



Modelling the health impacts of disruptions to essential health services during COVID-19

Module 1: Understanding modelling approaches for sexual, reproductive, maternal, newborn, child and adolescent health, and nutrition



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ISBN 978-92-4-002769-5 (electronic version)

ISBN 978-92-4-002770-1 (print version)

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Acknowledgements

This guide was developed through a broad collaboration of technical focal points from the World Health Organization (WHO) and in consultation with key partner stakeholders. The development and production of the guide were coordinated by Melanie Bertram, Theresa Diaz, Raymond Hutubessy and Katelijjn Vandemaele.

In *Module 1: understanding modelling approaches for sexual, reproductive, maternal, newborn, child and adolescent health, and nutrition*, the models were written by Jon Pedersen (Mikro) and coordinated by Theresa Diaz (WHO), Danzhen You (United Nations Children's Fund, UNICEF) and Howard S. Friedman (United Nations Population Fund, UNFPA).

This module was developed through a collaboration of the following organizations and individuals: Elaine Borghi (WHO), John Borrazzo (Global Financing Facility for Women, Children and Adolescents), Kate E. Gilroy (MOMENTUM Knowledge Accelerator – JSI), Ulla Griffiths (UNICEF), Chika Hayashi (UNICEF), Ann-Beth Moller (WHO), Jennifer Requejo (UNICEF), Lale Say (WHO), Alyssa Sharkey (UNICEF), Kate L Strong (WHO), William Weiss (Johns Hopkins Bloomberg School of Public Health), Eva Weissman (independent consultant), Denise Lynn Buchner (independent consultant), and Debra Jackson (London School of Hygiene and Tropical Medicine).

The modellers were: Kaja Abbas (London School of Hygiene & Tropical Medicine), Zulfiqar Bhutta (The Hospital for Sick Children), Aatekah Owais (Centre for Global Child Health, The Hospital for Sick Children), John Stover (Avenir Health), Elizabeth Sully (Guttmacher Institute) and Neff Walker (Johns Hopkins Bloomberg School of Public Health). They provided details of their models and input into the document.

Introduction to the guide

Coronavirus disease 2019 (COVID-19) has a wide range of documented effects. It directly causes death and disability for some people infected. However, disruption to essential health services, resources allocated to mitigation and therefore away from essential health service delivery, and the overall impact on the economy and society must also be considered within the response to COVID-19. Understanding the magnitude of all of these effects is an essential part of developing mitigation policies.

Several epidemiological models have been created to assess the potential impact of disruptions to essential health services caused by COVID-19 on morbidity and mortality from conditions other than COVID-19 illness. This guide presents models that have been used to assess these indirect impacts. The effects have been studied in various settings, using a variety of models.

The guide is intended for people who need to understand what the models say, their construction and their underlying assumptions, or need to use models and their outcomes for planning and programme development and to support policy decisions for a country or region.

Of course, an overview of models on COVID-19 is a moving target. Modellers create new models and they revise and improve established ones. Since the field is rapidly developing, it is important to note that modellers may have to overcome limitations or concerns that may be voiced here about approaches. Thus, the document may be revised to reflect these changes if such changes occur.

This document provides an overview and description of models from a technical point of view. The focus is on what the various models do, how they do what they do and the underlying assumptions on which the models are based. The document includes modules on modelling the disruptions caused by COVID-19 to the essential health services of specific health areas or conditions.

Each module will follow the same structure as closely as possible for consistency:

1. introduction to modelling for COVID-19 service disruptions
2. service disruptions in the context of the health area or condition of interest
3. models used in the disease of interest, their strengths and weaknesses, and their interpretation
4. outcomes and use of modelling studies to date
5. conclusion and recommendations for the use of models in the response to COVID-19.

This version of the guide (version 1) includes only the module on sexual, reproductive, maternal, newborn, child and adolescent health, and nutrition. The next version of the guide will contain more modules on other health areas or conditions.

The annexes to the guide comprise a discussion of data sources in general and an annex for each model presented, which gives details of the particular model for modellers and statisticians who wish to have this information.



Module 1: Understanding modelling approaches for sexual, reproductive, maternal, newborn, child and adolescent health, and nutrition

Introduction to Module 1

COVID-19 has a wide range of effects. It causes death and illness, but its indirect negative effects are just as important, such as the disruption to health and society, the resources that have had to be allocated to its mitigation and away from other areas, and the overall impact on the economy and society. Understanding these effects and how policies can eliminate, reduce or mitigate them is crucial.

This module focuses on the effects on health services and societal mechanisms related to maternal and child welfare and survival, as well as sexual, reproductive and adolescent health and nutrition. The effects of COVID-19 have been studied in various settings, using a variety of models. This module provides a technical overview and description of such models. The focus is on what the various models do, how they do what they do and the underlying assumptions on which they are based.

The modelling of the impact of COVID-19 on health outcomes reviewed here has four main processes:

- the dynamics of the disease
- the disruption caused
- mitigation measures
- health outcomes.

In principle, these represent four black boxes, with pathways between them. Models differ in the extent to which they let one or more of the boxes remain black or they open the elements of those boxes, and how they portray the pathways.

For example, the Lives Saved Tool (LiST) was first used for modelling the health impact of health service disruptions related to COVID-19. The model assumed specified levels of disruption expressed as a decrease in coverage of health interventions, and used established knowledge of the effects of interventions on health outcomes. Neither the dynamics of the disease itself nor the actual disruption level experienced in countries was modelled. This is considered a hypothetical scenario. On the other hand, there is the more integrated model of the Institute of Health Metrics and Evaluation. This model combines disease dynamics, population change, economic dynamics and effects, disruptions and health outcomes in an

attempt to mimic as closely as possible realistic disruption data and interactions between multiple competing considerations of policies.

We can distinguish between the following types of models.

- **Models that try to estimate health outcomes depending on levels of disruption.** Such models may assume likely levels of disruption, or base disruption levels on data from particular countries or regions. Other implementations of the same models, as the epidemic develops, may use disruption data from countries to predict specific outcomes.
- **Models that link a specific type of health intervention with disease dynamics (risk–benefit models).** This category includes models that estimate the balance between lives saved by enabling children with a critical disease or injury to seek health care, and COVID-19-related deaths that may occur as a consequence of the care seeking.
- **Models that estimate the consequences on other diseases of disruptions caused by COVID-19.** Here, a main focus is models that try to understand how HIV prevalence may be associated with disruptions caused by COVID-19.
- **Models that integrate disease dynamics, disruptions and outcomes.** These models may limit their focus on a narrow set of outcomes or they may try to construct a comprehensive picture of the health and societal effects of COVID-19.

The purpose of the models may vary, from advocacy linked to what might happen given realistic levels of disruption, to the prediction of what will happen given what is known about the disease and development of disruptions. Models may also focus on the costs and benefits of possible mitigation strategies or policies, measured by different metrics such as lives saved or lost, or economic costs.

The above list of models does not include models of the COVID-19 pandemic dynamics. Several reviews of such models are available. A good source is the multi-model comparison collaboration that has produced both a policy and technical report (1,2). Comparisons of models of the pandemic itself are also available in the literature (3–5).

The target audience for nearly all of the models is public health professionals engaged in COVID-19 management and mitigation from a technical or policy point of view. The model of the Institute for Disease Modelling aims to provide health professionals and families with an individual-level tool to assess the benefits and risks of various care-seeking activities.

Disruptions to sexual, reproductive, maternal and child services caused by COVID-19

Disruptions and changes associated with COVID-19 that affect health have a broad range. In this section, we discuss this range and the available data. The focus is on how data on these disruptions and changes can be used in the models, however, rather than on an assessment of the disruptions themselves. The broader issue of how to monitor the disruptions and their effects is discussed in Part 2 of the World Health Organization (WHO) publication *Analysing and using routine data to monitor the effects of COVID-19 on essential health services: practical guide for national and subnational decision-makers* (6).

Disruptions fall into three main categories:

- social change affecting factors that influence health
- supply of health services
- demand for health services.

Social changes include, for example, shortage of income for households, which may mean they do not have enough money to buy all the food they need, thereby leading to deficiencies in nutrition. These changes may also include shifts in behaviour, such as changes in the number of marriages entered into, alcohol or drug use, sexual behaviour or domestic violence. In addition, social changes may include government-enforced lockdowns that limit health service provision.

The availability of health services may decrease because health personnel fall ill or become fully engaged in treating COVID-19 patients, or because critical resources, such as medicines, are lacking, or the government mandates that specific non-COVID-19 health services are not to be provided.

The demand for health services may change because of fear of seeking services, or difficulties in accessing them. Furthermore, disruptions to transportation or lack of funding for transportation may also constrain access to services and decrease demand.

Few quantitative data are currently available that describe the disruption to health services caused by COVID-19. There are three related reasons for the lack of such data. First, most countries do not have up-to-date data on what the situation was immediately before the pandemic. Most of the data available for societal factors and supply and demand for health services come from surveys, generally done only intermittently. Thus, to a large extent, estimates in early 2020 or in 2019 are projections of the trends seen in past data. Second, few surveys have been done that have estimated the current status of, or trends in, the coverage of health services or health outcomes during the pandemic. Several rapid telephone and online surveys are being carried out but they have neither the detail nor the depth that large-scale surveys have, such as the Demographic and Health Surveys or the Multiple Indicator Cluster Surveys. Third, the pandemic has disrupted the ability of countries to collect routine data. A study carried out by the United Nations Department of Economic and Social Affairs and the World Bank, published in June 2020, found that statistical offices in low- and middle-income countries were often not able to collect survey data through face-to-face interviews and that they did not receive administratively collected data, such as vaccination statistics from health centres. Any individual-level data collection related to the pandemic that was being done was mainly through telephone interviews (7).

Annex 1 describes the data sources on sexual, reproductive, maternal, newborn, child and adolescent health, and nutrition that can support modelling.

Measuring disruptions over time

The COVID-19 pandemic and its associated disruptions have occurred over the course of the past year, while the response to prevent transmission in many countries has happened over less than a year. The pandemic has indirectly resulted in changes in disease prevalence and service coverage during that time.

Epidemiological models of COVID-19 typically have a one-day time cycle for incidence or cases, since the generation interval is measured in days. Most countries supply data on incidence on a daily or near-daily basis. The frequency of administrative reporting of disruptions varies, but for some indicators, data may be reported on a daily, weekly or monthly basis.

In contrast, many disease models that are traditionally used to support service planning use service coverage measures and have been developed with one-year time cycles, meaning that adaptation to the modelling of service disruptions and their impact is being seen only on a yearly cycle. The reason for the one-year time cycle is partly because the available data for interventions and their impacts are usually collected only annually, and partly because the demographic models that have traditionally been used to supply the numbers of births and deaths, and population size also have, at best, a one-year resolution. This timing mismatch between the impact modelling and the progress of COVID-19 and associated service disruptions may, in some cases, lead to misrepresentation of the effects of the pandemic.

One approach to deal with this problem has simply been to distribute effects of the pandemic over the year. Thus, a 50% drop in coverage of health services or interventions for six months would equate to a 25% drop in coverage for 12 months, or one can use half of the impact. This approach may be satisfactory for interventions whose impact has a short time scale (such as oral rehydration for treating diarrhoea) if only the total impact is of interest. This approach would not be useful, however, if the interest were in exactly when the impact occurred. For interventions that have a more complex impact over time, and delayed effects, such as immunization or family planning, this averaging approach may be unsatisfactory, and time resolution modelling is needed. For example, a sharp drop in family planning coverage due to disruptions in the supply chain may result in a spike in unintended pregnancies (and, later, a spike in demand for maternal health services), even if that sharp drop lasts for a short time. This situation is most acutely seen when the disruption is to short-term family planning methods such as condoms and oral contraceptives.

Choice of baseline and counterfactual scenario

Several of the models presented in this module depend on comparing how health systems perform during the COVID-19 pandemic with how they would have performed in the absence of the pandemic. This comparison is between real performance and a counterfactual one. A counterfactual scenario is the state of some entity, such as a level of service provision, that

would have been seen in the absence of some event. In the present case, the event is the pandemic. The loss in health due to the pandemic is the difference between predicted health outcomes in a counterfactual scenario and the outcomes in the pandemic scenario. The choice of counterfactual scenario for coverage of services is not easy, and several options exist.

1. **The situation in mid-2019** – this option establishes a flat baseline from the 2019 level. The benefit is that software, such as Spectrum and LiST, typically provides estimates for the mid-year of any given year. The same is true for World Population Prospects and other relevant data sources.
2. **The situation in early 2020** (i.e. immediately before the start of the pandemic) – similar to the first option, this option also establishes a flat baseline. The benefit is that this period may be seen as a so-called natural starting point. However, as noted, because mid-year estimates are what is available, the situation in early 2020 can generally be arrived at only by interpolation.
3. **Extrapolation of the pre-COVID-19 trend** – in this option, the pre-COVID-19 trend is extrapolated to the period of interest, such as mid-2020 or later, depending on the history of the pandemic in each country.
4. **The flat trend from the last available data point** – for example, the coverage rate of use of magnesium sulfate for pre-eclampsia may not be known for 2019 and is available only for an earlier date; for example, 2017. Therefore, 2017 is used as the baseline. For another intervention – say, tetanus toxoid vaccine – data may be available for 2018, and that year is used for the baseline. Thus, this option results in a variable baseline.

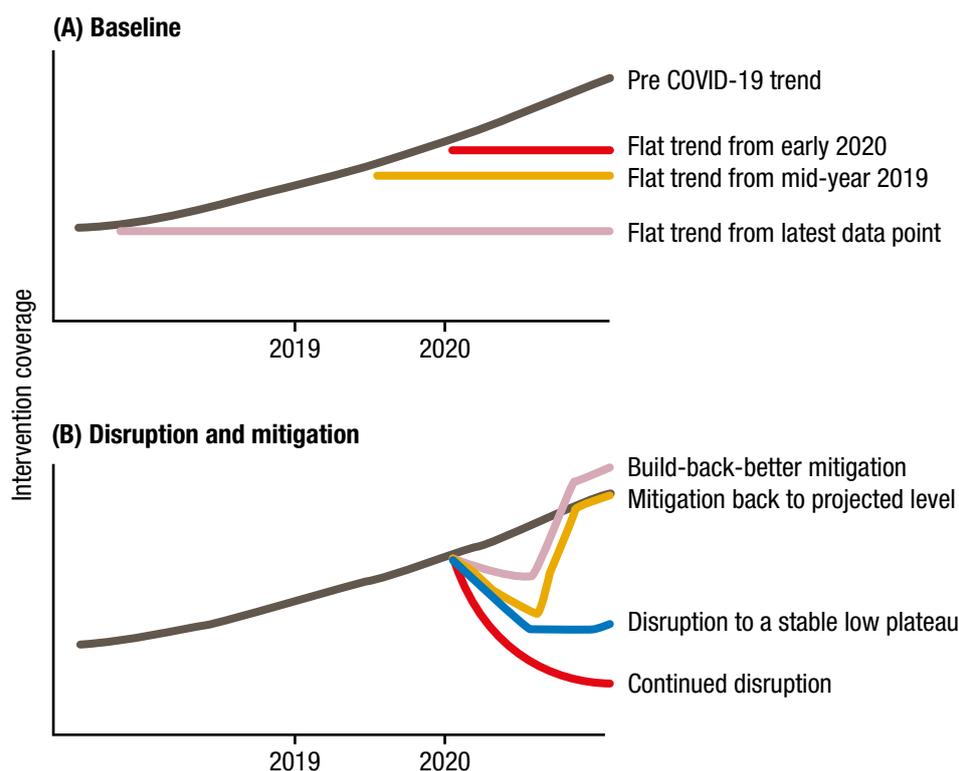
The four options are illustrated in the top panel of Figure 1 (panel A), which shows them in terms of the coverage of an intervention that is assumed to have been steadily increasing.

In some of the models presented later, the counterfactual scenario can be seen to some extent as a baseline – that is, the measured state at some point in time; for example, the level of service provision measured just before the pandemic began. In such cases, the impact of the pandemic is considered to be the difference between the baseline and the observations made during the pandemic. However, even when using baselines from before the pandemic started, there is a counterfactual assumption for the measurement of impact because one has to assume the progression of the service level in the absence of the pandemic.

Since most countries had a pre-COVID-19 downward trend in mortality and morbidity and the population at risk is growing in most countries because of population growth, the fourth option would give the lowest estimates of the impact of COVID-19 on service coverage because it is based on the lowest coverages and population size. In contrast, the first, second and third options would generate progressively larger estimates of the impact of COVID-19.

A good example of the possible scale of the differences in estimates of the effects of a disruption is found in a paper on indirect deaths caused by an outbreak of Ebola virus disease in Sierra Leone in 2014 (8). The authors calculated scenarios of the impact of the outbreak on service coverage with two different baseline assumptions. The first assumption was that the

Figure 1. Pre COVID-19 trends in coverage of an intervention (grey line) and (A) at baseline, assuming flat-line projections of coverage due to COVID-19 service disruption, and (B) with disruption caused by COVID-19 and mitigation, showing different potential coverage changes that may occur



trend in coverage would have continued in the absence of the outbreak. The other assumption was that the trend in coverage would have remained flat at the 2014 level. The baseline coverage of the fourth antenatal care visit for pregnant women was 95.5% in the first scenario and 89.5% in the second. The pre-Ebola (i.e. 2012–2013) coverage level was 74.2% (8). Thus, the choice of the baseline may have as large an effect as the disruption itself. Other interventions during the Ebola outbreak had smaller differences, reflecting that antenatal care visits had had the largest coverage increase before the epidemic.

Thus, the effect of the choice of the baseline will be different for 2019. It should also be noted that for many countries, the health coverage measures and epidemiological indicators before COVID-19 were already based on modelling. Estimates of service coverage, population size and demographic trends come from censuses and surveys in most cases. Countries typically carry out censuses every 10 years and surveys intermittently. For any given year, measures have been extrapolated from existing data using models of varying complexity. Thus, even option four, the flat trend from the last known data point, has been arrived at by extrapolation.

Under-five mortality is a good example. A key indicator in the present context, the United Nations trend estimates of under-five mortality up to the year 2019 were based on data points

where only half were three years or newer, and the average extrapolation from the last available data point was 4.5 years (9). Therefore, to establish the pre-COVID-19 level of under-five mortality, a prediction is needed for all countries that do not have a good-quality vital registration system. The picture is similar for other outcome indicators and service coverage measures.

Evaluation of the impact of mitigation strategies may use a double-counterfactual approach. The first is the initial counterfactual situation without COVID-19. The second is the scale of the disruption if the level of disruption after mitigation is based on scenarios rather than empirical data.

An issue to consider is whether the coverage of health interventions during the pandemic would decline to a new stable level, continue to decline as the pandemic progresses, or recover fully or partly without direct mitigation efforts. In many models, the disruption is assumed to plateau and then stay at that level until mitigation takes effect (Figure 1). Modellers and policy-makers may find that the scenarios for the coverage of health interventions in the lower panel of Figure 1 (panel B) are useful for advocacy and planning.

1. The build-back-better scenario supposes that there is a drop in service coverage but that mitigation leads to coverage levels that are better than the pre-COVID-19 trend. A variation would be that the level goes beyond only one of the flat baselines.
2. Disruption to service coverage followed by mitigation that brings coverage back to the pre-COVID-19 trend is another possible scenario.
3. A pessimistic scenario is that a disruption results in a stable plateau much below the pre-COVID-19 trend. Some of the short-term models take this approach and do not take account of mitigation measures.
4. A more pessimistic scenario, included for completeness, is that the disruption continues and worsens into the future. In this scenario, the health-care system of a country would be so damaged by the strain of coronavirus that it faced a breakdown.

The impact of the disruptions caused by COVID-19 on health services is the difference between what would have been the service level in the absence of COVID-19 – that is, the baseline or counterfactual scenario – and the actual level during the pandemic. The magnitude of the impact depends to a large extent on how baselines and disruptions are conceptualized and measured. In Figure 2, the impact is shown as the area between the baseline and the disruption/mitigation curve for a particular period. It is clear that the location of the baseline and the path of the disruption and mitigation both affect the total impact. The four panels of Figure 2 each represent a different baseline, and the impact is measured in terms of service delivery.

In panel A of Figure 2, the baseline is the projected trend of service delivery (grey curve). The total service decline can then be represented as the dark area between the baseline and the actual service delivery during the pandemic (red curve). However, using the actual service delivery depends on having frequent (e.g. monthly) measurements of the health system's performance. An alternative is to use the value for performance at a single point in time – in

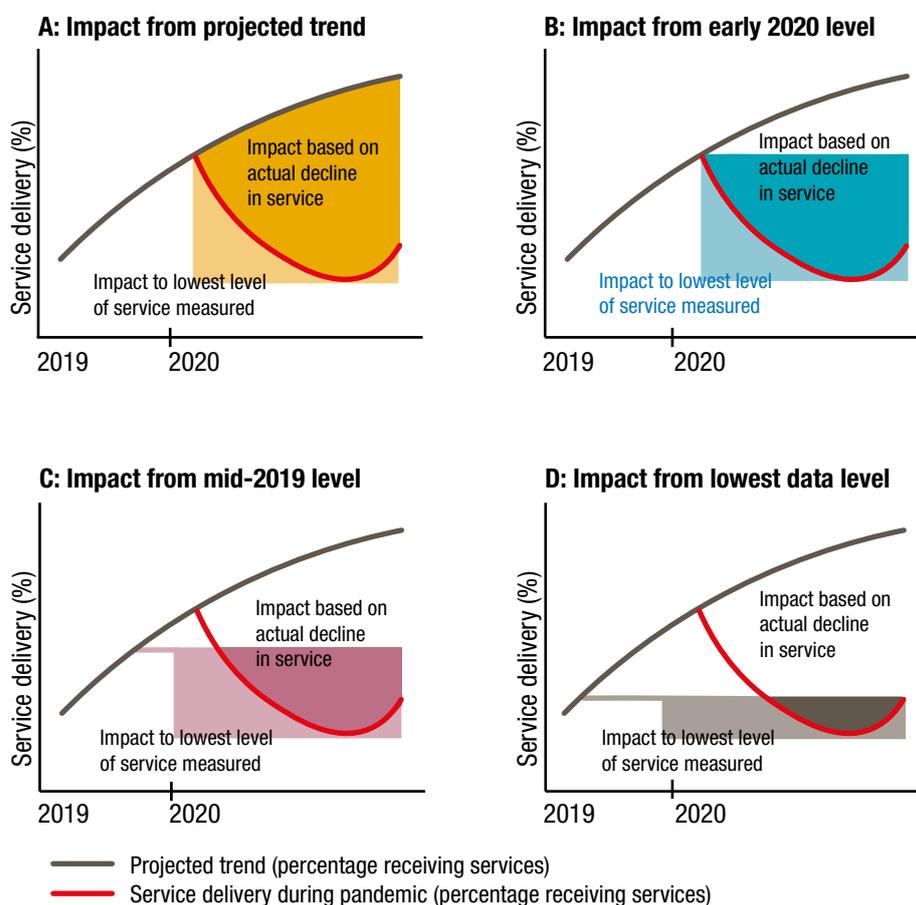
Figure 2. Impact modelling with different baseline scenarios

Figure 2, corresponding to the lowest level of service provision during the pandemic – giving the impact calculation at a so-called flat bottom. The additional impact measured by this assumption is shown by the lighter colour below the decline curve. Several models described in this module use the flat-bottom approach because of a lack of data for the service delivery over time. An exception is the SickKids model, which uses the actual measured values for the first two quarters of 2020 and estimates for each quarter after that.

Panel B of Figure 2 shows the impact when the level of service provision in the beginning of 2020 is used as baseline. The overall impact will be lower than in panel A because the assumed increase in service delivery during 2020 is not included in the estimate. If there is a declining trend in service provision before the start of the pandemic, then this impact will be lower than the one in panel A.

Panel C of Figure 2 is similar to panel B except that the baseline is the level of service provision in mid-2019. In a situation where service provision is increasing before the pandemic, the estimate will be lower than that with a baseline that is a trend (panel A) or a baseline set at the beginning of 2020 (panel B).

Panel D of Figure 2 is based on the latest observed level for the specific service under consideration. That will typically be from a survey such as a Demographic and Health Survey or Multiple Indicator Cluster Survey. The impact is smaller than the previous impacts in panels A, B and C. How much smaller it will be depends on how long ago the level was measured and what the trend is. Several of the models described in this module use the latest observed level to calculate the impact of disruption. In practice, this difference will depend on how far back the level of the service was measured and what the trend is.

Several of the assumptions related to the disruption are critical to the modelling and are not simply incidental inputs. For example, the paper on the possible indirect effects of COVID-19 based on LiST found different effects of disruption to vaccination from those based on the London School of Hygiene & Tropical Medicine model, partly because the disruption scenarios were different (10).

Overview of the models used

The models discussed here address various aspects of the effects on mother and child health of disruptions caused by COVID-19 to health services delivering interventions. A brief overview of the models and their purposes is given in Table 1. The details of each model can be found in Annex 2.

The models in Table 1 range from a general-purpose population and intervention projection tool, to detailed modelling of particular aspects of the COVID-19 pandemic.

The first model in Table 1, Spectrum, is a general population projection tool to which several modules have been added. LiST is one such module that estimates the impact of health interventions on women and children. LiST has a separate entry because it is the preferred tool for estimating impact. It is also used directly or indirectly by some of the other models. For example, the Adding It Up model leans heavily on LiST, although it also extends the modelling for impact of coverage changes in reproductive health services.

The benefit–risk assessment model developed by the London School of Hygiene & Tropical Medicine focuses on the effect of stopping child immunization for six months in Africa. Still, the model is of general use because it models the risk of infection from visits to health centres to children, their carers, their households and health personnel.

Somewhat similar to the benefit–risk assessment model, the model of direct and indirect effects of COVID-19 and response in South Asia attempts to model both the pandemic and its indirect effects. This model also includes modelling of the responses and mitigation but these are a set of independent models that do not interact with each other.

In contrast, the model developed by the Institute of Health Metrics and Evaluation is integrated, in that the disease modelling and socioeconomic modelling are done together. The model also differs from the others as it aims to project for a longer period (up to 2030) and produces estimates with a one-month resolution.

Several of the models address the same or similar topics. The results, however, are not the same, although in general, the models all lead to similar conclusions. There are three reasons

Table 1. Models for estimating the effects of COVID-19 on sexual, reproductive, maternal, strengths and weaknesses

Model	Developer	Main purpose
Spectrum	Avenir Health	Support planning and evaluation in demography, family planning, HIV, and maternal and child survival
Lives Saved Tool (LiST)	Johns Hopkins University	Estimate the impact of changing intervention coverage on health outcomes for mothers and children
Benefit–risk assessment model	London School of Hygiene & Tropical Medicine	Compare the health benefits of sustaining routine childhood immunization in Africa with the risk of acquiring COVID-19 infection when visiting service delivery points for routine vaccination
Adding It Up	Guttmacher Institute	Estimate the need for, use of, costs of and impacts of sexual and reproductive health services in low- and middle-income countries. Compare scenarios of changes in service coverage
Direct and indirect effects of COVID-19 pandemic and response in South Asia	SickKids, University of Waterloo, Aga Khan University and Cytel	Assess the direct and indirect effects of the COVID-19 pandemic and response in South Asia
Integrated model of the COVID-19 pandemic and socioeconomic shocks	Institute of Health Metrics and Evaluation	Estimate the development of COVID-19, economic performance of affected countries, SDG-indicators and health outcomes in an integrated way up to 2030

COVID-19: coronavirus disease 2019; SDG: Sustainable Development Goal; SEIR: susceptible, exposed, infectious, removed

newborn, child and adolescent health, and nutrition: their purpose, target population and

Target population	Main strengths	Main weaknesses
Total population as well as subgroups by age and sex	<ul style="list-style-type: none"> • Many add-on modules are available that model specific aspects of population and health • Modules are integrated • Free software; manuals can be downloaded 	<ul style="list-style-type: none"> • Projections are for one-year intervals
Women, and children up to the age of 5 years	<ul style="list-style-type: none"> • It is by far the most developed tool for ascertaining the impact of health interventions on children and women in low- and middle-income countries • Underlying assumptions are well described and documented • The user can change certain parameters, such as coverage, child mortality and intervention effectiveness • Free software; manuals can be downloaded 	<ul style="list-style-type: none"> • Does not account for the multiplicative effects of combinations of interventions • Does not account for long-term synergies from a generally improved health system • Projections are for one-year intervals • Typically used to model the effect of gradual improvement of coverage but not large decreases, which may cause problems in the accuracy of the predictions • For immunizations, herd immunity is taken into account only when coverage is increasing but not when it is decreasing. Hence, lives lost when coverage is decreasing may be wrongly estimated
Children and the general population	<ul style="list-style-type: none"> • Takes into account the risk of COVID-19 infection itself • Deaths from not being vaccinated are counted on a cohort basis • Relatively easy to extend it beyond immunization to other child health interventions 	<ul style="list-style-type: none"> • Developed early on in the pandemic, the two scenarios have proven to be overly pessimistic • Produces estimates for all African countries; if only interested in a single country, work is needed to separate the code
All women of reproductive age (15–49 years), with estimates broken down by age (adolescents 15–19 years and all women 15–49 years)	<ul style="list-style-type: none"> • Includes a more comprehensive package of sexual and reproductive health services and takes into account interactions across services • Stata code for the updates of Adding It Up is available to anyone interested 	<ul style="list-style-type: none"> • Designed for advocacy; less suited for decision-making for specific programmes • Population development is not modelled, so not suitable for projecting several years into the future • Percentage reduction is applied equally to each intervention considered; however, some of the reductions are cascading
Direct effects: general population; indirect effects: women, children and adolescents	<ul style="list-style-type: none"> • Uses data from real-time information from country health monitoring systems to assess disruptions from COVID-19 • Integrates a COVID-19 prediction model • Estimates mortality for age groups 5–9 years, 10–14 years and 15–19 years • Source code can be obtained from the developers of the model 	<ul style="list-style-type: none"> • Epidemic model is not broken down by age • Consists of five models, which, on the conceptual level, are linked, but in practice are estimated separately
General population	<ul style="list-style-type: none"> • Uses available empirical data to assess disruptions • Is part of the institute's extensive modelling framework, which makes the modelling consistent 	<ul style="list-style-type: none"> • The level of detail within each part of the model varies considerably • While there is considerable documentation of the sources of information available on the web, the inner workings of the model are far from clear. In other words, it is difficult to precisely understand how the sub-models and statistical approach were specified and used • The source code for some of the code (such as the COVID-19 SEIR model) is available on GitHub, but the code has few comments and little documentation

for the lack of detailed agreement: (i) the conceptualization of disruption and mitigation; (ii) the structure of the models; and (iii) the underlying data used. While the conceptualization of disruption and mitigation and model structure will be dealt with elsewhere in this guide, the underlying data merit some general comments.

The models depend in some way or another on population data, and the usual source for such data is the World Population Prospects 2019 (11), which provides age structure, the number of births and other information needed. It is not the only source, however; for example, the Institute of Health Metrics and Evaluation uses its own population projections.

The models also depend on data on the effectiveness or impact of particular interventions and do not necessarily use the same sources for these.

Outcomes and use of the models

Annex 2 provides some key outcomes and findings from the models described in Table 1. Most of the modelling was done during the first wave of the COVID-19 pandemic and was used in various policy briefs and other publications and communications for advocacy purposes. In retrospect, several of the models used assumptions about declines in service coverage that were too pessimistic.

Using LiST, it was projected that reductions of about 15% in the coverage of key high-impact maternal and child health interventions and 10% wasting at six months in 118 low- and middle-income countries could result in 253 500 additional child deaths and 12 200 additional maternal deaths (12). Reductions approaching 45% would result in 1 157 000 additional child deaths and 56 700 additional maternal deaths. Using Spectrum, Avenir Health estimated the impact of different lengths of disruption to family planning (e.g. 3, 6, 9 and 12 months of disruption) with different levels of service reduction (ranging from 5% to 40%). The models estimated that between 13 million and 51 million women who would have used modern contraceptives would be unable to do so because of the effect of the pandemic. This reduction in contraceptive use could have serious consequences for women and lead to between 325 000 unintended pregnancies, assuming minimal disruptions for three months, and 15 million unintended pregnancies, assuming severe disruptions for 12 months (13). The Guttmacher Institute estimated that a 10% proportional decline in the use of short- and long-acting reversible contraceptive methods in low- and middle-income countries due to reduced access would result in an additional 49 million women with an unmet need for modern contraceptives and an additional 15 million unintended pregnancies over the course of a year (14). The benefit–risk assessment model found that, in a high-impact scenario, for every one excess death attributable to coronavirus infections acquired during routine visits to vaccination clinics, 84 deaths (95% uncertainty interval: 14–267) in children could be prevented by sustaining routine childhood immunization in Africa. In a low-impact scenario that approximates the health benefits only to child deaths averted from measles outbreaks, the benefit–risk ratio to the households of vaccinated children would be 3 (95% uncertainty interval: 0.5–10) (10).

However, these models used various scenario-based disruptions and not actual data. The SickKids model, on the other hand, did use some routine district-level data.

These models have been used less often to guide country planning and policies, although this may be their best use. To date, the LiST country-level models have been used by the Global Finance Facility in country briefs (15) and to facilitate country dialogue about potential strategies to maintain services. The SickKids modelling was done at the request of the six most populous countries in South Asia (Afghanistan, Bangladesh, India, Nepal, Pakistan and Sri Lanka) to provide them with information that would help to guide their decisions on when to ease or lift COVID-19 mitigation measures.

To address the continued need to use models for country planning and policy development, a new tool – the benefit–risk model for maintaining essential reproductive, maternal, newborn, child and adolescent health services in the COVID-19 pandemic – is under development by WHO to help countries to prioritize and implement strategies to maintain essential services. This model combines the LiST models and the benefit–risk assessment models of the London School of Hygiene & Tropical Medicine. LiST is used to estimate the lives saved at different levels of service provision. An adaptation of the benefit–risk assessment model estimates the lives lost from COVID-19 as a result of visits to health centres. The combination of these two models allows the trade-offs (between the risk of lives lost to COVID-19 and lives saved by mother and child health interventions) to be estimated when trying to maintain immunization coverage and other health services provided at health facilities. While the original model of the London School of Hygiene & Tropical Medicine also allows for estimates of the trade-offs, the combined model has built in the whole range of likely intervention trade-offs that may need to be evaluated. This model was tested in several low- and middle-income countries and is being revised ahead of release to the public. Details of the model are provided in Annex 2.

Regardless of which model is used, they all demonstrate that reductions in the coverage of maternal, child and reproductive health services generally result in a greater loss of lives than maintaining or scaling up services.

Conclusion and recommendations

Most models of the effects of COVID-19 on maternal, newborn, child and adolescent health rely on Spectrum and LiST. The dependence may be direct, as in the direct application of LiST and of, in part, the SickKids model, or indirect, such as in the Guttmacher Institute model. Thus, key assumptions in LiST – such as distributions in the cause of death in individual countries, the affected fraction (proportion of the population affected by a given disease or ailment) and the effectiveness of the interventions – are very important. LiST probably represents, as well as is currently possible, the state of knowledge on these issues.

All models have weaknesses, mostly related to assumptions and data availability

All models have weaknesses in their assumptions on exactly what coverage losses have happened or will happen during the pandemic. Such weaknesses are partly because the models were conceived and developed relatively early on in the evolution of the COVID-19 pandemic, when fewer data were available, and partly because the models have a global or regional scope, where collecting data for all countries becomes a considerable challenge.

For individual countries, however, it is probably not necessary to rely on general assumptions. It may be feasible to obtain data from national or district health information systems or similar routine administrative reporting and topical surveys. All the models allow country-specific

disruptions to be entered into the model. However, the main problem is whether or not the data from these sources are available in a timely manner and are of good-enough quality to be useful.

All models have to choose a baseline for modelling disruption. Most models use data from the most recent Demographic and Health Survey or Multiple Indicator Cluster Surveys as a baseline for estimates of intervention coverage. In practice, this means that rather than 2019 or 2020 as a baseline, the baseline is put back a few years. This practice will likely result in an underestimation of the impact of the disruption. In general, the models use a resolution of one year. When shorter units, such as half years or quarters, are needed, the outcome measure in question is simply distributed across the year. The exceptions are the explicit COVID-19 pandemic models, where the resolution is either days or the generation time of the disease. From a policy perspective, given the very rapid development of and changes caused by the pandemic, models that gave estimates with a shorter time span than a year would be helpful. However, most countries probably do not have data that can support such modelling.

Some of the models are probabilistic and incorporate uncertainty directly into their modelling, while others are deterministic, in that they provide a single estimated output for a fixed set of inputs. Models that include uncertainty explicitly in the modelling typically do not include estimates of overall population size or structure. An exception is the Institute for Health Metrics and Evaluation model that uses a probabilistic population model and the model of the London School of Hygiene & Tropical Medicine that models all aspects of the population except for its initial size.

Country-specific models may be the most useful for modelling the indirect impact of COVID-19

Spectrum and LiST have been designed principally for the modelling of single countries. SickKids provides results for a set of countries within a region. Other models, for example Adding It Up, do not currently supply results for single countries and provide only global and regional results.

Models that only provide aggregate results do so by aggregating the results from individual countries internally. It varies how easy it is to separate the aggregation code from the country-specific code and isolate the results for a single country.

Therefore, country-specific models can be the most helpful for advocacy as well as decision-making on the priorities for maintaining essential services. The WHO risk–benefit tool under development, which merges the benefit–risk assessment model and LiST, is an attempt to make modelling easier at the country level while taking into account both the risks of seeking health care and the benefits of doing so.

The models show that the indirect impact of COVID-19 from service disruption will result in loss of life that can potentially be avoided

Overall, regardless of what model is used, they all show that reductions in coverage of maternal, child and reproductive health services during the pandemic generally cause a greater loss of life than maintaining or scaling up services. It is difficult to compare the results of the models directly because the time periods of estimations, outcome measures and underlying assumptions vary. That, however, does not detract from the overall message that maternal, child and reproductive health services should be supported and maintained during the pandemic.

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Annex 1: Data sources for SRMNCAH

Current sources of data

The World Bank has developed high-frequency phone surveys in cooperation with various countries. These are surveys of households to collect data on jobs and job losses, food security and access to health services.

The Global Financing Facility has, since late March 2020, carried out monthly surveys of its staff in 36 countries, to collect qualitative information on the impact of the COVID19 pandemic on essential health services for women, children and adolescents (1).

The United Nations Children's Fund (UNICEF) collects data to inform the COVID19 response, by collecting qualitative data from 85 country offices on disruptions in each country (2). UNICEF typically presents the data as estimated or assumed ranges of drops in services. However, the data derive from the expert opinions of UNICEF staff or government officials rather than actual measurement. The data may give a fair idea about whether or not the disruption is small or large, but require considerable deliberation to be included as inputs to quantitative models. The modelling results based on such data may also give an impression of higher precision in model outputs than is the case.

The Global Fund to Fight AIDS, Tuberculosis and Malaria collects biweekly data for disruptions in HIV, tuberculosis and malaria programmes from 106 countries, in much the same way as UNICEF does more generally, and with the same caveats (3).

For a modelling input, the Institute for Health Metrics and Evaluation uses the University of Maryland global Facebook survey, which collects data from individuals on COVID19-like symptoms, as well as on some individual adaptations such as wearing masks and social distancing, and reducing visits to health centres (4).

The World Health Organization (WHO) also conducts surveys on the effect of COVID19 on the supply of health services. Relying on WHO staff in the countries, these are similar to the surveys from UNICEF, The Global Fund and others.

More recently, UNICEF has launched the Multiple Indicator Cluster Surveys (MICS) Plus initiative that uses the respondents from the regular MICS as a sample frame for telephone surveys (5). The questions are taken partly from the standard survey and are partly specific to the COVID19 pandemic, such as on self-protection from the infection, and the frequency of distance learning for schoolchildren.

There are also several country-specific initiatives. A good example is Nigeria's Multi-Source Data Analytics and Triangulation Platform, which collects data from several sources, among them the district health information system. There were, for example, 4.6 million outpatient visits to health facilities in July 2019, but only 3.8 million in July 2020 (6).

Many of the various survey tools that have been developed for understanding disruptions due to COVID19 can be found at the PhenX Toolkit website (7).

Overall economic decline and increase in poverty

The World Bank has produced estimates of declines of GDP and concomitant increases in the number of people who are poor (8). The estimates are highly uncertain and depend, among other things, on assumptions that COVID19-related economic stress in countries will result in effects on the poor in the same way as previous changes in the economic performance of countries. The estimates are also based on assumptions about how inequality will change as a consequence of the pandemic.

A more recent World Bank model uses the expenditure distribution from the most recent household income and expenditure survey in each country, and estimates how the expenditure distribution changes given the assumption of equal percentage-wise GDP drops across the expenditure groups. The procedure allows estimates of the increase in poverty and of the number of households that cannot meet their food-energy requirements (9).

Similarly, the International Monetary Fund (IMF) has provided estimates of the economic trajectories of countries, but has stressed that the “there is a higher-than-usual degree of uncertainty around this forecast” (10). This organization appears more uncertain than the World Bank on the size of the growth in poverty, although it does not model it. The IMF’s June 2020 estimates of GDP growth for the year were negative for all European countries and all North and South American countries except Guyana. China, India, Indonesia and Viet Nam were projected to have weak positive growth, as were some other Asian countries. The IMF portrayed African countries as having varied growth rates, with some countries expected to have positive growth while others would see a decline.

In the October 2020 version of the World Economic Outlook, the IMF gives a slightly more optimistic outlook than in the June revision (11). It also changes the outlooks for individual countries. The most substantial changes are perhaps for China and India – China with a much more optimistic outlook, and India, a more pessimistic one. Given the spring 2021 surge in COVID19 cases in Europe, it is likely that the estimates will change yet again in the next revision.

The World Bank and IMF estimates illustrate the difficulties of the so-called now-casting of an event such as the shock from COVID19 (12, 13). Now-casting is predicting up-to-date estimates of important indicators in the absence of direct measurement. It depends on modelling, which, in turn, depends on the use of covariates whose values are measured, and that are good predictors. However, the modelling depends on assumptions about the world as it was before the pandemic.

Since now-casting models are typically predictive rather than causal, there is no guarantee that the predictive power of the covariates will remain in the new situation, or that the model structure will remain adequate. Additionally, even if the models retained their validity and predictive power, error propagation would lead to increasingly greater uncertainties in the forecast accuracy as the period of the forecast increased (14).

An evaluation of the forecasting of economic crisis and the accuracy of short-term predictions during recessions finds that neither the IMF nor the private institutions that do forecasting are

very good at it (13) Another analysis finds that the average absolute error in IMF GDP forecasts is about 2% (14) Still, in the absence of validated, real-time data, there is little that modellers can do but depend on models representing the best available judgement.

Taking a different approach from that of the World Bank and IMF, the International Food Policy Research Institute (IFPRI) estimates the impact of COVID19 on poverty with its MIRAGRODEP model (15). Its starting point is a series of disruptions (labour market disruption, trade shocks and total factor productivity shocks), which are exogenous inputs to a computable general equilibrium model. The model translates the shocks into impacts on production trade, consumption, and so on, which in turn lead to changes in prices, remittances, employment and productivity. Then, the real income arrived at in the model is translated into poverty estimates, using the income distribution for each country. Finally, the model estimates nutritional intake from household consumption patterns. Rather than assuming uniform shifts in income in each country, IFPRI tries to model the different ways in which COVID19 may have effects, and their impact on the income distribution. It also uses country-specific consumption profiles. In principle, the modelling is much more realistic than estimates of shocks to GDP or GNI with general poverty effects. The model has been used to estimate the effects of the pandemic on mother and child health. Unfortunately, it still relies on data that are currently uncertain estimates, underlining the need for better data on shocks due to COVID19.

In summary, the various disruption estimates are uncertain, and even when they are quantitative, such as the number of people who are newly poor, they are little more than estimates of whether disruptions are large or small. The approach that many modellers have taken – namely, to build scenarios of possible effects, rather than to predict possible effects – is therefore prudent.

However, for individual countries, it may be better to collect data on the actual effects and to use these as the input.

To help countries to measure and monitor effects, WHO has published *Monitoring effects of COVID19 on essential services for reproductive, maternal, newborn, child and adolescent health and nutrition (RMNCAH+N)* and *Revealing the toll of COVID19: a technical package for rapid mortality surveillance and epidemic response* (16, 17).

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Annex 2: Specific sexual, reproductive, maternal, newborn, child and adolescent health models

2a. Spectrum

Spectrum is policy modelling software that implements a set of models related to population, health, disease and poverty. It is developed and hosted by Avenir Health, and can be downloaded and used by anyone free of charge (1). Spectrum runs on Windows-based machines.

At the core of Spectrum is DemProj, a cohort-component population-projection tool. From a population age and sex distribution for a given year, it is able to project the population size and structure into the future by applying age-specific fertility and mortality rates and, optionally, age-specific migration rates. It is designed to allow a change in fertility, mortality and migration over time, such as for a decline in fertility.

Several other cohort-component population-projection programs exist. In contrast to some, Spectrum operates the projection on a single-year progression and single years of age. Thus, to obtain the population in year $t+1$, the age-specific mortality rates for single years are applied to each single-year age group in year t . Of course, the exception is age 0, which the model calculates by applying age-specific fertility rates to each single-year age group of women of fertile age.

The World Population Prospects 2019, in comparison, uses five-year projection periods and five-year age groups in the basic projection (although it is in the process of changing to a one-year projection method). Estimates for in-between years and single years of age are presently then interpolated. Spectrum and the World Population Prospects do not necessarily, therefore, give precisely the same results.

The chief merit of the Spectrum system is the many add-on modules that model specific aspects of population and health. In addition to DemProj, Spectrum includes the following modules geared towards impact (1):

- FamPlan: family planning
- LiST: lives saved tool (child survival)
- AIM: AIDS impact model
- Goals: cost and impact of HIV intervention
- Resource Needs Module: costs of implementing an HIV/AIDS programme
- RAPID: resources for the awareness of population impacts on development
- TIME: tuberculosis impact model and estimates
 - epidemiological and cost-effectiveness analysis of tuberculosis control strategies
- Malaria: impact of malaria interventions
- STI: estimation of burden and trends in sexually transmitted infections

- NCD: non-communicable diseases and mental health, substance abuse, and neurological disorders

Researchers have used several of the modules for modelling the impact of COVID19. The most important is LiST because it directly addresses the impact of service coverage changes on child and maternal survival. LiST will be discussed separately below, and some of the others will be touched upon since they are used in some of the other models.

Assumptions in Spectrum

Most of the assumptions inherent in Spectrum pertain to the various add-on modules and will be discussed later when relevant. Nevertheless, some of the demographic assumptions also merit mentioning.

As noted, Spectrum operates on a 1 x 1 basis – that is, the projection moves forward one year at a time, and single-year age groups are used. In the context of the rapid development of the COVID19 pandemic, a finer time granularity might have been useful, at least in principle. There are no data, however, that easily could support that. Disruption data may, to some extent, be available retrospectively, but future disruption is very difficult to predict. To model the population would require data on the seasonality of births and deaths. Moreover, the within-year stochastic variation and the general uncertainty around population data for many countries are so large that within-year modelling is fraught with difficulties.

As a demographic population projection tool, DemProj functions as expected. It is useful to understand how DemProj deals with mortality, though. In the case of using the default data that come with the World Population Prospects 2019, DemProj will use the life table that the United Nations Population Division used to make the population estimates. The life table may be strictly empirical for countries with good civil registration and vital statistics systems. It may be model life table-based, with one or two mortality rates being used to select the appropriate table.

If one replaces the default data, then the age-specific mortality rates in DemProj will be controlled through the life expectancy at birth and standard model life tables. The user may select the most appropriate life table within the sets of Coale-Demeny and United Nations life tables. DemProj does not directly allow for the use of custom life tables, although this restriction can be circumvented by editing one or more of the default model life tables. A full life table is needed for both genders, not an abridged one.

For the relatively short horizon projections that are needed in the COVID19 context, using country-specific life tables that differ from the patterns in the model life tables will not make a great difference by itself. Life table-driven differences in results will be much lower than the general uncertainty surrounding the modelling. An exception would be if a population projection were made outside of DemProj and a user wanted to replicate that as closely as possible for consistency. A typical example would be a central statistical office or a health ministry that has its own national projection.

Countries in sub-Saharan Africa, particularly in the Sahel region, have age patterns of mortality that appear to be shifted towards later deaths in reality than in standard model

patterns. The use of DemProj for Sahelian countries would, in principle, produce a slightly wrong age pattern for the mortality of children. However, as noted, the projection period is short – only one year – so large discrepancies will not develop. Moreover, when one is using the default country data, the Population Division has already taken the Sahelian age pattern into account. LiST is also not using the default neonatal, infant and under-five mortality statistics, but rather the most recent estimates by the United Nations Inter-agency Group for Child Mortality Estimation (IGME), where the problem has been corrected to some extent.

Disruptions in Spectrum

Spectrum itself is agnostic with respect to how disruptions are modelled. In DemProj, disruptions will be modelled as changes in the underlying rates (mortality, fertility, migration) for the population model. In other modules, much the same is the case. The assessment of the scale of disruptions may be based on scenarios or may be empirical. For example, for family planning, scenario-based projections early in the pandemic posited that very large numbers of women would be unable to access the services (2). A recent estimate using the FamPlan module of Spectrum, informed by mobility data from Google, found much lower but still significant numbers (3).

Use of Spectrum

Spectrum is a self-contained Windows program. Spectrum and its sub-modules are programmed in Delphi, a compiled language. Thus the source code is not immediately available for the user to change. Users must therefore customize Spectrum to their purpose by changing the assumptions.

2b: The lives saved tool (LiST)

The lives saved tool (LiST) answers the question: “Given what we know about how health interventions work, what is the impact of changing the coverage of an intervention?” The metric of LiST is lives saved, either of children or women.

Traditionally, planners and policymakers have used LiST to understand the impact of increasing the coverage of particular interventions. For COVID19, the first use has been to model massive decreases in coverage.

In an application of the software published in May 2020, coverage reductions and increases in wasting over a period of 6 months were modelled as increasing under-five deaths by between 250 000 and 1 160 000 (4). In 2019, about 5 200 000 children under five died (5). Similarly, according to the same paper, maternal deaths would increase by between 12 000 and 57 000. In 2017, about 295 000 women died from maternal causes (6).

LiST is a well-established modelling tool that was first developed in 2003. It integrates with the DemProj module, which provides the underlying demographic dynamics of the population under study. It is developed by the Institute for International Programs at the Johns Hopkins Bloomberg School of Public Health.

LiST is currently by far the most developed tool for ascertaining the impact of health interventions on children and women in low- and middle-income countries. It is also the most-used such tool.

The LiST model has been described in several publications. The overall structure is simple and stable, although it is continually being updated, not the least concerning COVID19. Current data on population structure by age and sex, and fertility and mortality are the starting point, together with the current coverage of interventions and prevalence of risk factors.

Deaths are the sum of deaths from all causes. Deaths from a specific cause may be reduced by increasing the coverage of interventions targeting that cause. However, an intervention typically does not affect all the possible deaths from a cause. For example, rotavirus does not cause all deaths from diarrhoea, but only around 20%. In LiST terminology, this is the affected fraction. Finally, the intervention, rotavirus vaccine, is about 50% effective, so if the 100 children who had died from diarrhoea had been vaccinated, 10 children ($0.2 \times 0.5 \times 100$) would have been saved by the vaccine.

Here, the demographic model supplies the total deaths, the estimates of the cause of deaths supply the total diarrhoea deaths, and scientific literature on causes of death, diarrhoea and vaccination feed the affected fraction, and the effectiveness of the vaccine. Finally, the change in the coverage of the intervention is applied (the percentage of children in the relevant age groups vaccinated).

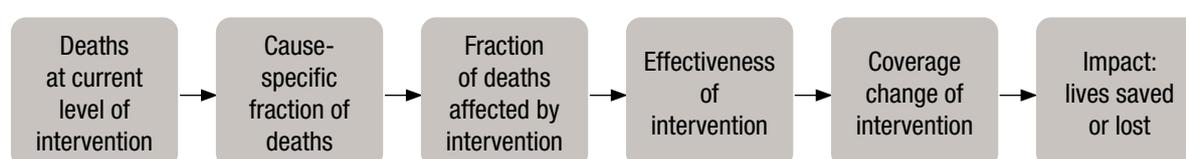
The overall structure is shown in Figure 3. Each arrow represents a multiplication.

If there are 10 000 deaths from diarrhoea, if the rotavirus vaccination is increased from 0% to 50%, if the diarrhoea deaths caused by rotavirus make up 20%, and if the effectiveness of the vaccine is 50%, then the lives saved are $10,000 \times 0.5 \times 0.2 \times 0.5 = 500$.

Rotavirus vaccination is not the only intervention targeting deaths from diarrhoea. For example, both zinc and oral rehydration prevent deaths from diarrhoea. An estimation of the lives saved by each intervention in isolation would lead to an overcounting of the lives saved, so when several interventions contribute to a reduction in deaths from a given cause, they are computed in sequence, but with the lives saved at each step deducted from the total deaths available for saving. The order of the sequence of calculation is irrelevant.

LiST does not account for the multiplicative effects of combinations of interventions. It also does not account for long-term synergies from a generally improved health system.

Figure 3. The basic structure of the Lives Saved Tool (LiST)



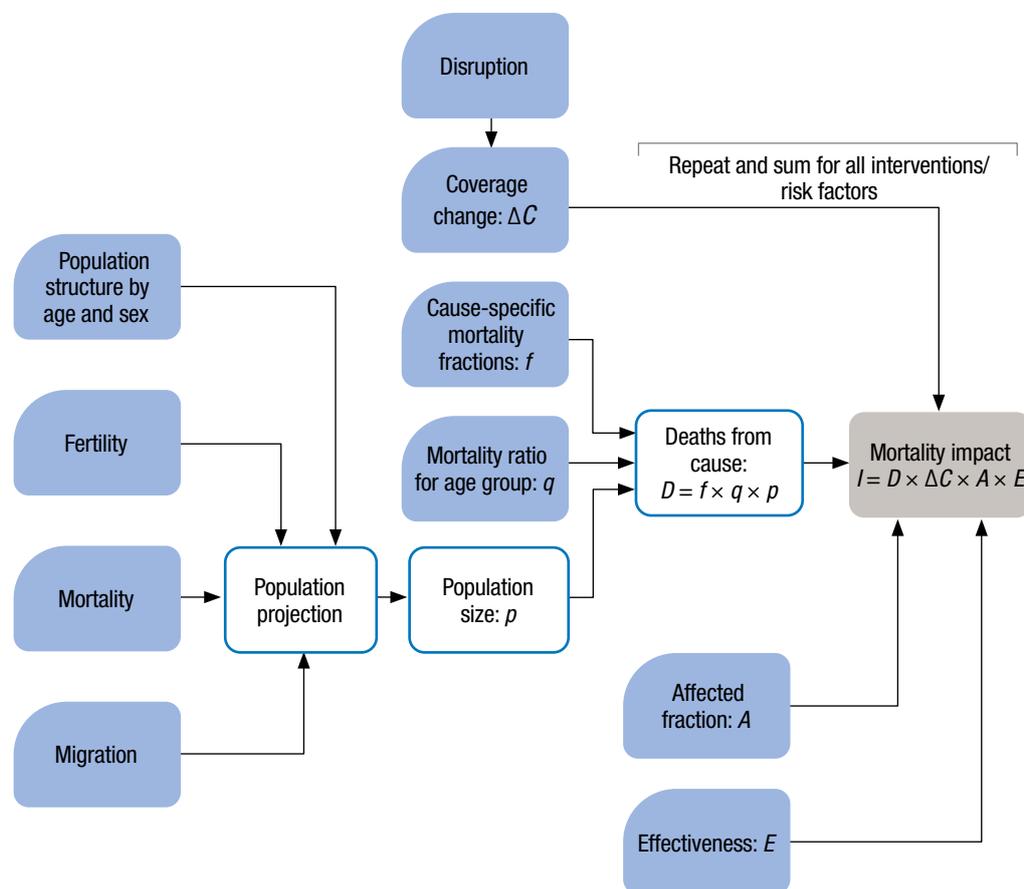
The number of interventions in LiST is high (there were 77 in the August 2019 version), and the overall causal structure is complex. However, the interventions, their affected fraction and their effectiveness are well documented, and the pathways well described (7).

For some interventions, the pathways are somewhat more complicated than just described because they operate through risk factors. Risk factors influence the probability of death directly, and may in turn be influenced by interventions. But risk factors are not interventions. Risk factors include birth order, breastfeeding, low birthweight and stunting. Some risk factors may themselves be counted as outcomes. One such example is stunting, but this not modelled directly in LiST.

The structure of LiST is shown in more detail in Figure 4, which identifies the different assumptions, marked in green, and the computations within the model. All the assumptions can be changed by the user, while the computational framework cannot.

The population projection is based on the available data on population size, fertility and mortality, and migration. The user is free to enter or change those, or to download standard ones from the Spectrum website.

Figure 4. Assumptions and computations in LiST



To conceptualize the COVID19 pandemic disruption in LiST, the user must change the coverage rates of interventions. Mitigation is similar. Disruption is a reduction in coverage; mitigation is an increase. The original use of LiST for COVID19 used a general disruption factor – that is, pre-COVID19 coverage rates were simply decreased by a common disruption factor. However, in practice, this entails using the disruption factor on each of the coverage rates. In the model itself, there is no global assumption of increases or decreases. Thus, the system does not force all coverage reductions to be the same.

An important set of assumptions in LiST are the cause-specific mortality fractions – the cause of death distribution for the relevant age groups. These groups are neonatal, 1–59 months, maternal deaths for women aged 15–49 years, and stillbirth. In the case of stillbirths, only the distribution of antepartum and intrapartum stillbirths is used. The causes of death are taken from the World Health Organization (WHO) Maternal and Child Epidemiology Estimation (MCEE). The data are country-specific, and the user may also edit them.

A slightly confusing aspect of LiST and its integration with DemProj is that there is a requirement to enter baseline child mortality, even though DemProj will already have these data. LiST will use the latest IGME estimates for the neonatal mortality rate, the infant mortality rate and the under-five mortality rate.

The moment LiST is run, the child mortality estimates provided with LiST will be used, rather than those found in the dataset that DemProj is using. One reason for this behaviour is that World Population Prospects data do not include neonatal mortality.

The affected fraction and effectiveness, both of which can mostly be changed, come from studies of the various interventions. They are country-specific in the default setup of LiST.

Inequity

The basic model in LiST assumes that the various factors that contribute to the impact of a change in coverage, as well as the coverage change itself, are equally and independently distributed across the population. The assumption is probably unrealistic, but given the lack of data on inequities, it is difficult to address the issue. LiST does have an equity tool where the user can simulate the impacts of changing coverage for all into the highest wealth quintile (8). However, possible differences in cause or affected fractions are not included.

Nevertheless, if the necessary data are available, it is quite possible to split a country into several regions, age groups or socioeconomic groups, and to run the analysis separately for each, perhaps with different epidemiological assumptions. The LiST manual offers some guidance on how to do that and, in practice, LiST is often modelled on both the national population and specific subgroups of interest.

The data that come with LiST can also be of considerable help in inequity analysis. A database with coverage data for subnational geographical areas, as well as for urban-rural residence and wealth quintiles, is available for many countries (9). Unfortunately, mortality levels and cause of death are not available because many surveys do not readily support the disaggregation of the measures because of sample size.

Uncertainty

As can be gathered from the discussion of the structure of LiST, the model is a deterministic one, based on the best available data on population dynamics, coverages and interventions.

Uncertainty estimates can be arrived at in at least two ways. One is a simple sensitivity analysis. This entails varying the inputs within reasonable bounds to determine the variation. LiST has a sensitivity analysis built in. The user should carry out a sensitivity analysis before using the results.

Another way is to vary the inputs in the model randomly. Thus, the values of coverages, effectiveness, attributable fractions, and causes of death are all estimated with uncertainty, and one may let each value be drawn from an appropriate distribution, with standard deviations, as found in the data or published literature. Stochastic uncertainty is catered for in the “More Tools” menu in Spectrum, where there is an option for uncertainty analysis for LiST.

LiST modelling does not cover all aspects of uncertainty, however. The population dynamics would also need to be probabilistic to get a realistic uncertainty estimate for lives saved or lost. One should, in principle, also allow for dependencies between the various interventions. For example, the coverage values of oral rehydration and zinc as a treatment for diarrhoea are probably highly correlated, as both may be obtained from a health centre. Moreover, their simultaneous use may have different effectiveness from the two considered separately. The effectiveness estimates often are based on very few studies, or even only one, and they may be tied to a limited locale or context.

The above caveats mean that the currently computed uncertainty intervals for LiST may be somewhat inaccurate. On the one hand, the omission of uncertainty in the population estimates will tend to make the uncertainty ranges too narrow. On the other hand, the correlation between values may work to increase or decrease the width of the uncertainty intervals.

In the context of COVID19, it may be wise to combine sensitivity analysis, focusing on different values of coverage drop or mitigation-related increase, with uncertainty analysis. This is so, even though data availability on coverage is rapidly improving.

Disruptions in LiST

In the May 2020 application of LiST for COVID19, data do not directly inform the disruptions, but reasonable scenarios were developed. There are two main pathways to worsened health outcomes: coverage decrease and decreases in nutritional status.

The coverage decrease may be determined empirically by collecting data on what the actual coverage is. As noted, LiST allows the coverage to be changed at the individual intervention or pathway level. So far, few precise data have been available. Moreover, the precise levels in early 2020 before COVID19 may be imperfectly known for many countries.

In the May 2020 application, the coverage decrease is a function of four factors: reduction in the availability of health workers (h), reduction in supplies (s), reduction of demand (d) and

reduction in access (a). The factors are considered as working in a chain so that the total coverage reduction is:

$$1-(1-h)(1-s)(1-d)(1-a)$$

It is not evident that reductions would work in this way. If supplies decrease by 10% and available workers decrease by 10%, the total reduction would arguably still be 10% because 10% fewer workers could handle 10% fewer supplies. Similar arguments could be made for demand versus supply. An alternative model would be Liebig's law of the minimum (10). Used in biology and ecology, this states that when several resources are needed for something, the limiting factor is the scarcest resource. In the COVID19 disruption context, the determining decrease would be the largest decrease. As von Liebig points out, however, "a more comprehensive analysis would consider the interaction between components". At the moment, how the total reduction in coverage results from changes in each factor is an unresolved empirical question.

Coverage reduction in LiST is an exogenous input to the model, however, and the user is free to change coverage either by applying their own assumptions to overall decreases or by individually changing each coverage rate based on available data.

The LiST model itself is agnostic to the level of disruptions and the source of the disruption estimate.

In a recent application of LiST for estimating the effects of disruption on nutrition, and on child and maternal mortality, the baseline was set to the latest survey before the pandemic. The MIRAGRODEP model in Annex 1 was used to estimate 118 individual countries' economic changes. In turn, the changes were translated into changes in wasting and low maternal body mass index. The resulting estimates were used in LiST together with assumed health service delivery changes to estimate the impact of COVID19 for 2021 and 2022 (11).

For practical use in a single country, it makes sense to use country and item-specific coverage reductions instead of calculating an overall decline that sums up all coverage reductions.

Disruptions and crisis

LiST has typically been used to model the effect of a gradual improvement of coverage of interventions, because this is what has been seen in most countries. The COVID19 pandemic presents a new situation, with potentially large decreases in the coverage of interventions. To some extent, this may cause problems in the accuracy of the predictions.

The problem is evident when the neonatal mortality during the 2014–2016 Ebola epidemic in Sierra Leone is considered. The IGME finds no increase in neonatal mortality during the epidemic. Rather, both the rate and absolute numbers are presented as steadily declining. The IGME depicts the under-five mortality rate as slightly peaking in 2015, but the peak is arrived at by adding externally estimated crisis data to the trend derived from the existing survey data, rather than by using the estimates from surveys of child mortality. A paper using

LiST to estimate indirect mortality from Ebola finds between 2,600 and 3,000 neonatal excess deaths during 2014–2015 (12). In comparison, the IGME estimates about 8,600 neonatal deaths in Sierra Leone in 2015 (13).

One reason for the discrepancy between the estimates using LiST and those using existing survey data may be that the paper incorrectly estimated coverage change. Another may be that LiST is not so good at handling complex, interacting and extensive coverage changes. Finally, it is also possible that the survey data have not picked up any 2014–2015 increase in mortality. The surveys covering the period are the 2017 Multiple Indicator Cluster Survey (MICS) and the 2019 Demographic and Health Survey (DHS). The first does not show any peak for the two years 2014–2015 but has relatively low mortality overall. The IGME disregards estimates from the 2017 survey. The 2019 estimates are currently only available for five-year periods before the survey, which tend to flatten peaks in mortality. However, given the large increase derived from the LiST, one would expect some signal in the 2019 data.

On the basis of Sierra Leone data, it is difficult to form any firm conclusions on whether LiST works well in the context of crisis. There does not appear to be any systematic evaluation of LiST performance in such contexts. One reason for this is that there are few gold-standard data with which to compare.

The effectiveness of LiST interventions in the model can be seen broadly as either causal or predictive. Thus, the effect of zinc on diarrhoea has been established by randomized control trials, and the effect estimate may be considered an estimate of the causal effect. In contrast, estimates of the effect of breastfeeding promotion on breastfeeding, or of poverty on nutritional status, are predictive. While there is undoubtedly a causal link, the estimates available of the effect are basically a prediction, which is dependent on the data set used to make it. With rapid changes due to COVID19, the basis for the prediction may have changed. When causal links have been estimated, the results may be more trustworthy than when the links are only predictive.

The effects of vaccines

The LiST vaccine model differs from its general model shown in Figure 4. The general model entails that interventions have immediate effects, within the same year as the interventions occur. Vaccines, in contrast, are treated on a cohort basis – when a child is vaccinated, the protection follows the child as they grow older.

In the Spectrum version of August 2019 (v5.761), except in the case of measles, herd immunity is not considered in the model. In the October 2020 version (v5.88), herd immunity is considered for *Haemophilus influenzae* type b, measles, pneumococcal and rotavirus vaccines. Herd immunity is taken into account only when coverage is increasing, but not when it is decreasing. LiST may thereby erroneously estimate lives lost when coverage is decreasing. Loss of herd immunity effects will take place some time after the reduction of vaccination coverage. Therefore, this problem will probably be significant only if the projection is two or more years into the future. According to the LiST development team, a new version of LiST has been developed that handles herd immunity for all the vaccines under both increasing and decreasing scenarios.

Completeness

LiST is not modelling child mortality in its totality, despite its large number of possible interventions and risk factors. Thus, setting the coverage of all interventions to 100% or 0% will not result in a modelled under-five mortality rate that is as low or high as perhaps might be expected.

Using the example of Mali, the default LiST 2020 neonatal mortality rate is 32 deaths per 1,000 births and the under-five mortality rate is 94. Changing all coverages of Mali interventions in 2021 to 100% drops the neonatal mortality rate to 10 and the under-five mortality rate to 40. Similarly, letting all coverages be 0% makes the neonatal mortality increase to 60 and the under-five mortality to 160. So while 100% coverage of interventions could be expected to result in mortality rates close to those of, for example, Scandinavian countries, or at least towards fulfilling the Sustainable Development Goals (SDGs), the modelling results in higher levels. Similarly, with no interventions carried out, one would expect the mortality rates to go closer to early colonial levels in Mali.

As noted, LiST does not take synergies into account. Economic growth can be seen as a function of labour productivity, capital productivity and total factor productivity. The first two are relatively easy to estimate, while the somewhat elusive total factor productivity – being an expression of intangible aspects of the economy, such as logistics, governance and other factors that enable the economy to function – is often estimated as a residual. Lives saved can be seen in a similar fashion – that is, as a result of direct interventions and factors such as women's knowledge about caring for children, the organizational efficiency of the healthcare system, and general aspects of living conditions. LiST handles the direct interventions and risks, but probably not the overall aspects.

How well LiST performs in a given country probably also depends on the quality of the data on coverage of interventions, mortality, and cause of death. To illustrate, a similar analysis to that of Mali for Bangladesh gives results that are much closer to what one would expect.

Use of LiST

LiST is distributed as part of Spectrum, and can easily be downloaded (1). In the context of COVID19, there have been several adaptations and additions to the program, to capture the pathways that COVID19-related disruptions potentially influence health outcomes. The most recent version should be used.

The use of LiST itself is quite simple and well documented in its manual. The starting point is the baseline for a given country or region. This includes specifying the population structure and change (i.e. age and sex structure, fertility, and mortality rates).

The demographic projection tool in Spectrum comes with the World Population Prospects projections by the United Nations Population Division (presently the 2019 revision), or the user's own data may be used. In addition, contraceptive prevalence is needed.

The second major component is the cause of death distribution for the relevant age groups. LiST has the distributions already loaded, so the user does not need to enter them.

The baseline is completed by mapping out the current level of risk factors and exposure, and the current coverage of interventions.

When the baseline is finished, and a level of mortality is determined, the coverage can be changed for specific interventions to see how the number of deaths changes. In the traditional use of LiST, the change has typically been a gradual scaling up of interventions as health systems and general living conditions improve; in the context of COVID19, the change is more likely to be decreased coverage because of stresses on the health systems, or an increase in risk factors such as stunting and wasting.

Because of how it is structured with a population model at the base, LiST is relatively easy to integrate with other models of aspects of the pandemic. An example is the nutrition model referred to above. Another example is a recent study of the benefits and risks of infant feeding and mother-and-child contact, which finds that the benefits of breastfeeding and close contact far outweigh the risks (14). Yet another example is the WHO assessment tool discussed in Appendix 2f.

2b: The benefit–risk assessment model

The benefit–risk assessment model has been developed by the COVID19 working group of the Centre for the Mathematical Modelling of Infectious Diseases at the London School of Hygiene & Tropical Medicine (LSHTM), in consultation with Gavi, the Vaccine Alliance and other stakeholders. It aims to compare the benefits of routine childhood immunizations with the risks of acquiring coronavirus infections when visiting for these routine vaccinations during the COVID19 pandemic in Africa. The measure for both benefits and risks is lives saved or lost. If children are not vaccinated, a risk is incurred, in children's lives lost, and if children are vaccinated, the benefit is children's lives saved. But the risk is that children may get infected with coronavirus while going for routine immunizations, and subsequently may die from COVID19.

The results are presented as benefit–risk ratios. For example, Chad may avert 9,016 deaths by continuing vaccination, and by its continuation, may incur 98 extra COVID19 deaths, yielding a benefit-risk ratio of 9,016 divided by 98, which equals 92. The model provides estimates by countries and for the African continent as a whole. In general, the model shows the huge benefits of continuing routine immunization programmes.

COVID19 disruptions

The model treats disruptions from COVID19 as scenarios that are completely exogenous. Two scenarios are considered. Both assume complete cessation of immunization activities, but differ in how they restart immunization.

The paper by the LSHTM was developed in the early phase of the pandemic and published in April 2020 in the institutional repository (15) and the journal paper was first published in July 2020 (16). The two scenarios have proven to be overly pessimistic. The second pulse poll of June 2020, from the United Nations Children's Fund, found that seven countries (out of 82) had completely suspended outreach immunization, while only one had suspended fixed-post immunization. Similarly, 50% and 42% of countries reported disruption in, respectively,

outreach and fixed-post immunization (17). Another example is the reporting from the Nigeria national health information system. This shows a 20% drop in pentavalent immunization from January to May 2020, but a recovery by September 2020 (18).

Complete cessation of immunization is probably excessive given experience so far, but the assumption may easily be changed into less severe reductions in coverage.

In the published model the pandemic is assumed to last for five and a half months, with herd immunity reached with a 60% infected population. With hindsight, the period is relatively short. The period can be extended, though, and if nothing else is changed, this increase in the period of infection risk would increase the benefit–risk ratio. The progression of the COVID19 pandemic is assumed to be constrained by various measures, such as hygiene, masks and lockdowns, so that the prevalence of infected people in the community is constant throughout the period.

The model

The model consists of three main parts: a simple model of the pandemic itself, the risk of COVID19 deaths related to visits to health centres for vaccination, and an analysis of the benefit of vaccination. The first two provide the risk of COVID19 deaths and come together with the last in the calculation of the benefit–risk ratios. The model is depicted in Figure 5.

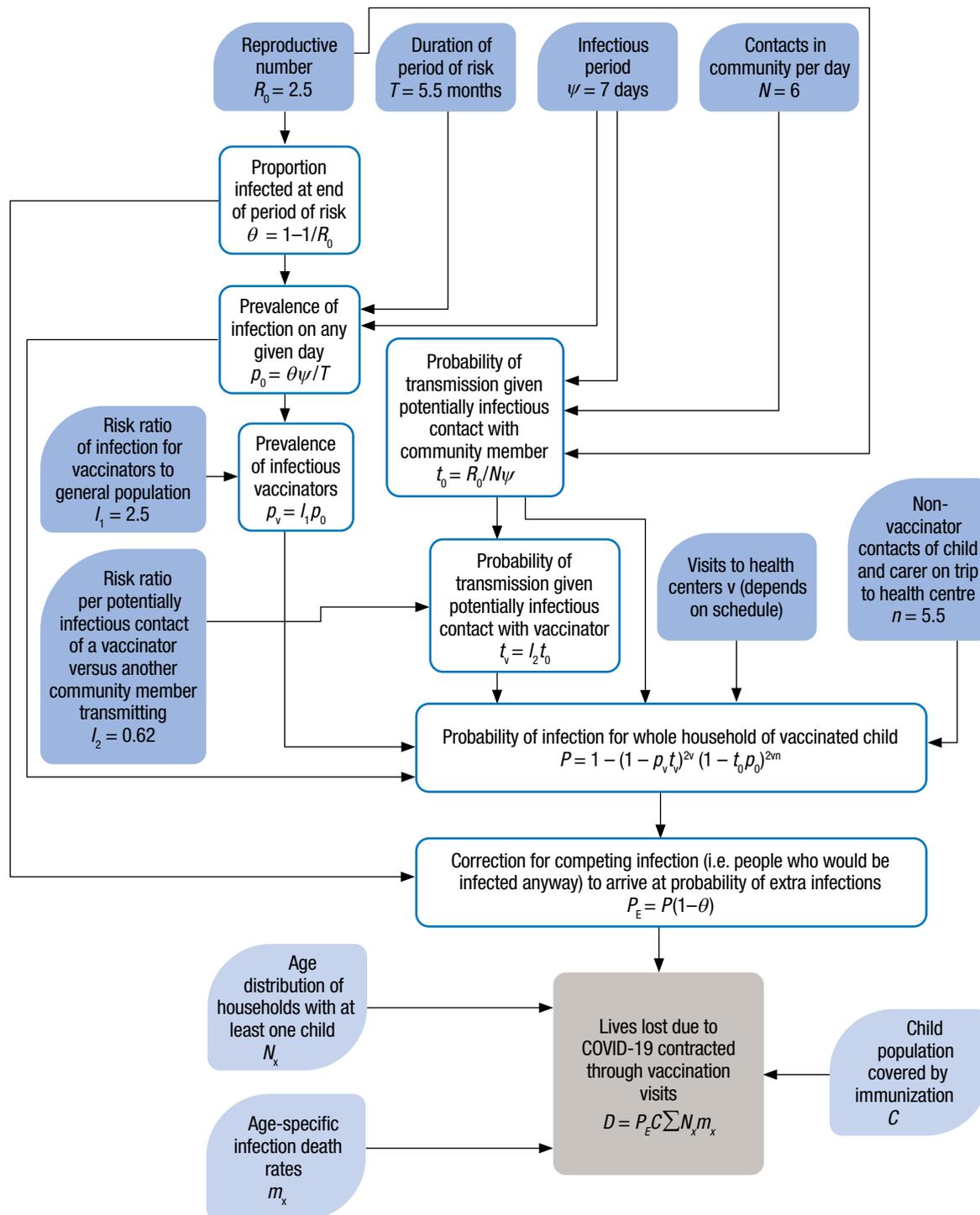
The calculation of lives lost due to non-vaccination takes its point of departure from the pre-COVID19 coverage, as supplied by WHO (19), and assumes that the vaccination stops completely. Deaths from not being vaccinated are counted on a cohort basis – a coverage drop means that a particular cohort of children does not get vaccinated. Two scenarios are described: a high-impact scenario and a low-impact one. They differ in how vaccination restarts.

The high-impact scenario assumes that immunization is suspended during a six-months period in 2020, and there is no later mitigation for the cohort. Therefore, the total extra deaths from, say, tetanus, is calculated as the deaths to the non-vaccinated fraction until they reach 5 years of age. The low-impact scenario assumes that, with the exception of measles, herd immunity protects the non-vaccinated fraction and that a catch-up campaign to mitigate the effects takes place after 6 months. Thus, the deaths from ceasing vaccination in the low-impact scenario are actually all measles deaths.

Two main sources inform the benefit of vaccination. One is a study of estimated lives saved by major vaccination against major pathogens by the Vaccine Impact Modelling Consortium (20) and another (for diphtheria, tetanus and pertussis) is a review of vaccine impact (21). These provide the number of child deaths avoided per vaccinated child for the different pathogens, and the confidence limits for these estimates. The information is used together with country-specific coverage rates to compute the number of deaths that may occur if vaccination is suspended.

The model of COVID19-related deaths proceeds in several steps. The first is a general model of the overall spread of COVID19 in the population, which results in an overall prevalence of

Figure 5. Outline of the Benefit-risk model



infection at any given time. The overall infection rate determines the chance that an individual may meet an infected person.

The model is not a complete COVID19 prediction model. Rather, it assumes a basic reproductive number for the disease and, from that, calculates the final cumulative percentage infected. The percentage who have ever been infected when herd immunity is reached is thus simply:

$$(1-1/R_0) \times 100$$

Where R_0 is the basic reproductive number, assumed to be 2.5 (22). Then, the ever-infected are spread equally over the pandemic's assumed duration, set to 5.5 months, and the percentage infected at any one time is about 2.5 (percentage infected at the end times the number days a person is infectious divided by the pandemic duration in days). The underlying assumption is that the disease will not progress unconstrained in the population but that social distancing, lockdowns, and other measures will flatten the curve. Still, the pandemic will not stop before herd immunity is reached.

The assumption is important, as an unconstrained epidemic with a basic reproductive number of 2.5 and a duration of infectiousness of 7 days would have about 40 days in the middle of the epidemic where the prevalence of infected people would be much higher, and reach slightly above 20% at its peak. Thus, in the case of an unconstrained pandemic, the number being infected by visiting a health centre would be substantially higher than that modelled by the LSHTM model because of the high prevalence of infectious people during that part of the pandemic.

Another critical aspect of the R_0 of 2.5 is the effect on the average prevalence in the population. If R_0 were higher, the prevalence in the population would also be higher since the total number of ever-infected would be higher. That would, in turn, mean that the probability of catching the coronavirus from travel and visits to health centres would increase.

The second step considers the extra infections of coronavirus that may occur if parents bring their children to health centres. The key equation in the model is the one that relates visits to infection. It is shown in Figure 5 as the "probability of infection for whole household of vaccinated child". It is the complement of neither being infected during immunization nor on travelling to and from the clinic. Since several visits are involved for a complete immunization schedule, and both the child and the caretaker are visiting, the probability of being infected must account for the number of visits, the probability of transmission given contact with the vaccinator, and the prevalence of infectious vaccinators.

The probability of being infected while travelling depends on the probability of being infected by a contact, which again breaks down into the prevalence of infected contacts and the probability of transmission given a contact. Of course, the probability of infection during travelling also depends on the number of contacts and number of journeys. Differences in risk between alternative modes of travel are not considered, but could easily be factored in. A key feature of the equation is that it is relatively easy to extend it beyond immunization to other child health interventions. Many interventions require a health centre visit or some contact between health personnel and the child and caretaker. What is needed is to model the benefit

of the intervention in terms of the number of visits needed for the intervention and the probability of transmission given contact with community members or health personnel, and the prevalence's of infection.

The task can be carried out by considering how the specific health intervention takes place. The general benefit assessment tool based on the LSHTM model and LiST does this. The tool will be discussed later in this document.

The complete household assumption

The model assumes that the secondary attack rate in households is 100% – that is, all household members get infected if one person in the household is infected. Some studies show that the rate may be considerably lower (23–25). The effect of reducing the household secondary attack rate in the model would be to increase the benefit of continued immunization. Different virus variants may have different secondary attack rates.

Mortality from COVID19

An important set of assumptions in the LSHTM model are the age-specific infection–fatality ratios. Together with the household age structure, the ratios are what determines the number of deaths from COVID19 in the model. The source for these ratios is a paper published in *The Lancet Infectious Diseases* in June 2020 (26). The ratios are shown in Table 1.

Table 1. Infection–fatality ratios used

Age group	Value (%)
Children (aged under 20 years)	0.00161
Adults (aged 20–59 years)	0.08464
Older adults (aged 60 years and above)	3.28379

Note that the rates are infection–fatality ratios, not case–fatality ratios. Thus, they are the ratios of deaths to all infected, irrespective of whether the infected have been diagnosed. The infection–fatality ratio is the correct measure to use in the model because the model estimates all infections, not just those that are diagnosed and confirmed. In contrast, readily available data from countries are often case–fatality ratios, which are the ratios of deaths to confirmed cases (27). Given that there is a large proportion of coronavirus-infected people who are asymptomatic, but who may still be infectious, the difference between the two ratios is substantial. Substituting the infection–fatality ratios with case–fatality ratios would yield estimates of COVID19 deaths that are too high.

The infection–fatality ratios used are on the low end of such estimates but benefit from being built on a wide range of available evidence. As more data become available, however, it is likely that the estimates will change. Increasing the fatality ratios in the model will reduce the benefit–risk ratios of vaccination. The benefit–risk ratios estimated in the model are so high, however, that higher infection–fatality rates would most likely not change the substantial conclusions.

Inequity

The benefit–risk model disaggregates only to the country level. There is no consideration of within-country differences. As with LiST, it is not difficult to model geographical regions, although each region would have to be assumed to be closed. Socioeconomic groups are more difficult to model than geographical regions, because they cannot be treated as distinct populations. One could, however, as a simplification, use different assumptions about the prevalence of infectious individuals in different groups.

Uncertainty

The benefit–risk model is stochastic, so uncertainty is built in. The model treats sensitivity to model assumptions and stochastic variation simultaneously. The basic reproductive number for COVID19 is thus assumed to be 2.5, but with a probability distribution. The basic assumptions can be changed by more than what is implicit in the probability distributions for each.

Use of the benefit–risk model

The benefit–risk model is implemented in the statistical programming language R, and anyone can download the source code (28). R itself is also free, as is RStudio, the most commonly used integrated development environment for the language (29). The current implementation of the model produces estimates for all countries in Africa, both in aggregate and individually. If one is interested in only a single country, it will require some work to separate out the code. The combination model of the benefit–risk and LiST developed for country use may solve that problem. The main downside of the approach, however, is that the combination model uses a deterministic, rather than a stochastic, framework. Uncertainty is therefore not accounted for.

2c: Adding It Up

Adding It Up, as described here, derives from an ongoing Guttmacher Institute project “that estimates the need for, impact of and costs associated with providing essential sexual and reproductive health services” (30). The Guttmacher Institute produces regular reports on such needs, impacts and costs. Its initial work on COVID19 is a scenario-based attempt to understand what the possible consequences of the pandemic may be for women of reproductive age, newborns and adolescents. The report is an adaptation of a 2019 report exploring the consequences of service disruption. The 2019 results are contrasted with what would have been the case given a drop in service coverage.

A report published in mid-April of 2020 found that, among other results, a 10% proportional decline in reversible contraceptive use would result in an increase in the unmet need for contraception by 49 million women, and 15 million additional unintended pregnancies (31). Concomitant maternal deaths were estimated at 28 000 and there would be an additional 168 000 neonatal (newborn) deaths.

To no small extent, Adding It Up follows the philosophy and algorithms of LiST. It employs the same basic structure as LiST (Figure 3), particularly the for maternal and newborn health, but

not for other outcomes. Family planning is, for example, treated differently. While LiST focuses on individual countries, Adding It Up emphasizes low- and middle-income countries, as a whole and regionally.

The critical characteristic of Adding It Up is the focus on reproductive and sexual health. Compared with LiST, Adding It Up includes a more comprehensive package of sexual and reproductive health services and takes into account interactions across services. The overall model may be seen broadly as population characteristics and sexual and reproductive health service coverage coming together to produce outcomes – and outcomes may have negative consequences. Lack of coverage of contraception, for example, may lead to unintended pregnancies that, in turn, may lead to unsafe abortions, as seen in Figure 6 to illustrate the structure of Adding It Up.

The main outcomes are the number of women in need of contraceptive, pregnancy-related and newborn care, and of treatment for the four major curable STIs, and the impact on unintended pregnancies, unsafe abortions, unplanned births, maternal deaths, newborn deaths, newborn HIV infections and the prevention of pelvic inflammatory disease.

The full Adding It Up model also includes estimates of cost for scaling up services, but that is not discussed here.

Adding It Up is designed for advocacy, and is less suited for decision-making for specific programmes. Particular to its advocacy purpose, Adding It Up's non-COVID19 application assumes an instantaneous jump in service coverage, from the current coverage rates to complete coverage. This jump is not assumed in other modelling work and reflects the specificity of Adding It Up's purpose.

An outline of Adding It Up is shown in Figure 7, which for simplicity depicts the model only for unintended pregnancies. The starting point is the age distribution of women of reproductive age. Women can be divided into several groups with respect to pregnancies, depending on whether or not they want to be pregnant, and whether or not they are using contraception. Unintended pregnancies are those that either result from contraceptive failure or when a woman does not want to be pregnant but, for some reason, does not use contraception (32).

Figure 6. General structure of the Adding It Up model

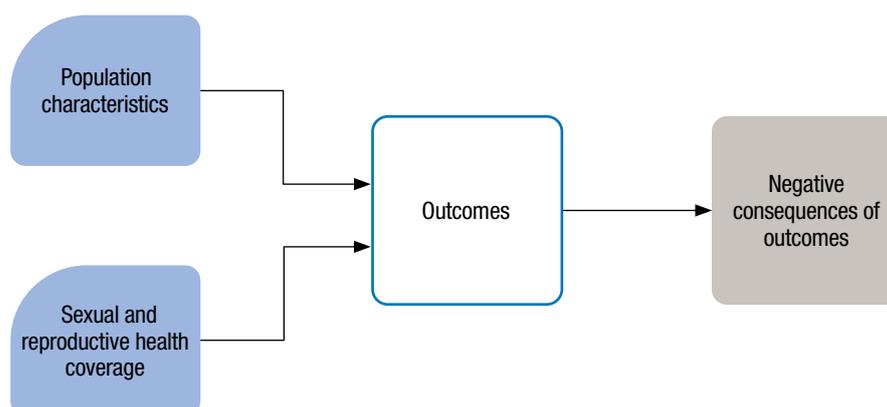
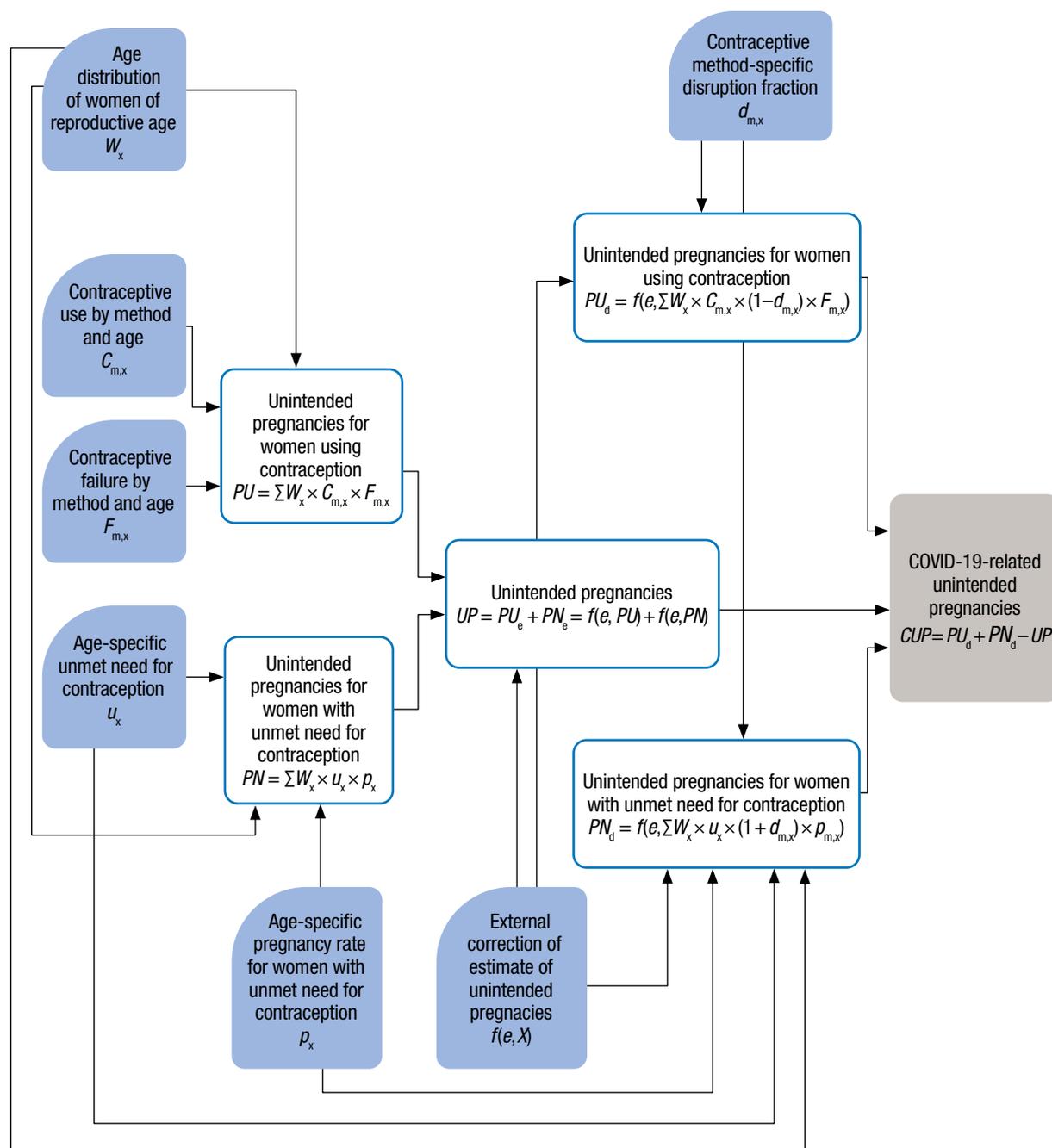


Figure 7. Outline of the Adding It Up algorithm for unintended pregnancies (draft)



Since the outset, pre-COVID19 crisis, Adding It Up has modelled unintended pregnancies as those that stem from contraceptive failure among women who use contraceptives, or pregnancies for women who did not want a pregnancy but who did not use contraception. The analysis is relatively fine-grained, in that age-specific use rates by the method of contraception are taken into account. The granularity is useful for COVID19 modelling because some methods are more affected than others by the pandemic. Sterilization is not affected at all, while disruption in the supply of condoms may have immediate effects.

Within an age group of women, the unintended pregnancies of those using contraception are the number of women in the age group multiplied by the method- and age-specific use rate and the corresponding failure rate. The total is then the sum across all age groups. Similarly, for women who were not using contraception but did not want children, the unintended pregnancies are simply the product of the number of women in the age group, the unmet need rate and the pregnancy rate among those with unmet need for contraception. The initial estimate of unintended pregnancies is thus a deterministic estimate from the available data for each country. The initial estimate is adjusted to a statistical estimate of unintended pregnancies for 2015–2019 that has been developed. A country estimate for a year is based on the available data for the year and the time trend for the country and presumed similar countries (33).

The COVID19 estimate is produced similarly, but assumes that when the supply or the accessibility of contraceptives is interrupted, usage rates decrease. Some women are shifted from contraceptive users to women with unmet need for contraception. A new initial estimate is thus arrived at, and it is shifted by the same fraction as the initial estimate with the external adjustment model. This process is different from that of LiST, where no external adjustment takes place.

For estimates such as child mortality, the estimation process is very similar to that of LiST.

Data sources

The model uses mostly the same data as LiST for the intervention-specific affected fraction and effectiveness, and extends the data when needed. It also sometimes use different data. For example, Adding It Up uses the WHO overall number of deaths for maternal deaths, but the Global Burden of Disease distribution of causes, which is different from the breakdown of causes used by LiST.

Adding It Up takes population estimates directly from the World Population Prospects 2019 and other recent sources as required. In contrast to LiST, the population development is not modelled. This is in line with the philosophy of providing scenarios for the current time period as there is then no need for detailed population modelling in addition to that of the World Population Prospects. This means that Adding It Up is not suitable, though, to projecting several years into the future. The COVID19 report is based on the 2019 yearly report, and therefore uses 2019 population figures. As noted before, the use of slightly outdated figures matters little.

Adding It Up also uses DHS and MICS data to obtain method-specific distributions of users and the proportion of the population in need of and covered by pregnancy-related and newborn health services.

The Guttmacher Institute is working to make the underlying data set available for researchers.

Similar to most of the other approaches, the model does not try to model disruptions but produces estimates for a general coverage-drop scenario. The published scenario uses a 10% proportionate drop in services.

Disruptions in Adding It Up

The 10% drop is applied equally to each intervention considered. In contrast, the LiST application considers that reductions in workers, equipment, access and willingness to seek care are multiplicative so that a 10% reduction across each of the four items would result in a 34% reduction overall. However, some of the reductions in Adding It Up are cascading. Thus the reduction in the supply of contraceptives leads to more unintended pregnancies and more births than before. That, together with a reduction of maternal and child health services, leads to more deaths of mothers and newborns.

Uncertainty

Adding It Up is a deterministic model and does not include sensitivity or uncertainty measures. Given the structure of the Stata source code, it would not be too difficult – albeit a lot of work – to build such features into the model.

Use of Adding It Up

The Stata code for the updates of Adding It Up is available to anyone interested (34). So far, the COVID19-specific modelling, including the complete set of country-level input data and output results, are not available.

2d: Direct and indirect effects of the COVID19 pandemic and response in South Asia

The model of direct and indirect effects of the COVID19 pandemic and response in South Asia has been developed by SickKids (The Hospital for Sick Children, Toronto), in collaboration with The Aga Khan University, Cytel, Medicus Economics and the University of Waterloo. It will be referred to here as the SickKids model. A report based on the model was published in March 2021 (35).

Rather than focusing on many countries, this model concentrates on some countries in South Asia, namely Afghanistan, Bangladesh, India, Nepal, Pakistan and Sri Lanka. In contrast to most of the other models discussed here, SickKids uses data from real-time information from country health monitoring systems to assess disruptions from COVID19. The SickKids model is not actually one model, but five. At the conceptual level, these models are linked but, in practice, they are estimated separately. The five models are of:

1. Development of the epidemic, giving estimates of mortality and morbidity, and the effect of responses;
2. Child and maternal mortality;
3. School-aged child and adolescent mortality;
4. Educational attainment; and
5. Economic impact of COVID19 control measures.

In this review, only the first four items will be discussed. The main outcome measures are maternal, child and adolescent health. Nevertheless, the five models produce several other measures of interest, to mimic the actual spread of the disease in each of the countries of interest.

The epidemic model

The purpose of the epidemic model that SickKids uses is to estimate the direct death toll of COVID19, the costs of admission to hospital and to the intensive care unit, and to explore the effects of possible mitigation strategies.

SickKids uses a full epidemic model that aims to mimic the actual spread of the disease in each of the countries of interest. This approach contrasts with that of the benefit–risk model by the LSHTM, in that the prevalence of infected people varies over time in the SickKids model, while it is constant in the LSHTM model.

The epidemic model is an extension of a susceptible–infected–recovered (SIR) model. In such a model, individuals in a population can be in one of three states or compartments, namely that of being susceptible to infection (S), infected (I) or recovered (R). The transition between the states is in only one direction, in the order of the letters, and people who have recovered obtain immunity and cannot be infected again. The model may be framed as having fixed transition rates, giving rise to a deterministic model. Alternatively, the transition rate may be conceived as a probability with a distribution, giving rise to a stochastic model.

A simple extension of the SIR model is the SEIR model, where the infected state is split into two: the exposed (E) and the infectious. Relevant to many diseases, including COVID19, the change implies an incubation period (the exposed period), when a person is no longer in the susceptible category but is not yet infectious.

Successful modelling of COVID19 needs a more detailed approach, though. A simple change is to divide the recovered state into recovered and fatalities, since COVID19 is sometimes fatal. Moreover, SickKids introduce two other states, namely the isolated cases outside of hospitals (Q) and those that require hospitalization (H). A critical aspect of those who need hospitalization is that they may or may not be in hospitals, depending on hospital capacity.

The exposed state's meaning is also redefined into exposed asymptomatic people who potentially may be infectious, while the infected state then is reserved for the symptomatic infected. The model, depicted in Figure 8, is derived from the COVOID (COVID19 open-source infection dynamics) model developed by Churches and Jorm (36).

The model requires several assumptions, which are empirically based to varying degrees. Some of the assumptions are country-specific, while others are intrinsic to the disease. The country-specific are either initial conditions, such as the number in each state at the start of the model run, or the number of hospital beds, or estimated from the calibration. Some assumptions are also fixed, either because there is a lack of evidence or because it is reasonable to assume a fixed value (Table 2).

Figure 8 Sick Kids COVID-19 model

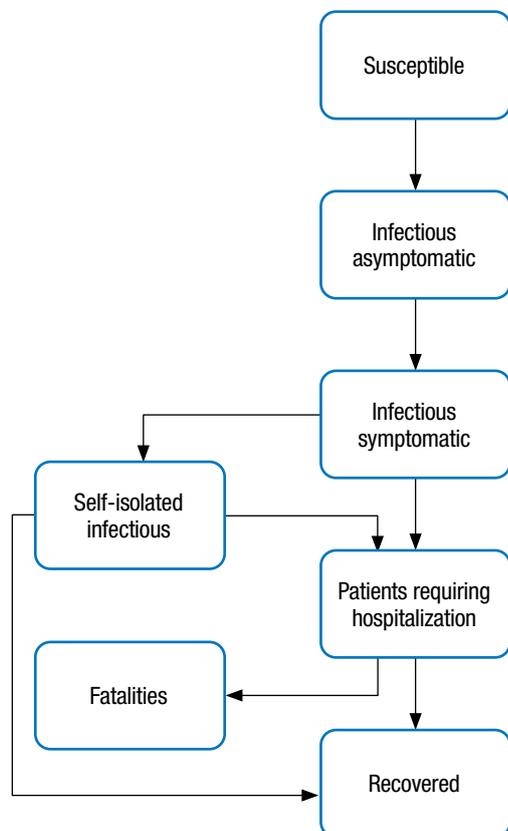


Table 2. Fixed empirical assumptions in the SickKids epidemic model

Assumption	Value	Note
Progression rate (the incubation time)	0.048305	Corresponds to 50% having developed symptoms after 14 days
Quarantine rate	0.03333	Expresses that there is a 50% chance of self-isolation within 21 days of the onset of symptoms
Recovery rate	0.05	Rate per day at which infected and symptomatic recover
Discharge rate	0.066667	Corresponds to a daily recovery rate of 2%
Mortality rate for people who need hospitalization but cannot get it because hospitals are full	The base mortality rate in hospitals multiplied by 2	The base mortality is estimated
Fatality rate for people needing hospitalization	0.5	The coefficient expresses the doubling of the fatality rate of people who need hospitalization but cannot get a hospital bed

The social contact rates for the individuals in the various states, the infection probability when an uninfected meets an infected person, and the hospitalization rate are estimated from the

calibration. The social contact rate and the infection probabilities are specific for each state. The contact rates and infection rate for the contacts between the symptomatic infectious and the susceptible are calibrated in the models, while the rates for the other transitions are fixed fractions of those.

In order to arrive at a model for each country, the model for each was calibrated, minimizing the squared difference between the model estimate and observed fatalities on a weekly basis. The procedure for doing so derives from a paper on the global optimization of computationally expensive functions using response surfaces, and tries to find values for the assumptions that make for the best model fit (37).

SickKids applies the model to each of the countries, thus establishing a model of the progress of COVID19 in each country. It also estimate the likely effects of mitigation measures such as lockdown, mask use, hand hygiene and social distancing.

To calculate the effects of pandemic control measures, SickKids makes assumptions about the effects of the various measures (Table 3).

Table 3. Relative risk reduction assumptions for control measures in the SickKids model

Measure	Relative risk (95% confidence interval)	Source
Smart lockdowns versus none (exposure)	0.38 (0.01–0.56)	Empirical/modelling study from Boston
Use of masks (transmission)	0.34 (0.26–0.45)	Meta-study of physical distancing, face masks and eye protection for COVID19, Middle East respiratory syndrome, and betacoronaviruses (38)
Hand hygiene (transmission)	0.50 (0.38–0.66)	Randomized control trial for influenza transmission among schoolchildren in Cairo (39)
Physical distancing – 1m or more versus less than 1m (transmission)	0.30 (0.20–0.44)	From meta-analysis (38)

As can be seen from the table, the effect of the measures on exposure and transmission may be relatively large, but the evidence base is not strong. However, this weakness reflects the state of the art, rather than criticism of the SickKids model.

The transmission dynamics of COVID19, as well as of fatalities, vary by age. The population over 65 years of age varies between 3% and 10% in the countries under consideration. A weakness in the model of the epidemic, therefore, is that it is not compartmentalized by age. The lack may be partly because the software package used cannot accommodate such a split, although the software developers plan this ability. Yet, since the model is calibrated separately for each country on fatalities, age-specific effects will, to some extent, have been taken into account.

The child and maternal mortality model

SickKids uses LiST and the family planning module of Spectrum to estimate the impact of service coverage reduction on mortality. The estimation process is the same as that described above for LiST, except for two critical differences between the LiST model and that used by SickKids. The first is that SickKids splits 2020 and the first six months of 2021 into six quarters, and estimates disruptions and impact separately for each quarter. One underlying assumption is that deaths in the baseline scenario can be distributed equally across the quarters. Another assumption is that service disruptions will have their effects in the quarter in which they occur. As noted, except for immunization, the latter assumption is probably true, while the first is more dubious. There is, for example, evidence of seasonality in child mortality in India.

The second difference is that SickKids uses district health information systems and health management information systems to estimate the disruption in the first two quarters of 2020. For the third quarter, it assumes 50% recovery from the second-quarter level. For the fourth quarter of 2020, an 80% recovery from the second quarter is assumed. For the first quarter of 2021, a 10% increase from the fourth quarter of 2020 is assumed. For the second quarter of 2021, a 20% increase from the fourth quarter of 2020 is assumed. Thus, in contrast to the other LiST applications discussed here, the SickKids model is empirically based for part of the period under consideration, and scenario-based for the remainder.

The baseline for the impact assessment is the most recent DHS or MICS, thus creating a variable baseline. Since these surveys are frequent in the region, the effect is probably not large, but may still contribute to an underestimation of the impact of the disruptions.

Adolescent mortality

In addition to under-five mortality, SickKids also estimates mortality for the age groups 5–9 years, 10–14 years and 15–19 years. LiST does not estimate lives saved or lost for adolescents. SickKids, therefore, uses another approach to arrive at these estimates.

The starting point is the cause distribution by the age and sex of the deaths in each country, as estimated by the Global Burden of Disease 2019 from the Institute of Health Metrics and Evaluation. The causes singled out were road traffic accidents, maternal causes for women aged 15–19 years, and HIV/AIDS, tuberculosis, typhoid and malaria. Road traffic accidents are in a particular category because mortality from these is likely to decrease during the pandemic. According to a study of the lockdown in Turkey, on which SickKids builds, people travel less during the lockdown, leading to fewer deaths across all age groups (40). The study also provides a breakdown by age. SickKids uses the age-specific declines and distributes them according to the severity of the lockdown. It is possible that there is considerable variation in how the pandemic affects road traffic accidents, and the study from Turkey is a weak evidence base. Not much other evidence is available, though (41).

For the maternal causes in adolescent women, the LiST and family planning modules of Spectrum are used for estimation, and deaths are distributed according to reductions in health intervention coverage.

SickKids models HIV/AIDS, tuberculosis and malaria using a similar approach to that for road accidents (finding a comparable situation and using that as a model). In this case, the model stems from the 2014–2015 Ebola outbreak in West Africa (42), where researchers modelled mortality from HIV/AIDS, tuberculosis and malaria examples with various levels of service disruption. SickKids uses 50% service reduction as a benchmark and scales its estimates linearly on that basis. Thus, if a 50% service reduction leads to a 40% increase in deaths, then a 25% service reduction leads to a 20% increase in deaths. For typhoid, SickKids simply assumes a case–fatality rate of 30% in the absence of treatment. Since data on service reduction for treating the diseases are not available, SickKids uses the proportion of facility-based deliveries as a proxy.

The appropriateness of the Ebola model is open to doubt, given the different epidemiological regimes in South Asia. Moreover, the West African model provides estimates for the entire 2014–2015 period. It is perhaps likely that the effects of service reduction will be somewhat delayed. For example, if antiretrovirals are interrupted in the first quarter of the year for people living with HIV, the impact is more likely to show up in the second quarter. It is possible, therefore, that the SickKids modelling somewhat overestimates the impact.

Educational attainment

Because of lockdowns and household income shortfalls, enrolment in schools may be expected to drop due to the COVID19 pandemic. The SickKids set of models tries to estimate the possible extent of this drop. It uses Indonesian data from the 1998 Asian economic crisis (43). The starting point is a table of change in drop-out rates in Indonesia from 1997 to 1998, by 1997 expenditure quintiles. SickKids then uses those rates on the enrolment data from the different South Asian countries. The final published report also includes estimates based on the West African Ebola crisis (35).

Rather than using expenditure quintiles, SickKids uses wealth quintiles – because these are what is available in the DHS and MICS. Expenditure quintiles should be more sensitive than wealth quintiles to households' current economic situations since the expenditure quintiles represent current expenditure whereas wealth quintiles are a measure of cumulative income. Because the Indonesian data analysis uses expenditure before the crisis, however, the difference may not matter much. Of greater concern is that the standard errors of the estimates are quite large in the Indonesian data. The Asian economic crisis was also an economic crisis, where the effect on school attendance presumably was mainly because of income shortfalls for households. In contrast, the COVID19 pandemic is a situation of both income shortfall and lockdown.

SickKids also tries to estimate an increase in teenage pregnancies. The evidence base is weak, and the assumption is that there will be a 28% increase. This figure is taken from a report from Kenya documenting the increase in teenage pregnancies in one refugee camp (44).

Uncertainty

The degree to which uncertainty is modelled appears to vary across sub-models. The epidemic model is fully stochastic and produces uncertainty intervals. The child and maternal

mortality estimates use LiST, and may also therefore produce estimates of uncertainty. There is no inherent modelling of uncertainty for adolescent mortality and educational attainment.

Use of the direct and indirect effects models

The source code, implemented mainly in R in addition to what has been modelled in Spectrum/LiST, is available from the authors. As noted, the core of the epidemic model can also be downloaded from the authors of that model. A very fast computer helps when using the full epidemic model.

2e: Institute for Health Metrics and Evaluation

The model from the Institute for Health Metrics and Evaluation (IHME) is not specifically on the effect of COVID19 on women, children and adolescents, but on achieving the SDGs generally. The results of the model are published as part of the Goalkeepers initiative of the Bill & Melinda Gates Foundation, which produces yearly reports on SDG progress. The report for 2020 naturally focuses on the COVID19 pandemic and its effects against the SDGs (45). Effects on child mortality, women's health, and so on, are of course a subset of the SDG indicators. The model covers the disease dynamics, and social and economic indicators in addition to the range of outcome indicators. It has four time tranches: the pre-pandemic period, the early pandemic (January to June/July 2020), the period between July 2020 and the end of 2021, and then 2022 to 2030. In the model diagram, the short-term phase (2020–2021) and the post-pandemic phase (2022–2030) are used. The first deals with the effects of the immediate disruption, and the second with the following possible setbacks.

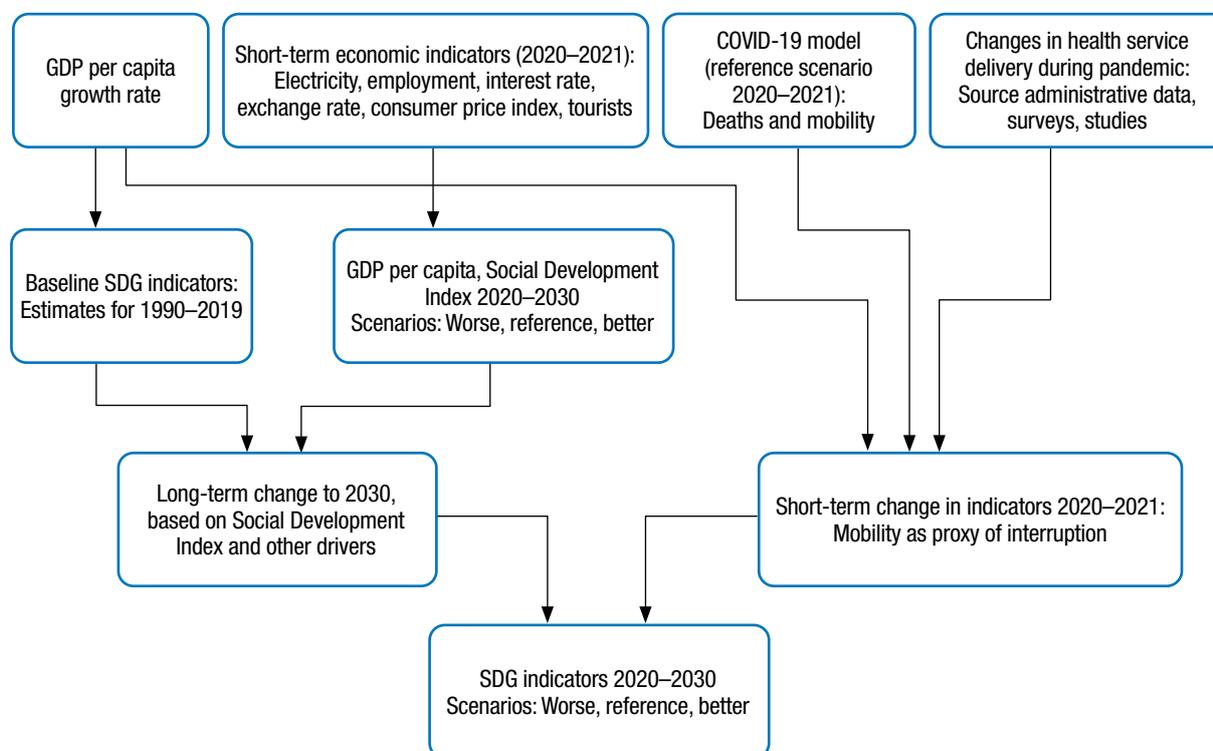
The overall structure of the IHME model (Figure 9) shows that the overall model is not a causal but mainly a predictive model, where proxy indicators are used extensively to predict outcomes (46). However, some parts of the model are more causal than others. Thus, the model of the development of the COVID19 pandemic has developed from a predictive model based on curve fitting to a susceptible-exposed-infected-recovered (SEIR) model assisted by curve fitting.

The level of detail within each part of the model varies considerably. For example, the GDP per capita is basically a set of data points, while the pandemic modelling box is a complex model in itself. Another characteristic of the IHME model is that it is based on available empirical data to assess disruptions rather than being purely scenario-based.

IHME commissioned 70,000 smartphone and telephone surveys, and also used monthly administrative data for data on health services, mobility and the monthly correlates of GDP.

The model of the pandemic

The main outputs of the IHME pandemic model are infections, testing, hospitalizations, intensive care unit use, ventilator use and deaths (47). The model itself is a relatively simple SEIR one where the infectious compartment is divided into two, namely into pre-symptomatic and symptomatic (see Figure 10).

Figure 9. Structure of the IHME model

GDP = gross domestic product; SDG = Sustainable Development Goal

The model is actually two models: one is used on existing data to calibrate the model, while the other uses the calibration for prediction. The model is built up by focusing on the rate of change in each of the compartments. The outcome measures are estimated from the relevant compartments. Predicted deaths, for example, are estimated from the predicted infections.

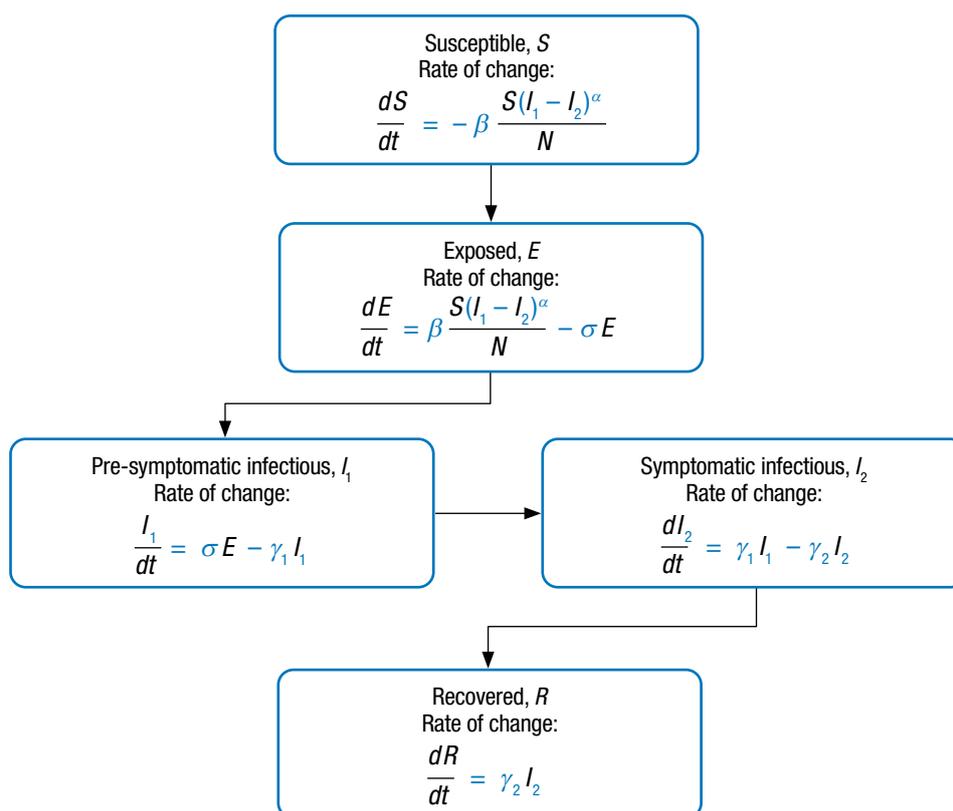
While the other COVID19 models described in this review use data from usually one selected public source to estimate the infection–fatality ratio, IHME performs its own meta-analysis of published data. Its final estimate is based on New Zealand, since the country has the lowest recorded infection–fatality ratio, and infection–fatality ratios are generally overestimated because many infections go undetected. Similarly, age-specific mortality rates were established using data directly rather than published estimates.

In general, the IHME strategy appears to have been that, if at all possible, estimates for parameters needed for the model should be estimated from existing data, or meta-analyses, rather than using a selected published source or scenario for each. In some cases, estimates from the Global Burden of Disease are used. The benefit of this approach is the nearness to data. The downside is that, even with the quite extensive documentation of the model, it is difficult to understand precisely how the sub-models and statistical approaches were specified and used.

When the model uses time series data for calibrating the model or for covariates, the time series are generally smoothed. The smoothing algorithm varies depending on the data.

The model differs from other similar models principally through the effort IHME puts into estimating β – that is, the product of the number of contacts and the probability of a susceptible person being infected when meeting an infectious person. To arrive at β for each geographical unit, a set of time-varying and a set of time-invariant covariates are used. The time-varying covariates include mobility, mask use, pneumonia seasonality, and testing for COVID-19. The time-invariant covariates were lower respiratory tract infections, altitude, smoking, air pollution (measured as the concentration of particulate matter with diameter less than 2.5 micrometers) and population density. The age distribution of the Global Burden of Disease was used to obtain age-specific deaths.

Figure 10. The IHME COVID-19 model



- α : Population mixing correction
- N : Population size
- σ : Transition rate from exposed to pre-symptomatic infectious
- γ_1 : Transition rate from pre-symptomatic infectious to symptomatic
- γ_2 : Transition rate from symptomatic infectious to recovered
- β : Product of number of contacts and probability of a susceptible person being infected by infectious person
- t : Time

Another aspect of the model worth noting is the α factor, which is used to account for incomplete mixing of the population – that is, to account for the fact that the disease is not evenly spread across population groups and locations.

The short- and long-term sub-models

The short-term change in the SDG indicators is driven by the pandemic itself, the change in health system coverage and short-term GDP changes. The long-term model is, in contrast, not based on the pandemic model.

The Socio-Demographic Index (SDI) plays an important role in the modelling. It is, for example, used in the projection of long-term change in SDG indicators to 2030. The SDI comprises three sub-indices: the logged lagged income per capita, the mean educational attainment in the population over the age of 15 years, and the total fertility rate (48). Each SDG indicator is modelled separately. The prevalence of stunting is described as being projected, with the SDI as the key driver. Similarly, the under-five mortality ratio was modelled using several covariates, such as Global Burden of Disease risk factors, selected health interventions and the SDI. The publicly available documentation does not reveal the exact model specification for the various models used.

Population

Unlike the other models discussed here, IHME does not use World Population Prospects 2019 as its population base. Instead, it uses its own probabilistic projection, which is also used in the Global Burden of Disease project. By using its projection, IHME maintains consistency across its various modelling efforts. While the population estimates are generally similar between IHME and World Population Prospects, there are discrepancies.

For Mali in 2020, IHME provides an estimate of 4.06 million children below the age of 5 years, while World Population Prospects reports 3.06 million. In contrast, the counterpart estimates for Ghana are quite similar, at 4.16 million for IHME and 4.17 million for World Population Prospects (49, 50). Thus, when IHME modelling gives different results from other models for specific countries, one should explore how much of the differences might be due to this variation in population estimates.

Uncertainty

In general, the IHME models and sub-models take uncertainty into account. The published results present the uncertainty as trajectories, which are called “better”, “reference” and “worse”. The calculation of each trajectory seems to be based on the 15th, 50th and 85th centiles of the SDI. However, the sub-models (such as the pandemic one or the population projection) have their own uncertainties associated with their estimates.

Use of the Institute for Health Metrics and Evaluation model

In contrast to the other models discussed in this review, the IHME model is not well documented in its totality. While there is considerable documentation of the sources of information available on the web, the inner workings of the model are far from clear. The source code for some of the code (such as the COVID19 SEIR model) is available on GitHub, but the code has few comments and little documentation. The code appears to be written either in R or Python. The main output from the model is readily available at the Goalkeepers website, however (45).

The integration with the rest of IHME's extensive modelling framework, such as the Global Burden of Disease and the population projection, is both a strength and a weakness. The approach makes the IHME modelling consistent, but it also appears monolithic and difficult to access and understand. While the overall framework is quite clear and well documented, it is more difficult to find each step's details.

The overall framing of the IHME COVID19 modelling of the SDG indicators is to advocate continued investment in achieving the goals. In contrast to some of the other models discussed in this report, the IHME modelling is not a policy simulation tool.

2f: Benefit–risk model merged with the lives saved tool (WHO)

To facilitate modelling of the risks and benefits of maintaining essential health-care services for individual countries, WHO has developed a modelling tool that uses and expands the methodology used by the LSHTM's benefit–risk model and LiST.

This tool takes the risk part from the LSHTM model and models lives saved or lost with LiST. The basic assumption is that contact with the health system for kinds of intervention other than immunization can be modelled in the same risk framework as for immunization. The merged model thus becomes a flexible tool for assessing how contact with the health-care system for various interventions may lead to increased COVID19 deaths (the risk) and lives saved from the interventions (the benefit).

The underlying assumptions are those that have already been described in the case of the risk model and for LiST. As noted, perhaps the most important in the case of the risk model is the assumption of the constant prevalence of infectious people throughout the pandemic. The combined model is, in contrast to the benefit–risk model, not a stochastic model and does not provide uncertainty estimates.

The model is basically an Excel spreadsheet into which all the relevant assumptions and country data are entered. It is geared for the use of up-to-date data on disruptions and coverage of interventions from individual countries. It is not designed for global or regional estimates. The COVID19 risk of using health services is modelled within the spreadsheet, while the disruption/coverage data are transferred to LiST. LiST then estimates lives saved or lost, and the data are transferred back to the spreadsheet for evaluation of the relative benefits and risks.

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