceptional depth and breadth of impact across health systems and, critically, the wider economy, which mean that standard 'within health sector' approaches to priority setting need to be extended to ensure that overall allocations to the health sector are optimal, considering all dimensions of population welfare including health, economic and social welfare[15]. Challenges in doing this, include:

1. The magnitude of the health impact from pandemics means that governments may wish to re-evaluate and rapidly change health sector funding levels, in order to maintain some semblance of 'health as usual' i.e. current levels of population health, for example, current levels of maternal mortality. Therefore, the **trade-offs may move beyond opportunity costs within the health sector to opportunity costs for other sectors**.

2. The health impact of pandemics such as C19 can rapidly evolve, and therefore **policy responses and the analytics to inform them need to be instantaneous**, despite the complexity involved.

3. **Health, interventions and economic policy goals interact with one another** and are 'dynamic' in the sense that ill health impacts on economic and social

welfare. Ill-health can impede the ability to work or exasperate economic inequities. Likewise, improvements in economic and social welfare can substantially impact health and health equity. For example, reduction in C19 attributable mortality is in part determined by the balance between policies to increase health system capacity and physical distancing. Likewise, economic welfare is in part determined by the balance between physical distancing and social protection policy.

4. Pandemic response policies such as physical distancing, are likely to have substantial short- to medium-term macro-economic and poverty impacts, so, to ensure economic welfare continues 'as usual', for example maintain current levels of employment, governments are likely to simultaneously **alter their ratio of present and future spending and investment policies**.

5. Much of the cost of C19 interventions and pandemic responses will be borne at the household level with implications for both household consumption and savings behaviour, labour supply decisions and consequential broader social and health ramifications of catastrophic losses to household income. Even where public expenditures are transferred to households and provide social protection, they eventually have to be paid for from household income, through taxation. Therefore, C19 policy may require **rapid changes to the balance between public sector and private expenditure across the economy, having short- and long- term implications for government budgets.**

6. Many mitigating behavioural responses to pandemics **exhibit important externalities,** which means that the actions of each individual directly impact the welfare of others. Typically, this requires a public policy response as individuals will not act in a way that necessarily benefits society as a whole. For instance, patients with mild C19 may not self-quarantine without incentives to do so.

7. Pandemic response policy is also likely to have **substantial distributional impacts**. For, example, there may be trade-offs between costs and benefits incurred by different socioeconomic groups, genders, ethnicities, urban/rural populations, those with differing health status etc. Therefore, heterogeneity of cost and the distribution of health benefits between sub-populations need to be considered.

8. **Responses to pandemics are also 'dynamic' over time,** for example the ability to exit physical distancing smoothly may depend on the credibility and understanding of government policy during the periods of stringent physical distancing. Likewise, the ability to stimulate improvements in 'demand-side' economic behaviour post-crisis may depend on government credibility in handling the economic consequences during the crisis.

9. Finally, it is highly likely that both health and economic impacts will heterogeneous across populations, and **responses to pandemics will need to reflect local health, social and economic constraints.**

In short, informing policy action for C19 and other pandemics is challenging, and needs to include evidence and the analysis of trade-offs within and between health services, but also inform social and economic policies (including financial protection and different sectoral objectives), across population groups, between the public and private sectors, and over time, conducted in an uncertain and rapidly evolving global context. As such, pandemic policy making requires additional processes to conventional HTA, evidence generation and review to understanding wide-ranging trade-offs that will be required across a broad range of sectors.

However, before moving evidence to policy challenges demanded by wider inter-sectoral interaction, we examine the generation evidence on the trade-offs incurred within the health sector: between the allocation of resources specifically to C19 services and new technologies versus those for other health conditions. During a pandemic 'business as usual' is, or should be, disrupted, but whether it is the exceptional use of bed capacity, or financing of C19 vaccines and treatments, pandemics can impose a clear 'health-health' trade-offs.

Assessing trade-offs across the health sector

Typically, health trade-offs are empirically assessed by establishing whether the implementation of an intervention results in a net improvement in population health. The extent of the 'opportunity cost' of C19 expenditure (and hence the net impact on population health) depends on: the extent to which underutilised health service capacity exists and can be employed; the extent to which other health services can be delayed or cancelled without causing harm; the extent of health impact gained from diverting additional funding to the health sector from elsewhere. To conduct these analyses a comparable measure of population health is required, measuring both the extent of both mortality and morbidity impact combined with populations' preferences for different health states. There is an extensive literature on different ways to measure population preferences for different health states, with many countries using standardised measures such as quality adjusted life years (QALYs) or disability adjusted life years (DALYs) as composite measures of health impact[16]. Importantly, these measures account for years of healthy life rather than deaths, weighing each year in full health equally. Estimates of DALYs averted for C19 for LMICs found that disability from C19 would increase DALYs lost by up to a third[17].

There is a debate as to whether all health vs health trade-offs compare like with like even when generic health measures are used. In previous pandemics, it has been argued that a 'rule of rescue', the moral action to save lives in immediate danger whatever the consequences for other health spend, should be applied[18], even if the impact on population is negative. Population preferences around the rule of rescue within the

health sector have been investigated, to assist in spending decisions around new life saving technologies, and may be considered during 'emergency phases' of pandemics, although this has been less explored in LMICs. For example, NICE in the UK, found that most (of a small council of citizens) prioritise immediate life-saving interventions above routine health interventions. However, this prioritisation was only agreed with strict definition of criteria, and even in these circumstances there should some consideration of the extent of impact on population health overall[18].

Empirical evidence on the net population health impact of C19 has suggested at least in the short term, C19 is incurring substantial opportunity costs for other health areas in LMICs, with health sectors not being able to sufficient address both underlying financial and non-financial constraints in the time required. A study on immunisation in LMICs found that every excess C19 death during routine vaccination would be traded for over 100 deaths in children if routine vaccination ceased[19]. Concerns have also been raised around the impact of C19 on TB and HIV[20,21]. This adds to the evidence from previous pandemics of adverse impacts on health services in LMICs; it was estimated that approximately 10,000 additional malaria deaths may have resulted from the cessation of malaria treatment in Guinea, Liberia, and Sierra Leone during the Ebola epidemic[22].

C19 stretches existing health sector capacity globally, but had C19 and other pandemics are likely stretch LMIC financial and health sector capacity is substantial. An early study estimates that if it had been unmitigated, the total health sector costs for C19 could have been extremely high, ranging from 58% to 122% of current annual health spend in five LMIC cities[23]. Barasa *et al.* assessed the capacity of the Kenyan health system to absorb those requiring critical care due to C19 and found that critical bed requirements of C19 surge varied from 12% to 145% of current capacity across different counties in Kenya[24]. Moreover, hospitals in LMICs typically run at high occupancy and focus on acute care, so displaced services may have a higher opportunity cost than in high income countries (HICs). Even if large temporary hospitals can be constructed, and supplies accessed, qualified health workers will be a critical resource in many LMICs; estimates range from 13 to 56 times current capacity at an unmitigated C19 peak[19].

In summary, while the within health trade-offs in LMICs are likely to have been substantial, but during the pandemic there was limited direct evidence available to assist policy makers respond in a way that considers overall population impact of their choices. There remains a need to ensure health economic methods are employed in pandemics to address this evidence gap; especially as new technologies are employed, and determine the optimal allocation resources between different diagnostic, treatment and preventative interventions during the health sector at different stages of pandemics[25]. Providing evidence alone however, is insufficient, importantly the production of evidence should be matched with 'evidence based deliberative processes'that build on current health technology assessment processes, but can respond with the rapidity required for pandemics.

Informing C19 policy choice considering trade-offs between health and wider economy

Economic models can inform policy makers about the extent of the economic impact of pandemics and responses to them. The 'health economics' and 'macroeconomics' professions apply different models to assess health and economic burdens. Micro-(health) economic models tend to integrate complex epidemiological models, but estimate societal costs by multiplying the time off work with rates of income loss per day off work measured by wages, or sometimes approximated using gross domestic product (GDP) per capita per day, known as the 'human capital approach'. They can also be linked with epidemiological models to estimate numbers of households placed below the poverty line as an immediate consequence of illness and health seeking behaviour[13].

Conversely, the macro-economic tradition focuses on estimating aggregate economic impact that includes the interactions between individuals and households, employing epidemic estimates produced by external models. Macroeconomic models account for consequential economic behaviour or adjustment, over time, including coping mechanisms such as household decisions to reduce costs and increase savings, workers' decisions to participate in the workforce, and producers' and traders' decisions to maximise profits, to address shocks to the economy (see Figure 1). Importantly, macro-economic models allow for interaction and feedback between different economic sectors, and global macro-economic models are also able to capture the consequences of pandemics on global movement and trade.

There is a long tradition of trying to integrate infectious disease modelling into macro-economic modelling to explore policy trade-offs within one model framework to inform policy makers; and incorporating health to economic to health feedbacks. Work from previous epidemics have included early studies of the macro-economic impact of the HIV pandemic[26–30], which relied on epidemiological projections by World Bank, but no integrated epidemiological model. Recent models employ more elaborate epidemiological models and produce broad ranges of estimates of both health and economic impacts including summary measures in non-monetary units (e.g. symptomatic cases/hospitalizations/deaths averted, work time absenteeism, etc.) and costs (e.g. combined impacts of work absenteeism, health costs, and public mitigation and suppression interventions in local currency units)[31–36]. However, there remain challenges in fully integrating the dynamic feedbacks between the progression of infectious diseases and the economy over long time periods. While most macro-economic models of pandemics incorporate the epidemic projections over time, it remains a challenge to incorporate the feedback between the resulting economic impact to the epidemic trajectory[37].

Even where the impacts of different pandemic policies can be estimated in an integrated manner, the optimal balance between health and economic policy outcomes is difficult to ascertain as it is inherently value laden. There is some evidence on how populations balance the two outcomes from high income countries (HICs). For example, economists have explored how populations value health and economic welfare using a

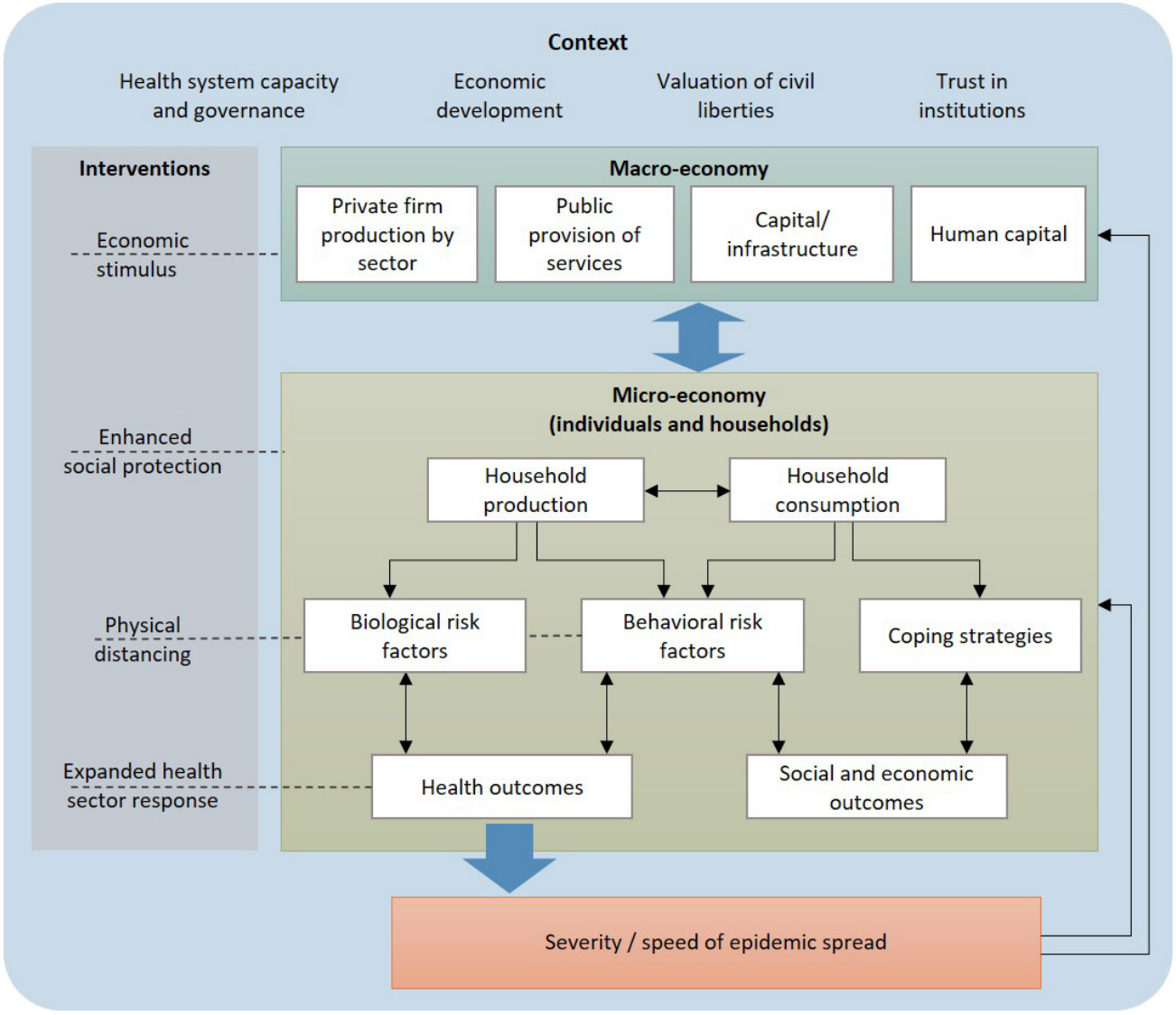

Figure 1. The scope of micro- and macro-economic models of Covid-19.

measure known as the value of statistical life (VSL). VSL estimates the amount individuals would be willing to pay for an improvement in survival, and can be used to convert health impact into monetary value: allowing for an estimate of net welfare[38]. VSL values are derived from surveys that aim to capture a population's willingness to pay for a reduction in annual mortality risk, and are reported to range between 20 and 140 times GDP per capita to avoid one death[39–41]. Studies in the US applying VSL values to C19 control suggest a net benefit which is higher for social distancing compared to suppression strategies and that social planners should be willing to pay approximately 26% of annual (US) consumption to avoid C19 deaths[39]. When VSL estimates are extrapolated to LMICs, net benefits that are considerably reduced compared to HICs, although still remain positive[42]. However, these estimates only point to a general direction as VSL estimates are not generally available for LMIC populations[42]. Moreover, VSL is controversial, as it is narrowly focussed on mortality and does not consider values around years of life lost and morbidity, and is highly sensitive to individual income. There have been other approaches taken to estimate benefits which are not covered here, but rely on measures of benefit related to the value of health to health sector payers, but in non-pandemic times[43]. The current evidence base and methods on the valuation of health versus economic welfare in LMICs therefore remains woefully inadequate, and even where models provide joint

health and economic outputs, careful decision processes are required to ensure these are weighed correctly (see section on governance below).

Estimating the impact of C19 without intervention – analytical approaches

The starting point of any empirical analysis of C19 policy on both health and economic welfare is to understand the base case, or the unmitigated C19 impact on the economy or poverty or the 'cost of illness'. Previous unmitigated pandemics have had substantial economic and poverty impacts. A challenge in estimating the impact of unmitigated pandemics is predicting how individuals judge and act when facing both perceived health and economic risks[44]. In simple terms, Figure 2 illustrates incremental impact on behaviour of public health policy in the face of C19, or other pandemic related risk. Figure 2 divides the population into four groups depending on the level of individual health and economic risk they face. Most of those with a high health risk but little economic risk may voluntarily choose to physical distance (all individuals above line 1). If individuals are altruistic that may increase their propensity to stay in (all individuals above line 2). However, for many either the economic risk will be too high, or the health risk too low, so they may not stay in and spread the disease and harm others (externalities). Likewise, those facing some of those facing either both high or low risks in both domains may chose not to distance. In this case public health policy may intervene and enforce physical distancing, or alternatively use social protection to reduce individuals' economic risk, resulting in all individuals above line 3 distancing. The central point being that the economic cost and health impact of the public policy are the costs of moving the line from 2 to 3, and the costs of illness and health impact of C19 are those above line 2.

During the early stages of the HIV pandemic, several macroeconomic studies aimed to estimate the costs of illness of HIV in LMICs. Estimates varied by setting, but ranged from approximately 1-5% of GDP[26–28]. For example, for Cameroon it was estimated that the loss of skilled workers from HIV would reduce annual economic growth by 1.7% per annum[45]. Similarly, macroeconomic studies of an unmitigated repeat of the UK flu pandemics from 1957 and 1968 was estimated to be short-lived and, in the worst-case scenario, to constitute a loss of 9.5% of quarterly GDP or a loss of 2.5% of annual GDP in the UK, most of which is due to population coping responses (self-imposed physical distancing)[32].

Micro-economic estimates of the cost of illness of C19 suggested that an unmitigated C19 epidemic would incur a substantial cost of illness in the first year[23]. Households affected by C19 incur costs due to time off work from sickness and incur costs from death. While many C19 deaths occur in older age groups, co-morbidities in working-age (and poor) segments in LMICs may mean that substantial proportions of households may still suffer income losses from an unmitigated C19 epidemic[23].

While unmitigated estimates are often used in the very initial stages of pandemics to alert policy makers to the extent of any catastrophic impact if nothing is done, they are often made on the basis of highly scarce data, and under considerable uncertainty. Moreover, they cannot be validated as a policy response quickly follows and therefore in reality 'and unmitigated epidemic cannot be observed'. Moreover, while unmitigated epidemics are argued to provide a useful comparator against which to measure the impact of interventions, even without government intervention they are unlikely to occur, as individuals within populations will act, and therefore unmitigated pandemics remain a conceptual construct, rather than a forecast of any real world consequence of pandemics.

Assessing the economic impact C19 intervention – analytical approaches

Micro-economic models of C19[46] and initial observational data suggest that the immediate direct impact on poverty of widespread physical distancing or 'lock down' will be

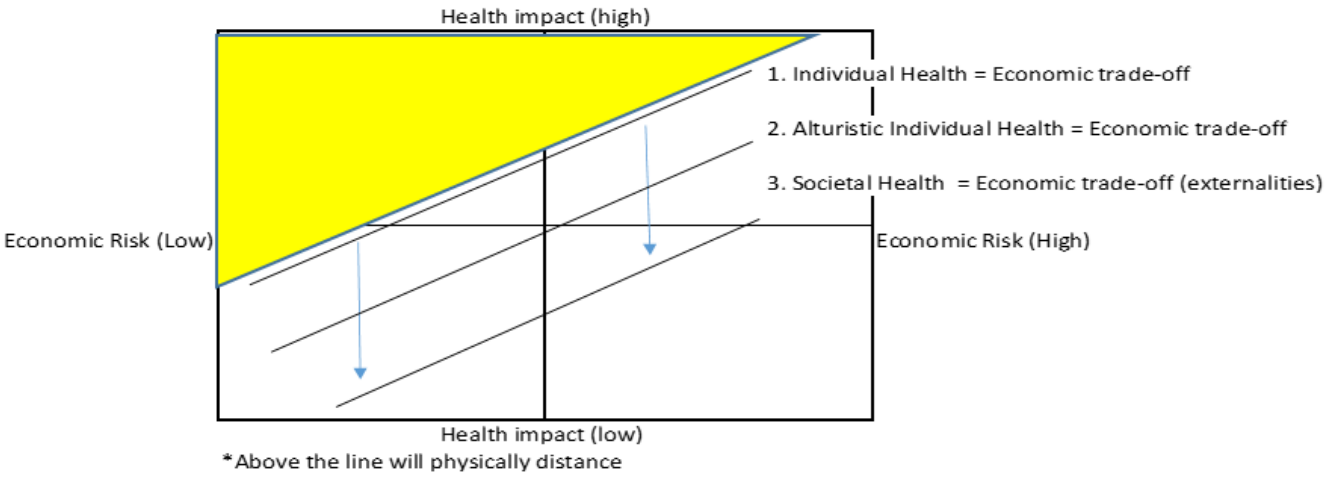

Figure 2. Incremental impact of Covid-19 response on compliance with physical distancing.

substantial in LMICs[47]. Two macro-economic modelling approaches have also been used to date to explore the macro-economic impact of such policies in LMICs. First, aggregate dynamic stochastic general equilibrium (DSGE) models have been used to focus on characterising optimal social planning and explore the balance between economic and health burdens at an aggregate level[40,41,48–50]. For example, the early use of DSGE models in the US suggested that the scale-up of testing could reduce the economic costs of current lockdown by 2% of GDP[41], and that the optimal levels of US teleworking could approach 40% at peak levels[40].

Second, multi-sector computable general equilibrium (CGE) models have explored the economic impact of C19 considering interactions between different sectors (e.g. social distancing-related sector-specific business and school closures, and private mitigation behaviours including reduced demand for entertainment, recreational activities, etc.) CGE model applications to infectious diseases are numerous and stretch back to the early stages of the HIV epidemic. The first global CGE applications to respiratory pandemic diseases appeared in the early-2000s, including analyses of SARS[51] and pandemic influenza[52]. Early studies of macro-economic impact in the UK estimated that the period of lockdown would reduce deaths by 95%, but increase the total cost to the UK economy, in 2020, to 29.2% of GDP unless additional mitigating economic policies were put in place to reduce economic co-harms of the suppression strategy[31]. In comparison, mitigation strategies imposed for 12 weeks would reduce deaths by 29%, but with a total cost of 13.5% of GDP.

Globally a 2.5% drop in GDP is estimated for LMICs, and if C19 continues, in the longer-term LMICs (excl. China) could suffer a 4.8% in GDP[53]. There is, however, still a dearth of work examining the integrated health and macro-economic impact of different public health policies in LMICs. None of the macro-economic studies for LMICs to date explicitly consider disaggregated impact for different population groups and specifically estimate the numbers of households falling into poverty. Yet, there is substantial evidence from other infectious diseases that suggests this impact may be high. For example, between 27-83% of households affected by tuberculosis in LMICs experience costs that are catastrophic (defined as exceeding 20% of household income)[54]. Households encountering catastrophic costs due to poor health often respond by adopting coping strategies, which can potentially cause further long term harm, including drawing high-interest loans, selling productive assets (such as livestock), or taking children out of school[55].

The need for context specific evidence from LMICs

Any health economic evidence generated to inform C19 policy needs to reflect the specific structural features of different LMIC economies and health sectors, including the values of specific populations. However, during a pandemic this presents a sizeable challenge given the large numbers of countries involved and limited capacity both to generate and conduct health economic analyses. We therefore identify below the critical and urgent context specific data needs required to inform the applications of modelling efforts outlined above to LMICs.

Population characteristics

Fundamentally, any modelling outcomes estimating economic and health trade-offs around the C19 response will be driven by the overlap between populations that are most at risk of infection, at risk of dying, at risk of transmitting C19 or provide most risk to the economy (or vulnerable to income-related shocks). Figure 3 extends Figure 2 to include not just the health risks faced by the individuals, but the risk that they cause harm to others. The yellow shaded area is the population who complies with physical distancing, but do not consider their harm to others. In this example a whole segment of the population who is at high risk of transmission, but has high economic risk and low individual health risk do not comply.

The three dimensions of risk factors are in turn are determined by a combination of biology and social and economic behaviour, that may be correlated (e.g. socioeconomically disadvantaged groups may be more likely to be in poor health and therefore

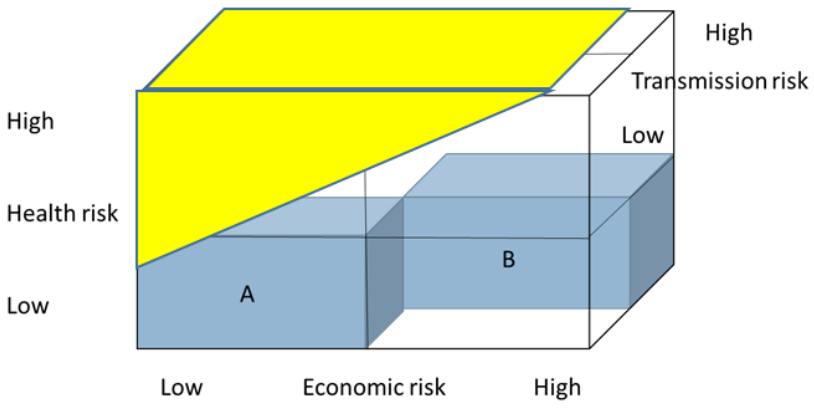

Figure 3. Impact on compliance, including transmission risk.

susceptible to severe disease). The challenge for LMIC policy makers, and the scientists/economists who support them, is to better identify these interactions, and develop an understanding that these relationships are dynamic. In other infectious diseases, the relationship between economic risk and these two dimensions of health risk, and the mixing between these populations has been pivotal in how pandemics progress over time, with diseases becoming endemic in populations with high economic risk[56].

Estimates of C19 transmission are best made estimated dynamically and predictions of the epidemic curve made by country. C10 transmission models currently rely on population specific demographic data[57] and often on non- context specific social contact patterns, using synthetic contact matrices that extrapolate survey data from other settings based on household and societal characteristics[58]. To estimate and understand both health and economic impact, setting specific data on how social contacts vary by population groups and socio-economic status is urgently required. For example, the probability of being infected by a particular person is likely to be higher for those in close and regular contact (e.g. household contacts) or those in overcrowded working and living conditions; but we know little about how those in these conditions interact with different population groups.

Household capacity and resilience

There is also an urgent need to understand the many context specific barriers that prevent individuals, households and firms from complying with C19 policies optimally and may make trade-offs between health and economic welfare more severe, particularly for poor populations. Epidemiological models can also be used to explore and identify between economic risk and disease, but still require primary data to identify explicit links between the specific constraint and disease related behaviour and progression[59]. Stigma and mental health issues may constrain the ability of individuals to protect themselves. The extent of trust in institutions and social values may influence the extent of adherence to physical distancing. Even when willingness is there, there may be demand side constraints related to economic status, including the affordability and allocation of goods that protect against C19 infection to those most in need, such as basic commodities for hand washing and face-masks. Housing conditions may also be a critical constraint; for example, in many urban informal settlements in LMICs, houses are crowded and one-roomed and have shared and/or outdoor toilets and water sources, making stringent physical distancing impossible.

There are also a wide range of factors that influence the resilience (and reduce the economic risk) of employed households to mitigate economic impacts, including access to loans at affordable interest rates, employment conditions, and the ability to sell assets[60]. However, for households relying on daily subsistence income, or on foreign remittances, the poverty impact of being unable to work may be severe. While many HIC countries have strong social protection mechanisms in place, many LMICs have weaker mechanisms for providing emergency transfers to populations[61]. There is a substantial body of economic evidence on the extent to which cash transfers and social protection in LMICs both impact health outcomes and reduce economic risk, which can support governments to design appropriate mechanisms[59,62–66], and methods such as benefit incidence than can capture the way in which costs and benefits of different public policies impact different population groups[67,68].

Health sector burden and capacity

Case fatality risks for C19 are also dependent on local health services and the existing disease burden/co-morbidities, which vary substantially by setting and may also be correlated with economic status[69,70]. Yes, there is a dearth of information on how different socio-economic groups are accessing both C19 and non-C19 services. In some settings the limiting health system constraint may, however, not be bed capacity, but staff, oxygen, medicines, or protective equipment[24]. Other elements of capacity such as the strength of the surveillance and testing systems may allow governments to exit physical distancing at an earlier point in the epidemic and reduce economic losses. However, depending on both physical and financial access these may also be less accessible to poorer populations. Previous studies on TB provide an example of how to characterise these constraints[25,71] and explore their impact on infectious disease trajectories and the eventual cost-effectiveness of different interventions[72].

Improving the governance for assessing C19 policies

LMIC governments will need to continuously refine their policies to align with how their populations value health, economic welfare and different dimensions of health. C19 has brought difficult trade-offs, commonly faced by the health sector, to the forefront of public scrutiny. There are several standard frameworks that are typically used to ensure that health policy processes operate in an evidence-based, accountable, and fair manner considering both economic and epidemiological evidence. The analytical frameworks for designing such processes have been developed in the context of HTA in HICs, but also applied in LMICs such as China, South Africa, India[31], Thailand and Indonesia[73].

Table 1 illustrates the types of health and economic trade-offs facing LMICs when making policy choices on social distancing, school closure and expanding health sector capacity to address C19. In their choices, policy makers would ideally maximize public goals such as health, economic welfare and social welfare - yet, in reality, choices impact differently on these goals. Formalised structured decision-making tools such as multi criteria decision analysis (MCDA) can support policy makers in making their choices, and Table 1 provides the starting point of this approach based on the public goals as mentioned in this paper. A complete MCDA would provide a comprehensive overview of the performance of policy choices on all public goals (possibly involving scoring of the performance and weighing of public goals), as input for the policy making process. Yet, given the urgency of C19 response,

Table 1. Framework for policy trade-offs in the Covid-19 response (with examples).

Policy choices/ public goals	Health		Economic welfare	Social welfare
	Impact on Covid-19 related health	**Impact on other diseases**		
Physical distancing[#]	Reduced infections in overall population	Increased mental health problems because of isolation; improved health through improved air pollution	Reduced household income and consumption through reduced tourism, export, foreign direct investment and inflationary pressure	Compromised civil liberties; unrest; food insecurity
School closure	Reduced infections in children; reduced infections in overall population	Increased mental health problems because of isolation Increased morbidity and mortality from delayed presentation and treatment delays	Reduced income if parents have to take time off work without compensation; loss of income for education sector workers if they are not compensated; increased demand for substitutes like online education	Increased exposure of children to violence and exploitation; poor nutrition if children rely on meals provided at schools; stress for teachers for creating and maintaining online learning; challenges measuring and validating learning.
Expanded health sector response	Reduced mortality and morbidity	Treatment delays	Increased health insurance premiums	Displacement of other public expenditure, such as on culture.

Various physical distancing policies are possible, depending on duration and restrictions. Such policies have different impacts on public goals and could be listed as different policy choices here.

policy makers may not be able to conduct a complete MCDA and will make the trade-offs in a more deliberative manner[74].

At the core of deliberative approaches is the recognition that policy makers are accountable to the populations they serve and thus need to ensure a legitimate decision-making process. Legitimacy here refers to the reasonableness, or fairness, of policy choices as perceived by stakeholders, which is an important prerequisite for broad societal support for these policies[74,75]. For example, the decision whether or not to enforce social distancing should include a consideration of the (potentially competing) interests of people and sectors with varying levels of health and economic vulnerability. Stakeholders are likely to have a wide range of social values and interests that result in different perceptions of what makes particular C19 policy choices valuable, for example limiting the spread of the epidemic, reducing impact on business, and limiting social expenditure. In such processes, stakeholders may reasonably disagree on what values can be used to guide decisions, often explicitly identifying a diverse range of criteria by which to assess policy[9].

The combination of the complex mesh of trade-offs, described in previous sections, and the wide range of social values, discussed above, indicates that there is a need for careful deliberative processes in which all stakeholders can meaningfully participate and their values be considered, informed as much as possible by evidence. Such processes should be transparent in the sense that there is clarity between which stakeholders and values are involved, what the available evidence is (and its quality), and how decisions are being taken. The decisions themselves should be made available to the public, including the evidence presented and its argumentation, to ensure public engagement, debate and support for the resulting C19 response. However, given the urgency of the decision-making, such broad consultative processes may not always be feasible and may depend on the stage of the epidemic. At the minimum, policy makers should include key stakeholders representing the health, economic and social dimensions of welfare in its advisory committee to adequately consider all related trade-offs, alongside scientific and economic evidence.

Conclusion

LMIC policy makers face major challenges in defining their optimal policy response to C19. We call for increased in investment in health economics evidence and evidence informed deliberative policy decisions that consider both health and economic impact. The need is acute in LMICs given the dearth of information and lack of access to both data and joint epidemiological and economic decision support models. There is a risk that countries are forced to rely on qualitative debate, or simple analytical approaches to make decisions, often with severe consequences.

We have highlighted the large body of previous work that can form the basis of that evidence generation to support C19 policy in LMICs, which demonstrates emerging collaboration between economists and epidemiologists, both within the scientific community and the policy arena. Critical priorities include: creating greater capacity (specifically in LMICs) to conduct combined economic and epidemiological modelling and support government decisions; parameterising models with enhanced

mapping of social contact data that includes economic status; tracking of the opportunity costs incurred in the health sector, including an improved understanding of the effectiveness of lower cost health sector intervention; economic evaluation to estimate the value of new C19 technologies that fully considers future risk; and communications to support decision makers and the general public understand the uncertainty and evidence quality of current models. However, ultimately, while scientists and academics can generate evidence, and enquire and explore the values of populations, trade-offs between health, populations and the economy require transparent and consultative processes if population welfare is to be protected during the C19 crisis.

Data availability

No data are associated with this article.

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Open Peer Review

Current Peer Review Status: ✔ ✔

Version 2

Reviewer Report 31 August 2022

https://doi.org/10.21956/wellcomeopenres.19889.r51682

✔ **Kalipso Chalkidou**
[1] Global Health and Development Team, Imperial College London, London, UK
[2] Global Health Policy, Center for Global Development, London, UK

The authors have addressed my comments.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 09 August 2022

https://doi.org/10.21956/wellcomeopenres.19889.r51683

✔ **Beverley Essue**
Institute of Health Policy, Management & Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

I'm happy with the revisions made and believe this paper is stronger and an important contribution.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of

expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 28 June 2021

https://doi.org/10.21956/wellcomeopenres.18017.r43687

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Sujata Mishra
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Overall, this is a very pertinent and timely article that discusses the challenges and need to integrate economic evidence with health outcomes and broader outcomes to provide an optimal background for priority setting for Covid-19 (or any pandemic) in a LMIC setting.

I would, however, urge that the authors consider pitching this piece as “Integrating economic and health evidence to inform pandemic policy in LMICs” taking Covid-19 as a case study as the lessons are certainly relevant for future pandemic preparedness planning.

The following comments are suggested to support strengthening the paper:

Introduction: Paragraph 2

1. Define UHC before using the acronym.

Broadening the assessment of health sector policy under C19: (*overall, this section could benefit from additional references).

1. Acknowledge that both C19 as well its evidence is rapidly evolving and needs urgent attention as the associated mortality and morbidity is relatively high in many LMICs. Thus, the within health-sector trade-offs need to be assessed instantly as compared to any other health issue. A challenge that is unique to the pandemic trajectory.

2. Elaborate on how you think health interventions and economic policy goals interact. In another place, the authors note that they can compete with each other, particularly in LMICs where there are limited resources to be allocated between sectors. Needs citations.

3. With most countries (including LMICs) making progress towards UHCs, how a pandemic like C19 affects government budgets is also a consideration for future planning needs and could

be raised here as well.

4. Some countries particularly LMICs with regions with higher population density, it may be impossible to adhere to physical distancing to begin with. Many of the resources including access to water, sanitation and sometimes food etc. are at the community level. How should this context-specific variability be accounted for in the modelling?

Assessing trade-offs across the health sector
Paragraph 1: Perhaps may be slightly misleading to have this data here. Is there an estimate for LMICs? Health systems in HICs and LMICs are quite different. So, I assume preventing C19 death in LMIC, may have a very different QALY and life expectancy as compared to UK. If the data point remains in the paper, consider adding this explicit caveat.
Paragraph 2: Is there evidence on how the rule of rescue has been applied during other health emergencies in LMICs? Is it equally applicable in LMICs and HICs? Needs a bit more elaboration.
Paragraph 4: "While many LMICs have now mitigated the C19, …" I believe the context has changed since this paper was submitted (and this review is overdue!) With multiple waves of C19 and vaccine inequalities, this statement needs revision.
Informing C19 policy choice considering trade-offs between health and wider economy (*This section would benefit from additional references).
Paragraph 4: Why does one see this reduction? Is it because LMICs have a lower willingness to pay for each additional life saved?

Estimating the impact of C19 without intervention – analytical approaches
Paragraph 1: First, I suggest using perceived health risk instead of a health risk. On most occasions, the true/actual risk (both health and economic) is unknown to the agent/decision maker.
Second, perhaps this needs more elaboration as to why someone with low economic risk may voluntarily choose to physically distance. I wonder if there may be moral hazard issues particularly if economic cost is lower. For example someone with health insurance, may behave riskier owing to the fact that he/she is protected financially for their risky behaviour.
Third, authors also need to discuss what happens to people who have higher health risk as well as economic risk (poor people with substantial financial and health burden)? Where do they lie in the figure? Will they also behave riskily? Will a social protection policy help in pushing these people to line 2?
Finally, consider adding references to the theory underpinning this figure. Has this figure/idea been used before while modeling cost of pandemic (e.g. HIV)?

The need for context specific evidence from LMICs
Population characteristics - Paragraph 1:
"Figure 3 extends Figure 1 to include not just the health risks faced by the individuals, but the risk that they cause harm to others." – I think the Authors mean Figure 2 instead of Figure 1?

Paragraph 2: I think it is important here to also identify people who have high economic risk and high health risk.

Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Partly

Is the Open Letter written in accessible language?
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Health Systems Research, Health economics, Health financing, Equity, Priority setting evaluation.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 29 May 2022

Anna Vassall, London School of Hygiene & Tropical Medicine, London, UK

We thank both reviewers for their comments, all of which we have addressed and greatly improve the paper.

Overall, this is a very pertinent and timely article that discusses the challenges and need to integrate economic evidence with health outcomes and broader outcomes to provide an optimal background for priority setting for Covid-19 (or any pandemic) in a LMIC setting. I would, however, urge that the authors consider pitching this piece as "Integrating economic and health evidence to inform pandemic policy in LMICs" taking Covid-19 as a case study as the lessons are certainly relevant for future pandemic preparedness planning.
Thank you for your comments. After a busy period conducting some of the work we originally suggested in this piece at the start of the pandemic, we are now responding to reviewer's comments. We agree with the above and have made edits that highlight this paper's broader relevance for future pandemics. While time has moved on, we think it remains useful going forward to map out the concepts and principles around integrating evidence. Without writing a new piece we would like to now ensure this letter is indexed in Medline etc, as part of the body of literature the authors produced during the pandemic. While we add some new references, we have not rewritten this piece as a review of the Covid response – it remains a viewpoint on the factors that should be generally considered in economic evaluation of pandemic responses. During the pandemic we published a living review of the literature integrating health and economics on C19economics.org. We have also recently submitted a systematic review of the

models used to integrate health and economic impact used in during the pandemic to another journal, and published an interim review: Saadi N, Chi YL, Ghosh S, Eggo RM, McCarthy CV, Quaife M, Dawa J, Jit M, Vassall A. Models of COVID-19 vaccine prioritisation: a systematic literature search and narrative review. BMC Med. 2021 Dec 1;19(1):318. doi: 10.1186/s12916-021-02190-3.
The following comments are suggested to support strengthening the paper:
Introduction

1. Paragraph 2. Define UHC before using the acronym. *Done*

1. Broadening the assessment of health sector policy under C19: (*overall, this section could benefit from additional references). *Done – we have now added further references*

1. Acknowledge that both C19 as well its evidence is rapidly evolving and needs urgent attention as the associated mortality and morbidity is relatively high in many LMICs. Thus, the within health-sector trade-offs need to be assessed instantly as compared to any other health issue. A challenge that is unique to the pandemic trajectory. *We agree and have now emphasised the importance of rapid analyses, by adding the following text:*

"Health impact of pandemics such as C19 can rapidly evolve, and therefore **policy responses and the analytics to inform them need to be instantaneous**, despite the complexity involved."

1. Elaborate on how you think health interventions and economic policy goals interact. In another place, the authors note that they can compete with each other, particularly in LMICs where there are limited resources to be allocated between sectors. Needs citations.

We agree with this statement and have added the following text:
"Health, interventions and economic policy goals interact with one another and are 'dynamic' in the sense that ill health impacts on economic and social welfare. Ill-health can impede the ability to work or exasperate economic inequities. Likewise, improvements in economic and social welfare can substantially impact health and health equity."

1. C19 affects government budgets is also a consideration for future planning needs and could be raised here as well.

We agree and have added text:
"Therefore, C19 policy may require **rapid changes to the balance between public sector and private expenditure across the economy, having <u>short- and long- term implications for government budgets</u>.**"

1. Some countries particularly LMICs with regions with higher population density, it may be impossible to adhere to physical distancing to begin with. Many of the resources including access to water, sanitation and sometimes food etc. are at the community level. How should this context-specific variability be accounted for in the modelling?

This is an important point. We now have elaborated with:
*"*Finally, it is highly likely that both health and economic impacts will heterogeneous across populations, and **responses to pandemics will need to reflect local health, social and economic constraints."**
Assessing trade-offs across the health sector

1. Paragraph 1: Perhaps may be slightly misleading to have this data here. Is there an estimate for LMICs? Health systems in HICs and LMICs are quite different. So, I assume preventing C19 death in LMIC, may have a very different QALY and life expectancy as compared to UK. If the data point remains in the paper, consider adding this explicit caveat.

Agreed, we have now changed the reference to one that relates to LMICs, see:
*"*Estimates of DALYs averted for C19 for LMICs found that disability from C19 would increase DALYs lost by up to a third [17]".

1. Paragraph 2: Is there evidence on how the rule of rescue has been applied during other health emergencies in LMICs? Is it equally applicable in LMICs and HICs? Needs a bit more elaboration.

We could not find a discussion of this in specifically related to LMICs. There has been some discussion of prioritising urgent services, those where health would decline substantially if not treated quickly, but we could not find additional material, so did not change the text substantially apart from being clear this work has primarily been considered in respect of HICs. See Blanchet K, Alwan A, Antoine C, Cros MJ, Feroz F, Amsalu Guracha T, Haaland O, Hailu A, Hangoma P, Jamison D, Memirie ST, Miljeteig I, Jan Naeem A, Nam SL, Norheim OF, Verguet S, Watkins D, Johansson KA. Protecting essential health services in low-income and middle-income countries and humanitarian settings while responding to the COVID-19 pandemic. BMJ Glob Health. 2020 Oct;5(10):e003675. doi: 10.1136/bmjgh-2020-003675. PMID: 33028701; PMCID: PMC7542611.

1. Paragraph 4: "While many LMICs have now mitigated the C19, …" I believe the context has changed since this paper was submitted (and this review is overdue!) With multiple waves of C19 and vaccine inequalities, this statement needs revision.

We agree and have deleted this sentence

Informing C19 policy choice considering trade-offs between health and wider economy (*This section would benefit from additional references).

1. Paragraph 4: Why does one see this reduction? Is it because LMICs have a lower willingness to pay for each additional life saved?

Yes, this is partially correct. LMICs have a lower ability to pay (and higher opportunity costs), so may be less willing to pay

Estimating the impact of C19 without intervention – analytical approaches

1. Paragraph 1: First, I suggest using perceived health risk instead of a health risk. On most occasions, the true/actual risk (both health and economic) is unknown to the agent/decision maker.

We agree and have now edited the text accordingly

2. Second, perhaps this needs more elaboration as to why someone with low economic risk may voluntarily choose to physically distance. I wonder if there may be moral hazard issues particularly if economic cost is lower. For example someone with health insurance, may behave riskier owing to the fact that he/she is protected financially for their risky behaviour.

This is a good point. We are supposing that those with a high health risk and low economic risk (in terms of income effect) may be able to distance, but we do not examine the reasons for that

low risk. It could be because they are able to work from home, or for reasons as you say that they are socially protected. We have added a reference (Sweeney et al, that examines this in more detail).

1. Third, authors also need to discuss what happens to people who have higher health risk as well as economic risk (poor people with substantial financial and health burden)? Where do they lie in the figure? Will they also behave riskily?

We do not know the answer to this question whether health or economic risk will be the most pivotal. We have edited the text to highlight this specific group, and that this is unclear.

1. Likewise, those facing some of those facing either both high or low risks in both domains may chose not to distance. Will a social protection policy help in pushing these people to line 2? Finally, consider adding references to the theory underpinning this figure. Has this figure/idea been used before while modeling cost of pandemic (e.g. HIV)?

We have now included text on social protection The figure has not been used in pandemics previously it is our own framing. However, several theoretical economic models have applied the same form, defining a behavioural function that considers both health and economic risk
The need for context specific evidence from LMICs

1. Population characteristics - Paragraph 1:
"Figure 3 extends Figure 1 to include not just the health risks faced by the individuals, but the risk that they cause harm to others." – I think the Authors mean Figure 2 instead of Figure 1? – *Done. Thank you for point this out*

1. Paragraph 2: I think it is important here to also identify people who have high economic risk and high health risk. - *Done*

Competing Interests: No competing interests were disclosed.

Reviewer Report 11 December 2020

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Timely and well written piece well worth indexing. A few comments on additional refs/points of

view (with apologies for self referencing!) below:

1. In the list (1-7) presented early on a few points on (1) where the *'health as usual' i.e. current levels of population"* may need explaining; on (2) where I I wonder if you could make your examples a bit more explicit/obvious? e.g. relationship between poverty and unemployment on one hand and neonatal mortality or preventable deaths? e.g. [1]; (3-4) Not sure how 3 and 4 are different.

2. In the assessing trade offs across health sector section, and though you do a lot of this below, I wonder whether you might want to references non COVID health costs of the COVID response. You do cite below work on TB HIV malaria vaccination MCH etc. from LMICs but also work on cancer and other NCDs n HICs - e.g. [2] not specific to COVID, [3] perhaps also worth citing this and this where these are summed up. Also [4] from OECD and this etc.

3. At the end of this section you discuss lack of evidence; and whilst you do introduce the importance of process later on I wonder whether it is the lack of evidence or rather of a process which brings all the evidence together - in a sense if the focus of media/gov is on COVID then the rule of rescue is applied to COVID alone with limited consideration of the invisible costs on other conditions...so we need a process first perhaps? Which may well also boost the evidence base? Again you discuss below but perhaps raise the issue (which is the centre piece of the analysis) early on?

4. Where you discuss micro (health) econ models, is it worth discussing here the trade offs of COVID tech adoption from drugs to tests to the vaccine(s)? E.g. this, [5], perhaps also [6] and Cam's piece?

5. On VSL - You do discuss the controversy of VSL - in the context of the UK a VSL approach would mean move to a Cancer Drugs Fund for absolutely everything NICE considers. I am not sure how one can put in perspective the magnitude of VSL estimates vs the reality of the NHS (and worse even) a LMIC health budget. Worth doing though.

6. Same section where you discuss health vs economic welfare indeed - I wonder also whether you want to discuss other refs here giving a negative net benefit or offer a more nuanced approach (i.e. suggest cut offs beyond which things cease to be CE etc.) - for HICs and LMICs eg [7], this, [8, 9] and similar work undertaken in Malawi. I have serious issues with VSL in the UK and LMICs (worse even extrapolating from overestimated UK and US estimates!) to the extent that it is explicitly uninterested in opportunity costs.

7. A lot of the early modelled estimates of HIV impact on economy ended up not materialising through the full cost approach continues to be used as an advocacy tool (albeit not very successfully as far as MOF are concerned) - esp the early modelled impact of loss of HCW from HIV, with the major returns coming in these analyses from longer lives rather than real GDP growth. Worth flagging? This reminded me - not sure if publicly available yet but you know this lit a lot better! [10]

8. I am not a fan of unmitigated and I wonder whether you might want to discuss "unmitigated" here - I and others discuss this here and I believe it is worth adding a sentence or two on what exactly unmitigated means in the real world and how useful (and

indeed how circular) such numbers end up being when used to inform policy OUTSIDE a more holistic in terms of evidence and of values process for which you call.

9. Linked to the above and the 490,000 deaths number, I think the whole issue with the way this outbreak has been dealt with is the over-reliance on single point highly uncertain estimates of impact on health due to COVID as opposed to a balanced approach to costs and benefits of different response options within and beyond health. It is this nuance which is missing when the whole discourse is driven by such estimates. This by Andrew in the FT sets it out nicely.

   So here I would caveat this estimate (which, arguably and based on some of the modellers' own assessments cannot be trusted for anything beyond a two week time horizon [11]) and also caveat the "prescription" for reducing the R, again modelled out ex ante but when assessed ex post based on (however imperfect) actual observations seem not to have worked that well (lack of evidence is not the same as evidence of things not working but it ought to moderate one's confidence levels!). A few references to consider and consider citing to this effect: [12], [13], this, this and even this next one where the authors seem to be arguing against their data - Fig 3 suggests to me one cannot declare NPIs have worked[14] and one more[15].

10. On use of HTA in LMICs perhaps (and forgive this includes one of mine!) [16] or say for India [17] and the 2014 HITA resolution by WHA.

11. In Table 1 I would as a minimum add increased mortality and morbidity (to follow on from treatment delays but also delayed presentation etc.) in the column on other health impacts of the policy response. Otherwise the table seems to suggest that the only mortality/morbidity effects come from COVID.

12. On governance worth also citing the WHO WB Gates iDSI CMCC work (which our Thai leads are trying to get published in peer reviewed journal).

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Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Partly

Is the Open Letter written in accessible language?

Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Health policy; health economics.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 29 May 2022

Anna Vassall, London School of Hygiene & Tropical Medicine, London, UK

REVIEWER 2
Timely and well written piece and well worth indexing.

Thank you for your comments. We have been busy with Covid work, and some time has passed since your review, but hope that the paper remains relevant as part of the broader range of work now conducted during the pandemic. We now have other papers reviewing work done in this area, so did not want to fully update this paper. However, we have made several edits to make this relevant for future pandemics. We are keen that the paper is indexed and have addressed your comments below.

A few comments on additional refs/points of view (with apologies for self-referencing!) below:

- In the list (1-7) presented early on a few points on (1) where the *'health as usual' i.e. current levels of population"* may need explaining; on (2) where I I wonder if you could make your examples a bit more explicit/obvious? e.g. relationship between poverty and unemployment on one hand and neonatal mortality or preventable deaths? e.g. 1; (3-4) Not sure how 3 and 4 are different.

Thank you for these references. We have referred now to maternal mortality to point 1 and in point 4, added in employment. It is correct that points 3 and 4 are very related, but we thought good to have one examining the consequences of the division between government and one on household expenditure, and another focusing on the impact on government expenditure over time.

- In the assessing trade offs across health sector section, and though you do a lot of this below, I wonder whether you might want to references non COVID health costs of the COVID response. You do cite below work on TB HIV malaria vaccination MCH etc. from LMICs but also work on cancer and other NCDs n HICs - e.g. 2 not specific to COVID, 3 perhaps also worth citing this and this where these are summed up. Also 4 from OECD and this etc.

Thank you for the references (again!). They are interesting and useful in this response for readers interested in HICs. As this paper focuses on LMICs we only included the ones from LMICs.

- At the end of this section you discuss lack of evidence; and whilst you do introduce the importance of process later on I wonder whether it is the lack of evidence or rather of a process which brings all the evidence together - in a sense if the focus of media/gov is on COVID then the rule of rescue is applied to COVID alone with limited consideration of the invisible costs on other conditions...so we need a process first perhaps? Which may well also boost the evidence base? Again you discuss below but perhaps raise the issue (which is the centre piece of the analysis) early on?

We very much agree Providing evidence alone, however, is insufficient, and importantly the

production of evidence should be matched with 'evidence based deliberative processes 'that build on current health technology assessment processes but can respond with the rapidity required for pandemics. We have added text to strengthen this point early in the paper.

- Where you discuss micro (health) econ models, is it worth discussing here the trade offs of COVID tech adoption from drugs to tests to the vaccine(s)? E.g. this, 5, perhaps also 6 and Cam's piece?

Agree and we have substituted the current reference for reference 6 to determine the optimal allocation of resources between different diagnostic, treatment, and preventative interventions.

- On VSL - You do discuss the controversy of VSL - in the context of the UK a VSL approach would mean move to a Cancer Drugs Fund for absolutely everything NICE considers. I am not sure how one can put in perspective the magnitude of VSL estimates vs the reality of the NHS (and worse even) a LMIC health budget. Worth doing though.

Agree that applying VSL without any empirical estimation from LMICs is limited. We have highlighted this is the text. Unfortunately, we could not think of a quick way of highlighting this concern further, although agree with the general point.

- Same section where you discuss health vs economic welfare indeed - I wonder also whether you want to discuss other refs here giving a negative net benefit or offer a more nuanced approach (i.e. suggest cut offs beyond which things cease to be CE etc.) - for HICs and LMICs eg 7, this, 8, 9 and similar work undertaken in Malawi. I have serious issues with VSL in the UK and LMICs (worse even extrapolating from overestimated UK and US estimates!) to the extent that it is explicitly uninterested in opportunity costs.

Agreed. We added text at the end of the VSL section and added in reference 9 to this section

A lot of the early modelled estimates of HIV impact on economy ended up not materialising through the full cost approach continues to be used as an advocacy tool (albeit not very successfully as far as MOF are concerned) - esp the early modelled impact of loss of HCW from HIV, with the major returns coming in these analyses from longer lives rather than real GDP growth. Worth flagging? This reminded me - not sure if publicly available yet but you know this lit a lot better! 10

Agree and we have added text. The issue with the initial estimation of HIV impact, is in part related to the issue below, that early estimates (even with HIV) tended to be of unmitigated epidemics with very little knowledge of infectiousness and transmission. It would be wrong to imply that early models got it wrong, they may have got it right given what was known at the time, but it is true to say that some of the forecasts overestimated the impact on African growth that followed (given all the drivers of growth). We could not find the reference below to ascertain which of these reasons (flawed models, uncertainty around disease, uncertainty around the economy, economic policy changes, health policy changes) led to a less catastrophic impact than some originally forecast.

- I am not a fan of unmitigated and I wonder whether you might want to discuss "unmitigated" here - I and others discuss this here and I believe it is worth adding a sentence or two on what exactly unmitigated means in the real world and how useful (and indeed how circular) such numbers end up being when used to inform policy OUTSIDE a more holistic in terms of evidence and of values process for which you call. Linked to the above and the 490,000 deaths number, I think the whole issue with the way this outbreak has been dealt with is the over-reliance on single point highly

uncertain estimates of impact on health due to COVID as opposed to a balanced approach to costs and benefits of different response options within and beyond health. It is this nuance which is missing when the whole discourse is driven by such estimates. This by Andrew in the FT sets it out nicely. So here I would caveat this estimate (which, arguably and based on some of the modellers' own assessments cannot be trusted for anything beyond a two week time horizon 11) and also caveat the "prescription" for reducing the R, again modelled out ex ante but when assessed ex post based on (however imperfect) actual observations seem not to have worked that well (lack of evidence is not the same as evidence of things not working but it ought to moderate one's confidence levels!). A few references to consider and consider citing to this effect: 12, 13, this, this and even this next one where the authors seem to be arguing against their data - Fig 3 suggests to me one cannot declare NPIs have worked14 and one more15.

This is a contentious issue, that was critical in the early forecasts of Covid impact. While unmitigated estimates are often used in the very initial stages of pandemics to alert policy makers to the extent of any catastrophic impact if nothing is done, they are often made based on highly scarce data, and under considerable uncertainty. Moreover, they cannot be validated as a policy response quickly follows and therefore in reality 'an unmitigated epidemic cannot be observed'. Moreover, (as your references suggest), while unmitigated epidemics are argued to provide a useful comparator against which to measure the impact of interventions, even without government intervention they are unlikely to occur, as individuals within populations will act, and therefore unmitigated pandemics remain a conceptual construct, rather than a forecast of any real-world consequence of pandemics.

In essence, we agree with your concern that early estimates need to be seen and responded to as highly uncertain. However, it is important to also recognise that even if early on pandemics are highly uncertain, it is a risk that is more important to policy, and faced with this policy may be precautionary. Precautionary policies do not necessarily fail to recognise uncertainty but can instead be seen as a response to it.

- On use of HTA in LMICs perhaps (and forgive this includes one of mine!) 16 or say for India 17 and the 2014 HITA resolution by WHA.

Agree and have added reference 16. Thank you for this reference.

- In Table 1 I would as a minimum add increased mortality and morbidity (to follow on from treatment delays but also delayed presentation etc.) in the column on other health impacts of the policy response. Otherwise the table seems to suggest that the only mortality/morbidity effects come from COVID.

Done

- On governance worth also citing the WHO WB Gates iDSI CMCC work (which our Thai leads are trying to get published in peer reviewed journal).

We could not find so were not able to add.

Competing Interests: No competing interests were disclosed.