Report 19: The Potential Impact of the COVID-19 Epidemic on HIV, TB and Malaria in Low- and Middle-Income Countries

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Summary

COVID-19 has the potential to cause disruptions to health services in different ways; through the health system becoming overwhelmed with COVID-19 patients, through the intervention used to slow transmission of COVID-19 inhibiting access to preventative interventions and services, and through supplies of medicine being interrupted. We aim to quantify the extent to which such disruptions in services for HIV, TB and malaria in high burden low- and middle-income countries could lead to additional loss of life. In high burden settings, HIV, TB and malaria related deaths over 5 years may be increased by up to 10%, 20% and 36%, respectively, compared to if there were no COVID-19 epidemic. We estimate the greatest impact on HIV to be from interruption to ART, which may occur during a period of high or extremely high health system demand; for TB, we estimate the greatest impact is from reductions in timely diagnosis and treatment of new cases, which may result from a long period of COVID-19 suppression interventions; for malaria, we estimate that the greatest impact could come from reduced prevention activities including interruption of planned net campaigns, through all phases of the COVID-19 epidemic. In high burden settings, the impact of each type of disruption could be significant and lead to a loss of life-years over five years that is of the same order of magnitude as the direct impact from COVID-19 in places with a high burden of malaria and large HIV/TB epidemics. Maintaining the most critical prevention activities and healthcare services for HIV, TB and malaria could significantly reduce the overall impact of the COVID-19 epidemic.

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1. Introduction

The course of the COVID-19 epidemic in Low- and Middle-Income Countries (LMICs) will be determined by the actions that countries take in the coming weeks and months. It is clear that actions taken to reduce the size of the epidemic, delay, or flatten its peak, could lead to substantial reductions in deaths if doing so allows more patients with severe conditions to benefit from supportive care in hospital [1]. However, the impact of the COVID-19 epidemic and actions taken in response to it will have far reaching consequences – including on other diseases, poverty, food security and economic growth – and consideration of these will have a strong bearing on the range of responses that are taken.

Here we aim to provide information on just one of these aspects – the potential impact of the COVID-19 epidemic on three other major health priorities; specifically, Human Immunodeficiency Virus (HIV), Tuberculosis (TB) and malaria. We conceptualise this potential impact as arising predominantly from disruptions in the usual activities and services that may result from: (i) the mitigation strategies being undertaken in response to the COVID-19 epidemic leading to the scaling back of certain activities and care-seeking; and, (ii) reduced capabilities of the health system, due to overwhelmingly high demand for the care of COVID-19 patients and interruptions in the supply of commodities as a result of disruptions domestically or internationally.

We aim to quantify the extent to which such interruptions could lead to increased loss of life and other significant health outcomes due to HIV, TB and malaria during the period of COVID-19 epidemic and in the years that follow. We emphasise that these are not predictions of the impact but simply modelled scenarios to examine what potential consequences *could* ensue in order that this can help inform planning for an overall response to these threats such that the worst of these outcomes can be avoided.

2. Methods

Following Walker *et al*. [1], we construct four scenarios that describe a wide range of possible trajectories for the COVID-19 epidemic in LMIC:

- *'No Action'* – in which there is no substantial intervention on the COVID-19 epidemic (provided as a counterfactual as all countries are responding to the COVID-19 epidemic);
- *Mitigation* – in which interventions capable of reducing the COVID-19 effective reproduction number, *Rt*, by 45% are used for 6 months;
- *Suppression-Lift* – in which interventions capable of reducing *Rt* by 75% are implemented for 2 months and then lifted;
- *Suppression* – in which interventions capable of reducing *Rt* by 75% are implemented for one year (implicitly assuming that pharmacological intervention becomes available by that time and that therefore there is no large COVID-19 epidemic in the next 5 years).

We also assume that there is a reduction in *Rt* of 20% that occurs irrespective of any intervention due to a spontaneous reduction in social contacts. The timings of the epidemic are representative of settings where there has been a total of 0.1 deaths due to COVID-19 per million population by 12/4/2020, which is the case for most countries in sub-Saharan Africa.

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The course of each possible trajectory is then divided into periods during which different types of disruptions to services may occur - disruptions caused by COVID-19 interventions limiting activities and disruption caused by the high demand on the health system due to the COVID-19 epidemic itself. We assume that there is "high demand" on the health system when the ratio of the number of persons currently requiring non-critical care in hospitals for COVID-19 to the prevailing capacity of hospitals exceeds 50%; and that there is "extremely high demand" when that ratio exceeds 100%. We create two versions of the 'Suppression' scenario that have the same COVID-19 outcomes but different effects on other health services. In one permutation we assume that this very long period of suppression is so well managed that no more disruption is caused than during the short-term application of 'Mitigation' or 'Suppression' interventions. In the other, we assume that substantial obstacles to the provision of other health services do accumulate during this long period of substantial intervention.

We then make further assumptions about how the programs for HIV, TB and malaria will be affected in such circumstances (Table 1). In the absence of firm data on most of these points, these assumptions have been designed to give a consistent representation of the extent of disruption in the program elements for each disease so as to allow the results to be comparable. In particular: routine services for prevention (Voluntary Medical Male Circumcision (VMMC), Pre-Exposure Prophylaxis (PrEP), Long-lasting insecticide treated nets (LLIN), Seasonal Malaria Chemoprevention (SMC)) are assumed to be at least partially suspended during any intervention; provision of on-going treatment (for HIV or TB) or new acute treatment (for malaria) is reduced by ~25% and ~50% in the 'High' and 'Extremely High' periods of health-system demand, respectively; and treatment that requires persons newly seeking care (HIV or TB testing and treatment) is reduced by 25% in the 'Mitigation' / well managed suppression scenario, and by 50% during the unmanaged suppression interventions. Diagnosis and treatment rates for TB are reduced in total further than for the other conditions, owing to the additional impact of Xpert MTB/Rif, a molecular diagnostic tool for TB, potentially being repurposed for COVID-19 diagnosis.

The impact on health of these disruptions is estimated using separate models (see Appendix). Each disease model is applied to two contrasting settings chosen so as to span a range between settings that would likely be impacted severely by such disruptions and those which would be less severely impacted. These settings are:

- HIV: The 'High Impact' setting is South Africa (HIV prevalence 20.4% among 15-49-year-old adults in 2018) and the 'Moderate Impact' setting is Malawi (HIV prevalence 9.2% among 15-49-year-old adults in 2018);
- TB: The 'High Impact' setting is South Africa (estimated TB incidence of 520 per 100,000 population in 2019) and the 'Moderate Impact' setting is Brazil (estimated TB incidence of 45 per 100,000 population in 2019);
- malaria: The 'High Impact' setting is one with a high burden (~386,000 cases per million people in 2018) and a seasonality of transmission typical of a west African country; and the 'Moderate Impact' setting is one moderate transmission (~7,000 cases per million people in 2018) and a seasonality of transmission typical of a country in eastern Africa.

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Further justifications for these assumptions and technical details of the models are provided in the Appendix.

The impact of the COVID-19 epidemic and of the disruptions are quantified as the *extra* deaths and as the *extra* years of life that are lost with respect to a scenario in which there is no COVID-19 epidemic or associated disruptions (and programs continue or expand in the manner that would have expected in this period otherwise), over a period of 1 year and a period of 5 years. The life-years lost when a person dies as a result of COVID-19 or of HIV, TB or malaria are computed with respect to the life-expectancy for that age of persons in the respective country setting.

	During when Covid-19 interventions limit activities		**During High demand on health system**		**During Period of Recovery**
	Mitigation, or Well-managed/Short-term Suppression	***Unmanaged Long-Term Suppression****	***High***	***Extremely High*****	
HIV	*Care Seeking Reduced:* - Rate of new ART enrolments reduced by 25%; -2% per month of those on ART become virally unsuppressed . *Prevention Services Partially Suspended:* -No new VMMC; -No new PrEP enrolments . *Reduced Social Contact*: - 10% reduction in chance of acquiring new sexual partner	*Care Seeking Reduces:* -Rate of new ART enrolments reduced by 50%; -1% per month of those on ART stop due to inability to attend appointments. *Prevention Services Suspended:* -No renewals of PrEP prescriptions.	*Care, Medicine and Diagnosis is Less Available at Facilities:* -No new ART initiations; -25% of persons on ART pre-epidemic have their ART use interrupted; -10% become virally unsuppressed due to lack of viral load testing. *Prevention Services Suspended:* -No new VMMC; -No new PrEP enrolments; -No renewals of PrEP prescriptions.	*Supply of Drugs is Interrupted:* -A total of 50% of persons on ART pre-epidemic have their ART use interrupted; -Condom use is reduced by 50%.	-All services and behaviours resume to pre-epidemic levels immediately.

TB	*Care Seeking Reduced*: - TB diagnosis rates decrease by 25% compared to pre-epidemic levels; -Patient delays before the first presentation to care increased by 25% compared to pre-epidemic levels. *Displacement of Gene Xpert Diagnostic Resource:* - Diagnosis rate for TB and DR-TB decreased by a further 45% due to non-availability of Gene Xpert machines, yielding overall reduction of 70%. *Reduced Social Contact*: -Transmission reduced by 10%.	*Care Seeking Reduced:* -TB and DR-TB diagnosis rates decrease by 50%; -Patient delays before first presentation to care increased by 50% compared to pre-epidemic levels. *Displacement of Gene Xpert Diagnostic Resource* -Diagnosis rate for TB and DR-TB decreased by a further 20% due to non-availability of Gene Xpert machines, yielding overall reduction of 70%. *Prevention Services Suspended:* - No new IPT for PLHIV.	*Care, Medicine and Diagnosis is Less Available at Facilities:* - Treatment completion rates decrease by 25% for first line and 25% for second line compared to pre-epidemic levels; - Patient delays before first presentation to care increased by 50% compared to pre-epidemic levels; - DR-TB diagnosis rates decrease by 50% compared to pre-epidemic levels; *Prevention Services Suspended:* - No new IPT for PLHIV	*Supply of Drugs is Interrupted:* -Treatment initiation rates decrease to 50% pre-epidemic levels; - DR-TB diagnosis rates decrease to 0% (this is also impacted by diagnosis not being available).	- All services and behaviours resume to pre-epidemic levels immediately.
Malaria	*Care Seeking Reduced:* -Treatment of clinical cases reduces by 25% compared to pre-epidemic levels. *Prevention Services Partially Suspended:* -LLIN mass distribution continues as normal;	*Care Seeking Reduces:* -Treatment of clinical cases reduced by 50% compared to pre-epidemic levels. *Prevention Services Suspended:* -LLIN mass campaigns halted; -SMC halted.	*Care, Medicine and Diagnosis is Less Available at Facilities:* -Treatment of clinical cases reduced by 25% compared to pre-epidemic levels; *Prevention Services Suspended*:	*Supply of Drugs is Interrupted:* -Treatment of clinical cases reduced by 50% compared to pre-epidemic levels.	-Treatment of clinical cases remains at reduced level for 2 months; -All other services and behaviours resume to pre-epidemic levels immediately.

	- SMC 50% normal coverage		-LLIN mass campaigns halted; -SMC halted.		

Table 1: Assumptions for how programmes are affected during each kind of potential Disruption and during the period of recovery. *These changes are assumed to be in addition to those changes that occur during the 'Mitigation' interventions. **These changes are assumed to be in addition to those changes that occur during the period of 'High' demand on the health system. VMMC=Voluntary Medical Male Circumcision; PrEP=Pre-Exposure Prophylaxis; DR-TB= Drug-resistant TB; LLIN=long-lasting insecticide-treated nets; SMC=seasonal malaria chemoprevention.

3. Results

1) Projections for COVID-19

The projections for cumulative deaths due to COVID-19 over the course of the epidemic are shown in Figure 1. In the 'No Action' counterfactual scenario, the deaths due to COVID-19 are predicted to occur mostly between June and August (though these dates are sensitive to when the epidemic takes off) with an estimated ~6,000 deaths per million population. In this scenario, many of these projected COVID-19 deaths would be due to lack of treatment due to hospital capacity being exceeded. In the 'Mitigation' scenario, we project a lower number of COVID-19 deaths (~4,400 per million). This is because the epidemic is 'flatter' – it has a lower peak and lasts for longer – which means that the capacity of hospitals can accommodate a higher proportion of the COVID-19 patients. The relative number of deaths in the 'No Action' and 'Mitigation' scenarios depends on the hospital capacity assumed and the extent to which the 'Mitigation' interventions result in more people receiving treatment; if hospital capacity is very low, for instance, then we would project less difference between 'Mitigation' intervention and 'No Action' scenarios.

Under the 'Suppression' scenario we assume that the interventions that are put in place reduce the effective reproduction number for COVID-19 to below 1 and hence that the epidemic is quickly brought under control. In this scenario we assume that those interventions are maintained until other means of preventing the epidemic (such as a vaccine) become available. In the 'Suppression-Lift' scenario, we project a delayed epidemic of a size similar that in 'No Action'. This is due to the assumption that the risk of transmission is the same following the lifting of interventions; but clearly if additional interventions or strategies are found to maintain control of the virus then this assumption would not hold and the 'Suppression-Lift' scenarios would be closer to our 'Suppression' scenario.

Under our modelling assumptions, these different epidemic scenarios induce different patterns of disruptions (Figure 2). In the 'No Action' scenario, there is a period of 6 weeks during which the health system is under 'High Demand', within which 'Extremely High Demand' is experienced for 4 weeks. For the 'Mitigation' scenario, there is a period of disruption caused by the interventions, and then a period of 'High Demand', but there is no period of 'Extremely High Demand'. In the 'Suppression-Lift' scenario, there is a 2-month period of disruption caused by the suppression intervention and the same sequence of health system demand as in the 'No Action' scenario but this is delayed by 11 weeks. In

the two scenarios for 'Suppression' interventions, there is no period of 'High Demand' on the health-system (because there is no large epidemic) but there is a 12-month period of disruption caused by the intervention, which could be either 'Well Managed' or 'Unmanaged'.

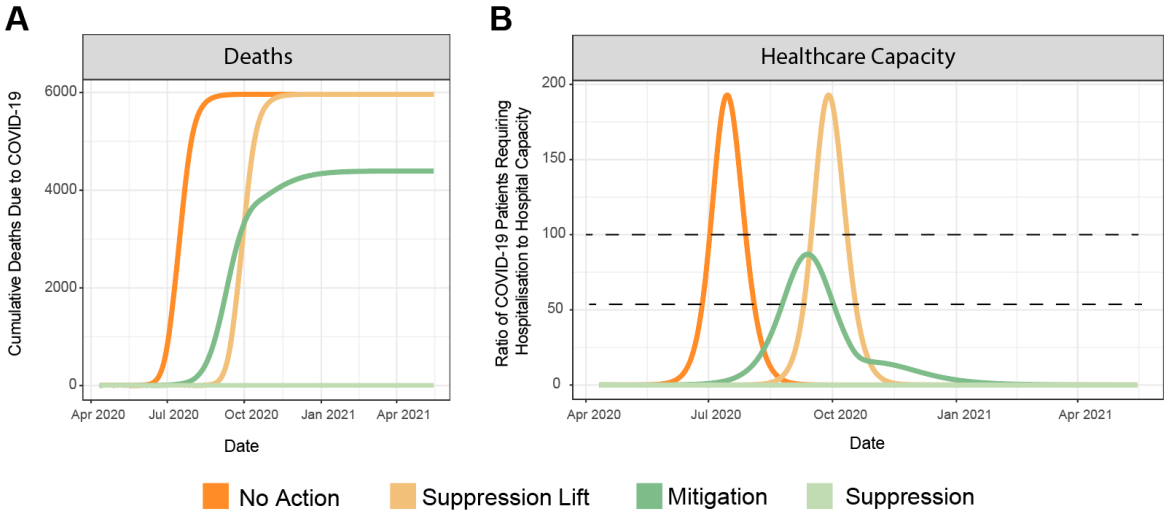

Figure 1: The impact of the COVID-19 epidemic under each epidemic scenario in respect of (A) Cumulative deaths due to COVID-19 per million population, and (B) The ratio of the number of COVID-19 patients requiring non-critical care in hospital to the total hospital capacity. Orange= 'No Action'; Yellow= 'Suppression-Lift'; Green= 'Mitigation'; Pale Green= 'Suppression'. In panel (B) the dashed lines indicate the threshold which are used to delineate periods of 'High' (50%) and 'Extremely High' (100%) Health-System Demand.

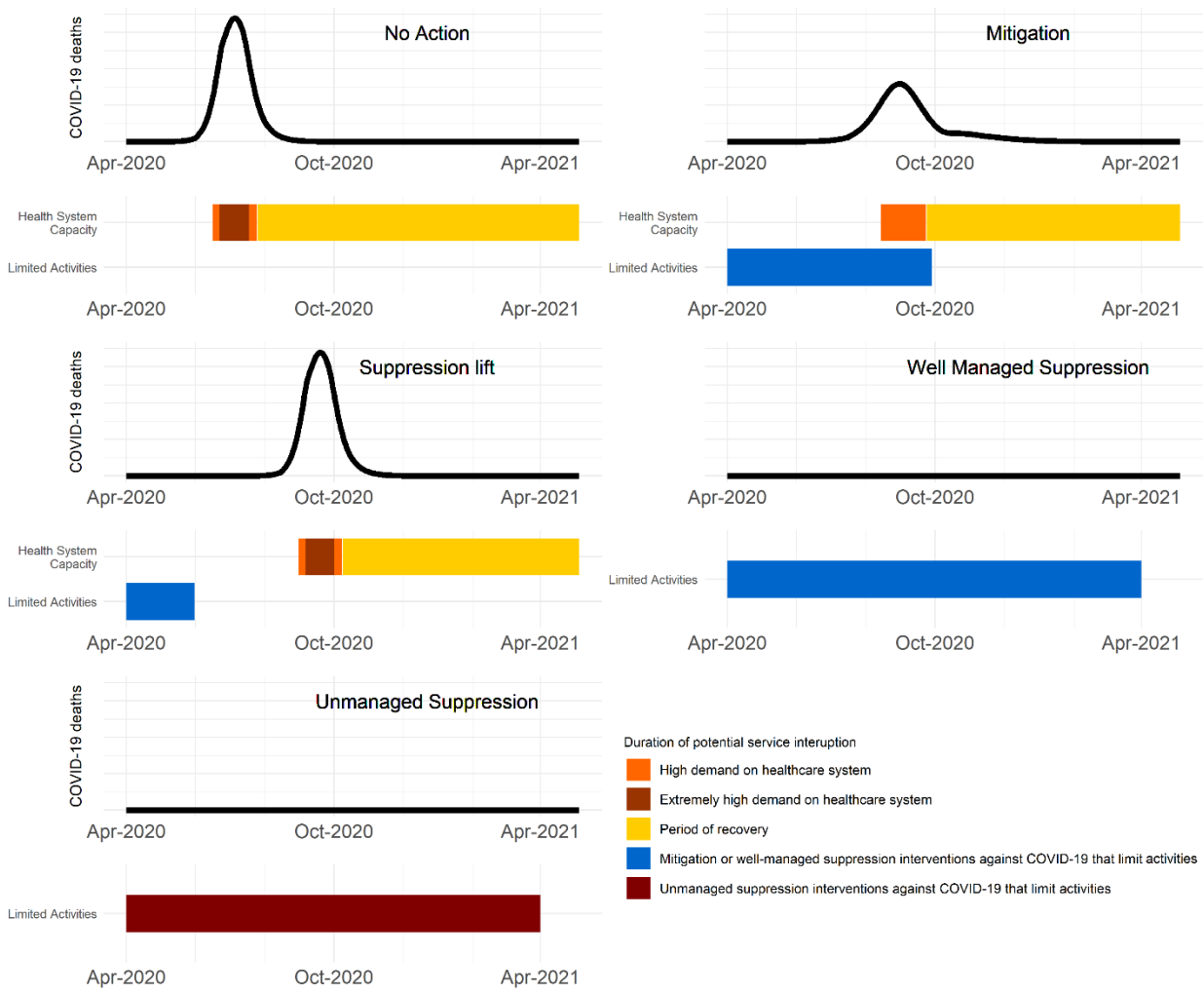

Figure 2: Potential course of the COVID-19 epidemic and the impact this may have. The black line shows the number of COVID-19 deaths per day in each scenario. The periods indicated with the shaded bars show the timings of the different types of disruption: Light Orange = 'High demand' on health system; Dark Orange = 'Extremely High' demand on health system; Yellow = Period of recovery; Blue = Mitigation or Well Managed Suppression interventions against COVID-19 that limit activities; Red = Unmanaged suppression interventions against COVID-19 that limit activities.

2) Projections for HIV

Figures 3 and 4 show the results of the disruption on HIV related deaths. Our predicted disruption in the HIV services in the 'No Action' scenario mainly results from the health system experiencing a period of 'Extremely High' demand which leads to some persons having their ART interrupted and thus an immediate increase in AIDS deaths. There remains an elevation in AIDS deaths after the period of disruption due to a combination of factors: some of those with their ART interrupted will have progressed to AIDS in that time and die later (despite ART being reinitiated); others that should have been initiated on ART will have been delayed on ART and progressed to a point where the ART gives less favourable survival outcomes; and, there is a substantial increase in HIV incidence during the disruption (due to reduced VMMC, condom use, and viral suppression) which will translate into additional AIDS deaths in later years. As a result, a substantial part of the impact on HIV will occur in

the years following the disruption and the consequences of increases in new infections would continue for decades.

Under the 'Mitigation' scenario we predict a much lesser impact because there is no period of 'Extremely High' demand on the health-system and so the worst outcomes of ART interruptions are avoided. In addition, during the period of 'Mitigation' interventions, the rate of new HIV infections does not increase substantially, despite there being no VMMC or PrEP services at that time, due to there being fewer contacts outside the home. There may however be differential changes to risks for key populations (e.g. female sex workers) that are not fully explored here.

The impact of the 'Suppression-Lift' scenario is predicted to be slightly greater than in the 'No Action' scenario, due to the additional disruptions during those 'Suppression' interventions that see more persons have unsuppressed viral loads and slightly fewer people initiate treatment. In the calendar year 2020, fewer deaths happen than in the 'No Action' scenario as the major health service occur later in the year and have effect in 2021.

In the 'Well Managed Suppression' scenario we assume that there are no significant program interruptions and so there is little predicted impact on excess deaths. In contrast, in the 'Unmanaged Suppression' scenario, the assumed year-long significant disruptions to the supply and access to ART, do lead to steady growth in excess deaths over this period. This scenario, however, also avoids the worst impact of ART interruption that would come during Extremely High Demand on the health system and so the impact is estimated to be lower than in the 'No Action' or 'Suppression-Lift' scenarios.

To a large extent, the impact in each case could be avoided by maintaining the ART supply for current patients. The overall impact of the disruption to HIV services is closely linked to the prevalence of HIV: in these scenarios, the additional number of deaths per million is twice as high in South Africa as Malawi because HIV prevalence is twice as high in South Africa.

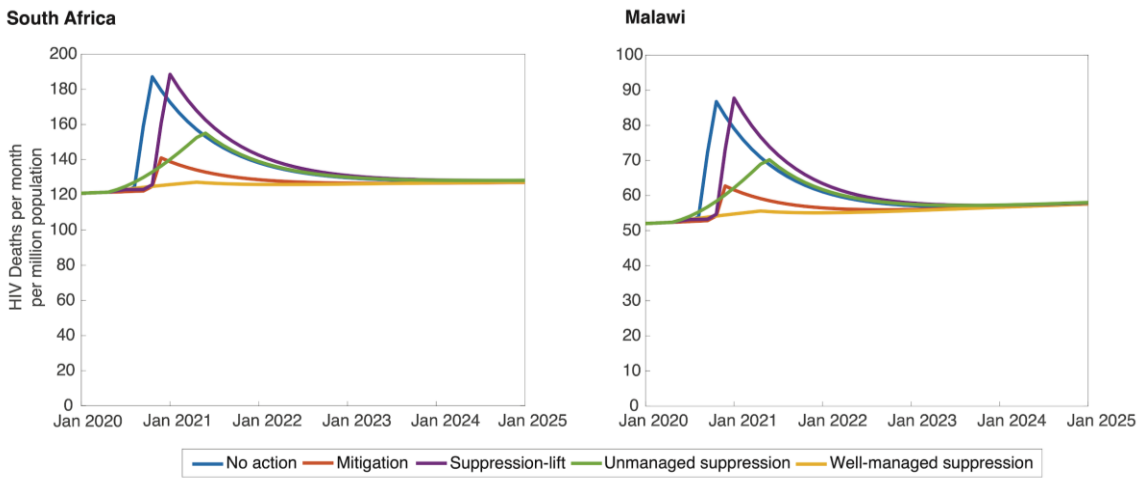

Figure 3: Total deaths per Million due to HIV in each of the settings considered ('High Impact': South Africa and 'Moderate Impact': Malawi), under each COVID-19 epidemic scenario: Blue= 'No Action'; Red= 'Mitigation'; Purple='Suppression-Lift'; Yellow= 'Well Managed Suppression'; Green= 'Unmanaged Suppression'.

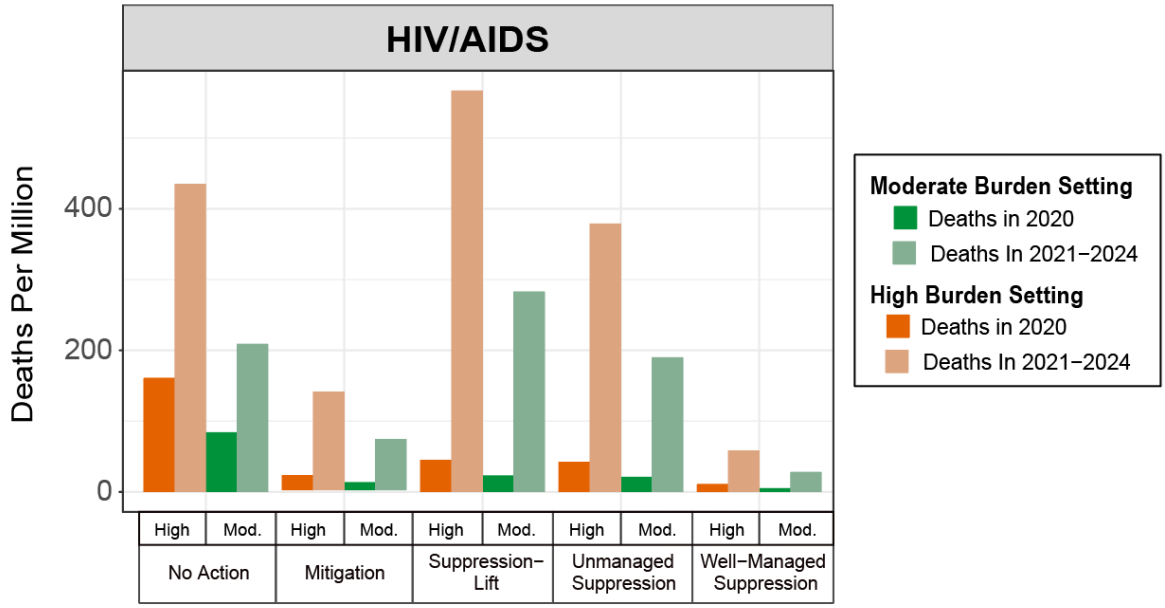

Figure 4: Excess deaths per million population due to HIV during 2020 (dark green and dark orange) and 2021-2024 (light green and light orange), under each scenario for the COVID-19 epidemic. Each set of bars shows the result for the 'High Impact' setting (orange) and 'Moderate Impact' setting (green).

3) Projections for TB

Figures 5 and 6 show the results of the disruption on TB related deaths. TB mortality rises rapidly as a result of service disruptions, driven by worsening outcomes amongst those on TB treatment (due to treatments being discontinued), and the increasing burden of untreated TB (due to reduction in treatment initiation, which in turn is driven by reductions in prompt health care seeking and diagnosis). We note that these results illustrate overall dynamical behaviour. In parallel modelling analysis by the Stop TB Partnership (in press), these dynamics are examined in further detail, and extended to the global level.

Broadly in Figures 5 and 6, TB mortality continues rising as long as service disruptions continue and begins a slow decline after services are restored. Depending on the duration of disruptions, TB mortality can remain elevated for several years. This is primarily because of the increased transmission of TB during the disruptions, leading to new cases in the following years. Upcoming modelling by the Stop TB Partnership shows how efforts that compensate for shortfalls in case detection (for example, ramped-up active case finding) would have the potential to accelerate that decline and reduce the overall impact of the disruptions.

The principal driver for the difference in excess mortality between the scenarios is the duration of service disruptions, rather than their intensity. The 'No Action' and 'Suppression-Lift' scenarios give rise to periods of extremely high demand that, despite their intensity, last for only a short period of weeks. These scenarios yield the lowest projected excess TB mortality. By contrast, the 'Well Managed Suppression' scenario sees disruptions lasting for one year, during which relatively smaller obstacles

to the programs are allowed to accumulate and give rise to substantially higher excess TB deaths overall. The 'Unmanaged Suppression' scenario adds to this burden by increasing the intensity of service disruption over this long duration.

In settings such as South Africa (the 'High Impact' setting), HIV coinfection sharply exacerbates the rate of TB mortality amongst those without TB treatment. Brazil (the 'Moderate Impact' setting) has an overall lower burden of TB as well as less HIV, and thus the increases in TB deaths caused by the reductions are much smaller than in South Africa.

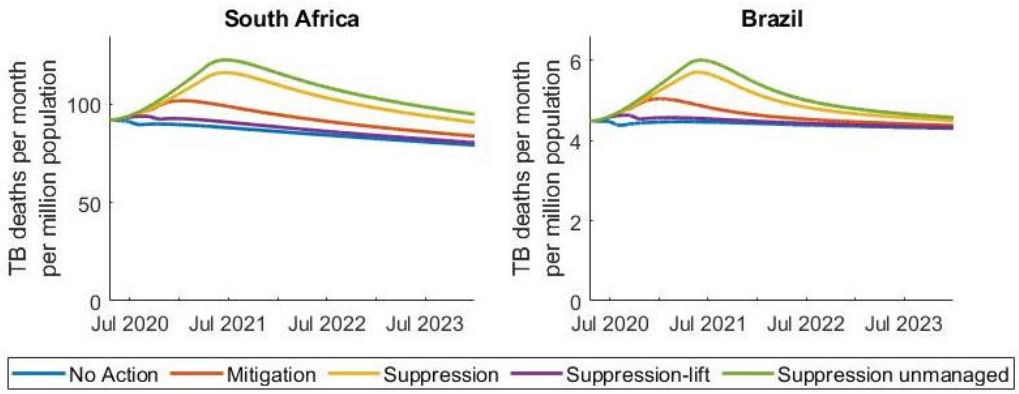

Figure 5: Total deaths per Million due to TB in each of the settings considered ('High Impact': South Africa and 'Moderate Impact': Brazil), under each COVID-19 epidemic scenario: Blue= 'No Action'; Red= 'Mitigation'; Purple= 'Suppression-Lift'; Yellow= 'Well Managed Suppression'; Green= 'Unmanaged Suppression'.

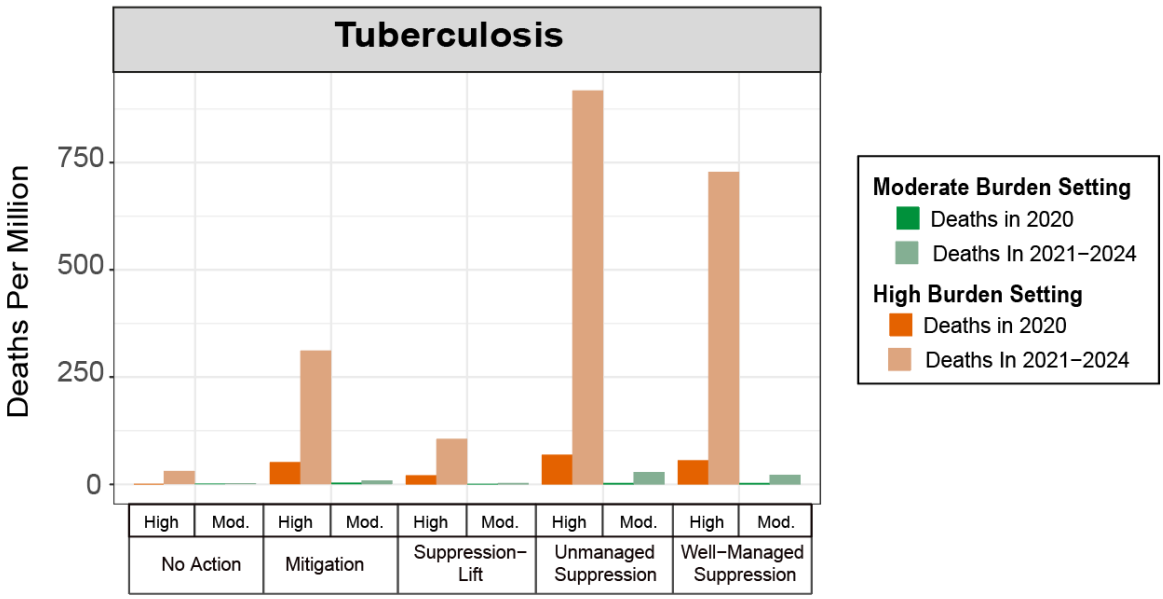

Figure 6: Excess deaths per million population due to TB during 2020 (dark green and dark orange) and 2021-2024 (light green and light orange), under each scenario for the COVID-19 epidemic. Each set of bars shows the result for the 'High Impact' setting (orange) and 'Moderate Impact' setting (green).

4) Projections for Malaria

We estimate that malaria mortality caused by disruption of services during the COVID-19 epidemic is likely to be concentrated in the year 2020 or early 2021 due to the acute nature of the disease (Figures 7 and 8). The impact of COVID-19 on malaria will vary substantially between regions according to the malaria burden but also the timing of the COVID-19 epidemic relative to the malaria transmission season and use of preventative measures. Here we examine the impact settings where malaria is highly seasonal ('High Impact' setting) and where there is a longer transmission season ('Moderate Impact' setting).

The widespread distribution of LLINs is one of the most important tools for preventing malaria. Mass campaigns typically occur every three years and their effectiveness and use likely wanes over time. It is assumed that mass LLIN campaigns were due in 2020 in both the modelled settings and so the impact of disrupting malaria prevention activities is likely to be greater in these countries compared to those which received LLINs in 2019.

In both countries, for a 'Well Managed Suppression' scenario, where LLINs are distributed as planned and there is a relatively modest reduction in case management, the number of additional deaths due to malaria is relatively small. Conversely, under the 'No Action' scenario, a disruption to LLIN deliveries during the peak of epidemic, coupled with lack of access to care for the period during which the health system is overwhelmed, is predicted to result in a large malaria epidemic in both countries. A similar situation is seen in the 'Mitigation' and 'Unmanaged Suppression' scenarios where we assume that LLINs would not be distributed due to the movement restrictions and social distancing in place for COVID-19. We find that this problem is most severe in the 'High Impact' setting because LLINs are due to be distributed at the start of a short but intense malaria transmission season.

It is assumed that the LLINs that are not distributed in 2020 are instead distributed in 2021, meaning that malaria prevention would increase in 2021. Therefore, the impact of disruptions on malaria are generally smaller over the five-year time horizon than the one year. Nevertheless, over a five-year period the impact of malaria is minimised under the 'Well Managed Suppression' scenario, for which there is no delay in the provisioning if LLIN (Table 1).

The impact of reduced case management of malaria varies between settings. In the 'High Impact' setting we predict relatively little difference between the 'No Action', 'Mitigation' and 'Unmanaged Suppression' and 'Suppression-Lift' scenarios as the health care is reduced in all scenarios during the short malaria transmission season. Conversely, in the 'Moderate Impact' setting, where a higher proportion of transmission occurs at the start of the calendar year, we predict a substantial difference between these scenarios, with the COVID-19 'Mitigation' and 'Suppression' scenarios increasing malaria death rates by ~20% and 30% respectively compared to the 'No Action' scenario (Table 8). The predicted impact of closed health centres will depend on how the proportion of clinical cases receive prompt treatment under normal circumstances which can be relatively low in some settings.

These differences between the two exemplar settings highlight the need to examine the impact of the COVID-19 epidemic on malaria in the local context.

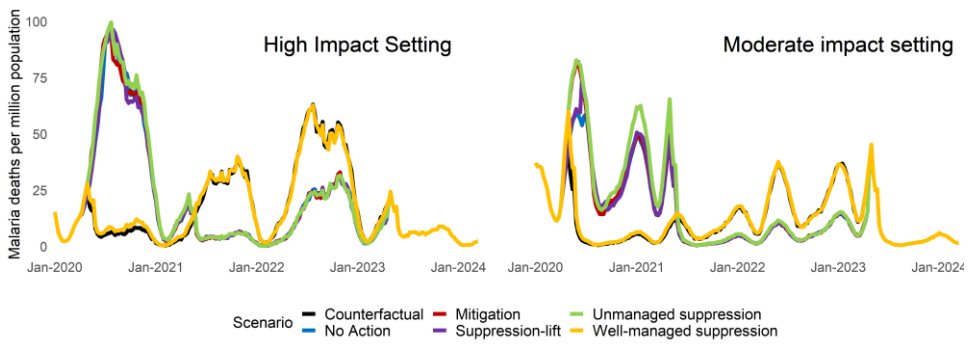

Figure 7: Total deaths per million due to malaria in each of the settings considered, under each COVID-19 epidemic scenario: Back = "Counterfactual" (projections without COVID-19 epidemic); Blue= 'No Action'; Red= 'Mitigation'; Purple= 'Suppression-Lift'; Yellow= 'Well Managed Suppression'; Green= 'Unmanaged Suppression'. In both settings LLIN mass distribution is delayed until 2021 in all scenarios other than the "Well Managed Suppression" scenario when it continues as normal in 2020.

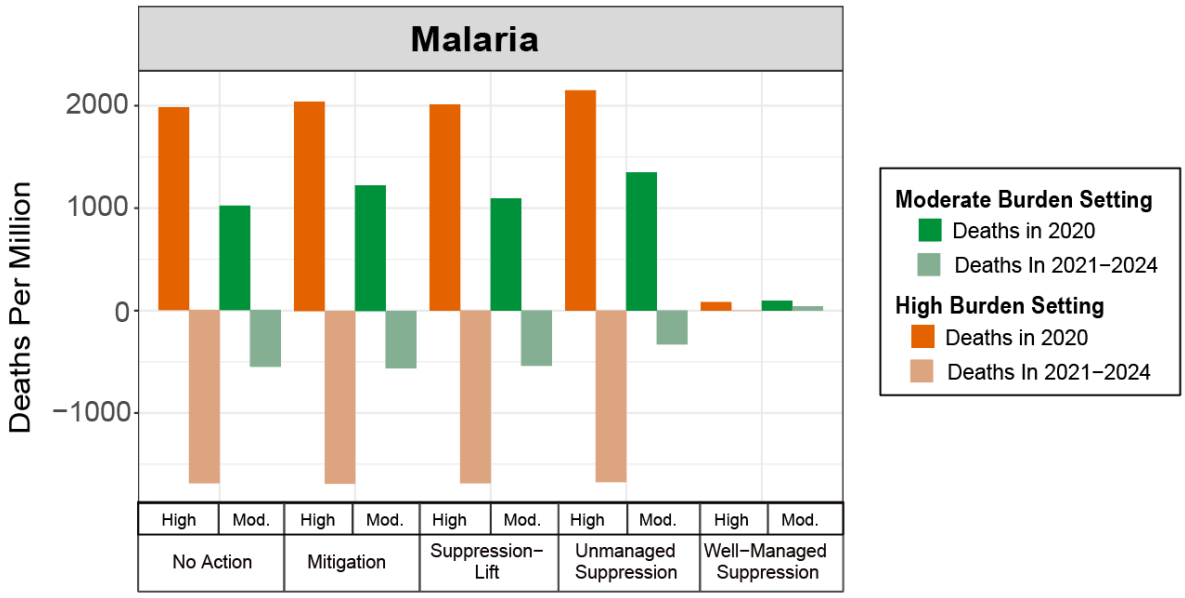

Figure 8: Excess deaths per million population due to malaria during 2020 (dark green and dark orange) and 2021-2024 (light green and light orange), under each scenario for the COVID-19 epidemic. Each set of bars shows the result for the 'High Impact' setting (orange) and 'Moderate Impact' setting (green).

5) Comparison of Projections for Each Disease

The impact of the COVID-19 epidemic on death and life-years lost can be compared with the impact of disruption of services on HIV, TB and malaria (Figure 9; Tables 2 & 3).

Overall, the magnitude of the impact of disruptions of HIV, TB and malaria are broadly similar to one another. It should be borne in mind that there is a substantial overlap between the deaths counted under HIV and TB in the 'High Impact' setting (South Africa) and the total excess deaths caused by HIV and/or TB is estimated in these models to be equal to approximately 65% of the sum of each cause when computed separately.

The predicted impact on malaria is similar in all scenarios (because the predicted impact in these settings is driven by a reduction in vector control which is incurred in all scenarios) whereas the TB impact is greatest where there are prolonged periods of interventions, and the HIV impact is greatest when there is a period of Extremely High Demand in the health system (causing half of individuals to have their ART interrupted).

The magnitude of excess deaths and the life-years losses caused by HIV, TB and malaria over five years are smaller but of a similar magnitude to those that would be expected to be caused by the COVID-19 epidemic itself. Settings in which malaria prevention interventions are particularly heavily impacted could see an increase in the life-years lost to malaria being approximately 40% that of the life-years lost to COVID-19 in the 'Mitigation' scenario (Figure 9(D)). If there was a setting that had as high a burden of HIV, TB *and* malaria as in each of our case-study countries, the number of life-years lost due to the indirect effects of COVID-19 on these three diseases could be up to 60% of the life-years lost to COVID-19 directly. In lower burden settings, the magnitude of the impact of disruptions is accordingly much less than the impact of the COVID-19 epidemic itself.

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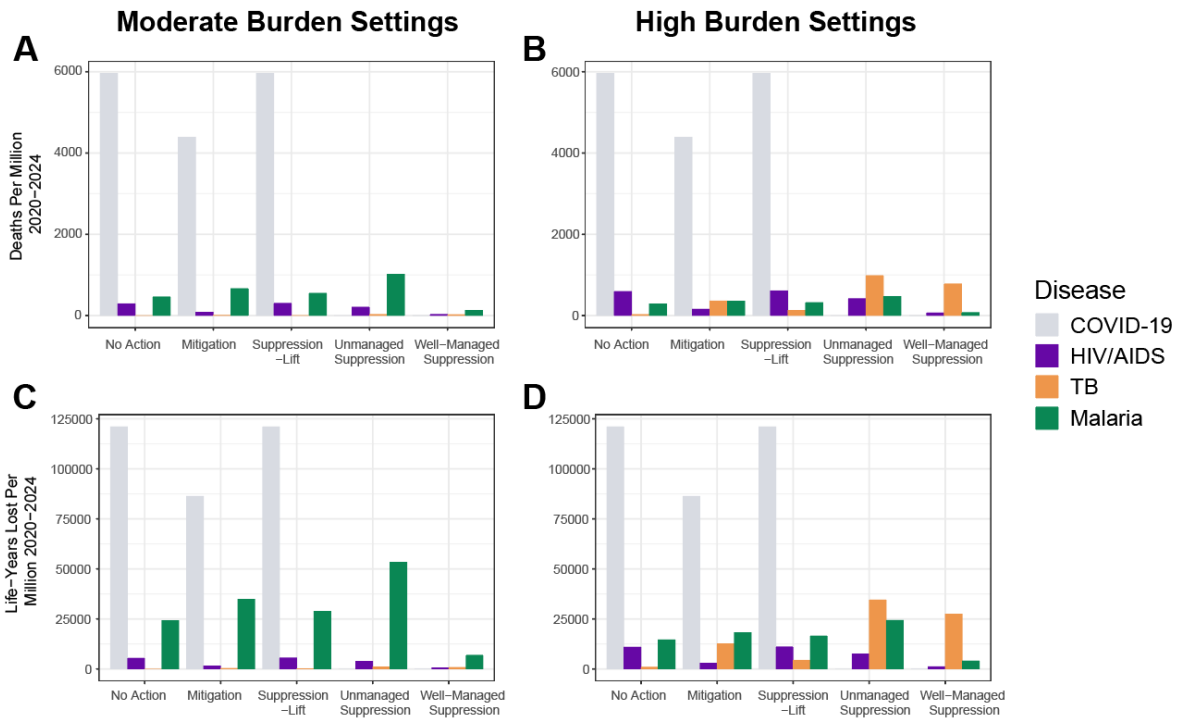

Figure 9: Excess deaths (A and B) and life-years lost (C and D) due the epidemic and the disruption during the years 2020-2024, caused by COVID-19 (grey), HIV (purple), TB (yellow) or malaria (green) in each scenario for the COVID-19 epidemic in the 'High Burden' (A and C) and 'Low Burden' settings (B and D).

4. Discussion

The COVID-19 epidemic will not exist in isolation and the direct impact of the epidemic and the indirect impact of its response will have major ramifications for the economy, poverty, food security and many other areas [1]. We have provided some quantification of the extent of those indirect impacts for HIV, TB and malaria, three of the major infectious diseases that are common in many LMIC.

In high burden settings, HIV, TB and malaria related deaths over 5 years may be increased by up to 10%, 20% and 36%, respectively, compared to if there were no COVID-19 epidemic. Indeed, it could lead to a loss of life-years over five years that is lesser but of the same order of magnitude as the direct impact from COVID-19, especially in places with a high burden of malaria and HIV/TB. Therefore, maintaining a continuity of services and recovering the programs should be a high priority to reduce the broader health impact of the COVID-19 epidemic, particularly in settings in which these diseases have a high burden. Indeed, it is important to note that these projections are not forecasts and the impact indicated here may be avoided with strategic planning, redeployment of resources and 'recovery' campaigns. For HIV, this means ensuring persons on ART can continue to access medicine even in periods of highest health system demand (e.g. multi-month scripting, dispensing away from health facilities [2]); for TB this means providing routes for persons to continue to seek care and be diagnosed despite interventions that promote social distancing; and for malaria it means prioritising preventative measures and ensuring LLINs and prophylactic treatments such as mass drug distribution or SMC are conducted at scale as soon as possible.

The results underscore the extraordinarily difficult decisions facing policy makers. Long term 'Suppression' interventions could avert the most deaths, through avoiding a COVID-19 epidemic, if they are well managed; but it could also lead to a large spike in deaths from other causes if it is not well managed. In either case, it will have enormous impacts of other kinds, in the worst cases risking jobs, livelihoods, food security and more. If such 'Suppression' interventions are not feasible, then 'Mitigation'-type intervention may lead to there being fewer deaths than in other scenarios - both from COVID-19 and the other diseases. However, a less effective or well managed implementation would not reap the same benefits in reducing COVID-19 deaths and could lead to greater increase in deaths from other causes. An intense but short period of suppression intervention (the 'Suppression-Lift' scenario) could generate a valuable delay in the epidemic that affords the opportunity to increase hospital capacity and engineer long lasting reductions in contacts. But if such changes were not possible, then the impact of the epidemic would simply be compounded by the disruptions incurred during the initial period of intervention.

We have presented short (one year) and medium term (five year) projections and examined deaths and life-years lost in order to explain the effects that arise from the assumptions being made rather than to point to these as the metrics that should inform decision-making directly. The decision making about the strategy for the COVID-19 epidemic and other health services is complicated by the need to draw comparisons between likely short-term effects and less certain longer-term effects, on the basis of partial information and when the set of possible decisions is still evolving. Future health benefits are often considered with a discount to reflect the natural preference for benefits in the near-term; we have not done that here as to do so would be to add a particular value judgement. The long-term impact on HIV may be under-stated in particular because additional deaths that result from new infections during the disruptions would not occur within the five-year time period. Furthermore, interruptions in ART may cause the development of resistance and so clinical outcomes of patients would continue to be affected in the longer-term.

The modelled scenarios for COVID-19 presented here are not predictions of the future, but hypothetical scenarios designed to allow this analysis to highlight the importance of maintaining different services during the COVID-19 epidemic. The major uncertainties in this analysis can be classified into three groups: (1) uncertainty about the scale of the COVID-19 epidemic (how far and fast will it spread and with what chance of death for those infected); (2) uncertainty about the extent to which other disease programs will actually be disrupted by the COVID-19 epidemic and the response to it; and (3) uncertainty about how those disruptions will impact on population health. Data on each of these points is accumulating and will allow projections such as these to be updated and refined.

In respect of the first of these issues - uncertainty in the course of the COVID-19 epidemic - it is worth noting that the observation of epidemics in so many settings around the world provides a very convincing reason to expect a similar trajectory to be followed in the low- and middle income settings of sub-Saharan Africa even if cases and deaths remain low to date. The scenarios that have been constructed do not provide an exhaustive account of all potential eventualities, but they do characterize a wide range, spanning from little action, to substantial mitigation, to suppression interventions lasting more than a year. As such they afford an investigation into the trade-offs between the extent of disruption due to intervention activities and periods of very high demand in the health system. One possibility that is not explored is of a very long duration epidemic and long-

disruption -- this would be expected to lie between the 'Mitigation' and 'Suppression' scenarios, but the long duration would present different challenges to the health system. Another possibility is that the high levels of death contribute to wider changes in behaviour and society that lead to very different types of disruptions than considered here. It should be noted that it is very difficult to produce reliable modelling analysis at a time when data are still very limited. In particular, understanding of the risk of mortality upon infection with SARS-CoV-2, how this is affected by underlying comorbidities, age, and how this may be different in Africa than China and how this might be affected by treatment, is evolving rapidly [6].

Whilst it is not clear what the effects on disease programs will actually be, it is apparent that disease programs are already making planned scale-backs of community-based programs (described in the Appendix) and experience in high-income settings has shown a substantial reduction in engagement with care during the periods of high health system demand [3]. Another major factor that could lead to reductions in health system capability during the periods of highest demand is shortages of staff due to COVID-19 illnesses [4]. Disruptions in supply chains have not yet occurred on a large scale, although there are reports of TB drug supplies already being affected. There is arguably a credible threat of substantial disruption given the reliance on international trade routes that could be affected by economic factors and travel restrictions, and even that prices of drugs rise due to speculation on their use for treating COVID-19 patients. The differences in results presented here for the different diseases should be interpreted with a high degree of caution as they will stem from the different assumptions being made, which are based on very little information.

Estimating the impact of some types of disruptions on population health is hampered by there being few data to inform the relevant mechanisms because (fortunately) such disruptions have not occurred before on the scale being considered here. On the other hand, the impact of some forms of disruptions can be predicted more confidently as informative data are available, such as the overall effects of a reduced coverage of malaria vector control prior to a long malaria season.

Overall, whilst the precise mechanism and effect sizes are uncertain, it is reasonable to conceptualise the risk of the potential for disruptions of the kind described here. Furthermore, this kind of effect has been observed before, for example during the Ebola epidemic in Guinea, where it now seems likely that more additional people died from malaria that year due to fewer treatments being administered than died from Ebola [5].

In order to create a simple analysis that is useful to those in as many different settings as possible we have considered just two 'case study' settings for each disease, which have a high or moderate burden of the disease (as described in the Methods) and most countries will be on a continuum between these settings for each disease. However, it is also the case that many more factors will determine the impact of these disruptions than this simple scale – including, the overall level of viral suppression for persons living with HIV, the relative sizes of the public and private sectors for TB treatment and the timing of LLIN distribution. A more detailed analysis of all these factors in specific country settings would be valuable in designing and prioritising the relevant mitigation strategies. The difficulty in comparing between diseases and settings and in constructing the relevant assumptions precludes a more precise comparison than just on the order of magnitudes of the relative effects.

This analysis is limited by the COVID-19, HIV, malaria and TB models being separate and so interactions between these disease are missed that could compound the impacts presented here (e.g. reductions in ART could lead to an increase in TB incidence and so worse TB outcomes; or the potentially higher risk of serious COVID-19 conditions developing for those with active or latent TB [18] or unsuppressed HIV viral load may make COVID-19 outcomes worse in settings with high HIV and TB burdens). The models do not share a common representation of the health system or the healthcare workforce, so it is not clear if the assumptions made here about limitations in service in the different diseases are really internally consistent, or under- or over-state the extent to which pressures from treating COVID-19 patients or reduced workforce availability translate into a reduced treatment for other conditions. We also do not consider how the increased stress of the health system may continue and affect other programs following the COVID-19 epidemic when it must reinstitute these HIV, TB and malaria programs that were postponed and cope with increased demand from patients who acquired disease during the epidemic.

In conclusion, to the extent that the COVID-19 epidemic and its response induce disruptions in the services for HIV, TB and malaria, there could be a substantial number of additional deaths and life-years lost, especially when considering the life-years that are lost in the years following the epidemic. In the short-term, maintaining the most critical services – treatment for HIV and TB (new and current patients) and resuming vector control for malaria as soon as possible – is a major priority and is likely to be one of the key ways in which the overall impact of the COVID-19 epidemic can be reduced. A major focus in the longer-term is likely to be improving the resilience of the health system to cope with shocks such as pandemics and the changes necessary may be far-reaching [7].

5. Supplementary Results

Covid-19 Epidemic Scenario		Covid-19	HIV		TB		Malaria	
			High	Moderate	High	Moderate	High	Moderate
Excess Deaths	No Action	5965	161	84	-1	0	1978	1018
	Mitigation	4393	21	11	51	3	2041	1225
	Suppression-Lift	5965	45	23	21	1	2009	1092
	Unmanaged suppression	0	42	21	69	3	2149	1348
	Well Managed suppression	0	11	5	56	3	82	93
Excess Life-Years Lost	No Action	121069	3060	1593	-52	-8	102253	53955
	Mitigation	86348	396	205	1809	88	105525	64906
	Suppression-Lift	121065	857	445	726	29	103871	57873
	Unmanaged suppression	10	794	402	2416	111	111097	71427
	Well Managed suppression	0	207	101	1979	98	4259	4947

Table 2: Numbers of additional deaths due per million capita due to COVID-19 and other causes during 2020 according to modelled scenarios. 'High' and 'Moderate' refer to the different settings that are being explored in each model (see Methods).

Covid-19 Epidemic Scenario		Covid-19	HIV		TB		Malaria	
			High	Moderate	High	Moderate	High	Moderate
Excess Deaths	No Action	5965	596	293	29	1	287	464
	Mitigation	4393	160	83	362	11	355	667
	Suppression-Lift	5965	612	306	127	4	323	553
	Unmanaged suppression	0	421	211	987	31	474	1018
	Well Managed suppression	0	69	33	784	25	79	132
Excess Life-Years Lost	No Action	121069	10992	5459	1041	22	14658	24199
	Mitigation	86348	2954	1541	12689	381	18243	34890
	Suppression-Lift	121065	11165	5639	4446	122	16570	28913
	Unmanaged suppression	10	7589	3825	34573	1115	24378	53360
	Well Managed suppression	0	1227	596	27460	866	4082	6980

Table 3: Numbers of additional deaths due per million capita due to COVID-19 and other causes during the five-year period, 2020-2024, according to modelled scenarios. 'High' and 'Moderate' refer to the different settings that are being explored in each model (see Methods).

5. Supplementary Methods

HIV Model

We used an established deterministic mathematical model of the HIV epidemic in South Africa and Malawi [8, 9] to quantify the impact of disruptions. The assumptions made for the disruptions in HIV services have been generated through discussion with the HIV Modelling Consortium, although there is no endorsement for any one particular set of assumptions. The disruptions incurred during when there is a 'Mitigation' or 'Well Managed Suppression' intervention are intended to correspond to what could occur through a combination of the intentional scaling back of services (for VMMC and PrEP), patients on ART being less able or willing to gain timely refill prescriptions, and a reduction in time spent away from the home leading to reduced acquisition of new sexual partners. The disruptions incurred during when there is a 'Unmanaged Suppression' intervention are intended to correspond to what could occur when, in addition, persons postpone seeking HIV testing or linking to ART programs or PrEP programs and a small proportion of those on ART do not continue to access medication. The disruptions incurred during when there is a 'High Demand' on the health system correspond to what could happen if viral loading testing is not available (due to the machines having been repurposed) such that the fraction of those of ART who become virally unsuppressed during the year remain so (when otherwise detection would have to lead to intervention and re-suppression); and also when the health system is unable to accept new patients to start ART, PrEP or VMMC. During when there is 'Extremely High Demand', it is assumed that disruptions in the supply of ARVs and condoms could lead to a fraction of those on ART not being able to access any medication and for condoms to be used less frequently than otherwise. Modelled changes in HIV incidence and HIV deaths in response to these different elements of the disruption are represented in Figure S1.

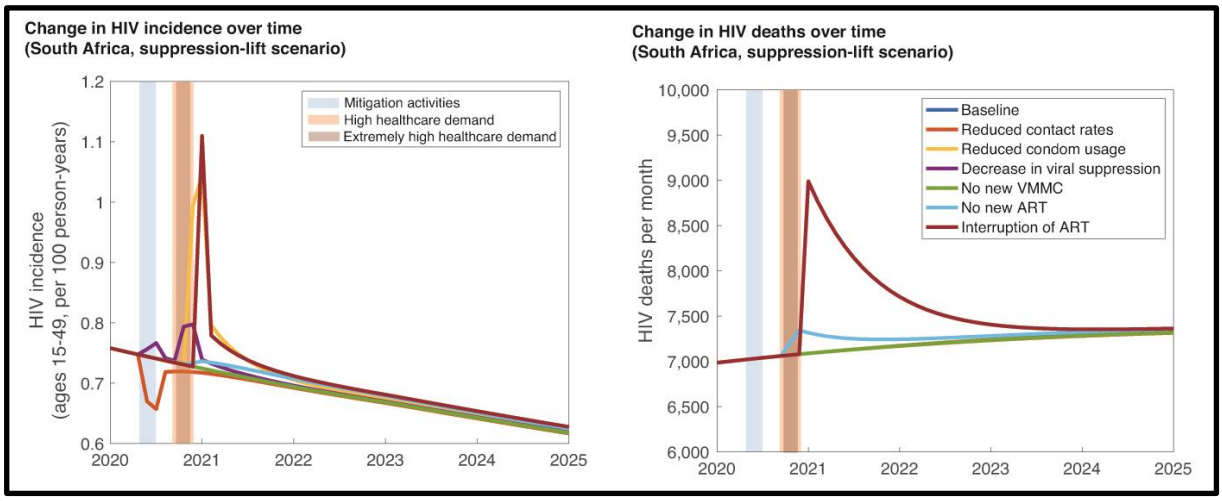

Figure S1: Change in HIV incidence and deaths over time in South Africa for separate elements of the disruption in the 'Suppression Lift' scenario.

Results are most sensitive to the risk of dying for people living with HIV (PLHIV) who have had their ART supply interrupted. This quantity is not well known. We assume an average monthly risk of death of 0.60% for this group. This implies a mean survival of 14 years which is approximately the survival time for HIV-positive persons who have never been on ART [10]. We also note that the monthly risk of death is likely to increase over time as individuals accrue time off of ART; however, this is not represented in the model. When the supply of ART is resumed at the beginning of the recovery period, those persons who have not progressed to AIDS re-initiate ART and do not suffer any long-term health consequences from the interruption. However, those who have progressed to AIDS by that time do not gain any benefit if they are restarted on ART.

Other important limitations to note include: (i) no interaction between HIV and COVID-19 infection are incorporated – that is, PLHIV are not assumed to be more or less likely to acquire or die from COVID-19: (ii) the effect of disruption on the risk of mother-to-child transmission is not incorporated; and (iii) possible increases in drug resistance due to ART regimens being disrupted are not incorporated. In each case, this would lead to greater impact of the disruptions in increased adverse outcomes for HIV, particularly over longer timescales. PrEP coverage is so low in the settings modelled that disruption to PrEP has no effect in the model.

TB Model

A compartmental, deterministic model of TB transmission dynamics was used, to capture the impact of the COVID response on TB [11]. The model incorporates the acquisition and transmission of rifampicin resistance, as well as the role of HIV in driving TB incidence. It also includes, in a simple way, interactions between symptomatic patients and the healthcare system, capturing (for example) the potential for repeat visits to a care provider before TB is diagnosed, and the ongoing transmission that occurs as a result of this diagnostic delay. The model does not capture the dynamics of HIV or ART coverage, instead taking this as a fixed input, informed by UNAIDS estimates [12]. The model is parameterised using World Health Organization (WHO) estimates for incidence in 2018 [13]) for the proportion of TB cases that were HIV-coinfected; and for the proportion of incident TB that was rifampicin-resistant. As the model does not have an age-structure, years of life lost are estimated by comparing total years-of-life lived with and without the disruptions being applied.

In terms of their effect on interpersonal contact rates, while the 'Mitigation' and 'Suppression' scenarios will reduce opportunities for community-based transmission, they will also intensify and prolong household exposure to infectious TB. Combining these factors leads to an estimate of a reduction in overall transmission, by 10%. The model also captures an initial patient delay before first presenting for care; it is assumed that this delay is extended during the period of mitigation/suppression intervention, to reflect associated difficulties in accessing care. Molecular diagnostic tools such as Xpert MTB/RIF [15] are widely used for TB diagnosis but may be increasingly used for testing for SARS-CoV-2 instead [16]. Meanwhile, persons with symptoms are also expected to reduce their care seeking. Accordingly, we assume that the probability of diagnosis drops by 70%, under the mitigation/suppression scenarios, allowing for some degree of clinical diagnosis in the absence of diagnostic tools. Moreover, Xpert MTB/RIF is used to detect rifampicin resistance, a function that cannot be performed using clinical diagnosis. Thus the proportion of cases having a drug sensitivity result is assumed to decline by 50% under high demand on the health system, or to 0%

under very high demand. Finally, disruptions in the supplies of TB drugs may be expected when the health system comes under stress [17]. In extreme conditions, drug stock outs may occur, leading to only a proportion of TB cases being able to access treatment. Here it is assumed that only 25% have access to treatment under such conditions. The model does not address potential interactions between COVID-19 and TB, although there is some early evidence for potential risks of increased severity of COVID-19, associated with pre-existing TB infection [18]. The modelling analysis presented here complements parallel analysis being conducted by the Stop TB Partnership (in press), that examines these TB dynamics in further detail, as well as extending it to the global level.

Malaria Model

An individual-based transmission dynamics model of malaria was used to predict the number of malaria deaths and lives saved under the COVID-19 scenario [19]. Models were parameterised using 2017 malaria prevalence and the LLIN usage estimated at the administrative 1-unit level from the Malaria Atlas Project [20] with LLIN usage expected to remain at the same level in the next LLIN mass campaign. The level of insecticide resistance in the local mosquito population (which affects the effectiveness of controls) was estimated for each administrative unit from data collated by the WHO [21] and combined with results from experimental hut trials to predict the epidemiological impact [22, 23]. The number of deaths and life-years lost were estimated from the incidence of severe disease and the proportion of clinical cases receiving treatment [24, 25].

COVID-19 could increase malaria morbidity and mortality by impeding routine prevention activities whilst also reducing treatment of clinical-cases, worsening health outcomes. Early reports suggest mass distribution of LLNs may be delayed as countries increase social distancing to reduce the spread of COVID-19. In many countries these campaigns typically involve large gatherings of people who congregate centrally to receive their LLIN. Similarly, Seasonal malaria Chemoprevention (SMC) activities, which distribute antimalarial medicine to children door-to-door in areas of highly seasonal transmission to prevent malaria illness, may also be disrupted. It is therefore assumed that these activities will be halted in 2020 when health systems are overburdened ("High" and "Extremely High Demand") and during any unmanaged COVID-19 suppression period. It may be possible to conduct both LLIN mass distribution and SMC during the mitigated or well-managed suppression COVID-19 scenarios, though population coverage (those receiving LLINs or SMC treatments) are likely to be reduced (here assumed to be 50% of 2017 levels). LLIN mass campaigns typically occur every three years. Here we examine the impact in two settings which both are assumed to have had mass distribution of LLINs planned for 2020 ('High Impact' setting in quarter 1; 'Low Impact' setting in quarter 2-3). Timing of LLIN distribution and seasonality of transmission is set to represent a typical west-African and east-African country for the 'High Impact' and 'Moderate Impact' settings, respectively. It is assumed all previous LLINs were distributed in a mass campaign in 2017 although both countries are also assumed to distribute a low percentage of their LLINs continually through routes such as antenatal clinics. Delayed campaigns are assumed to occur a year later than originally planned and again in 2023. All LLINs distributed were assumed to be standard pyrethroid LLINs. SMC takes place annually in a small region of the 'High Impact' setting with 70% of children younger than 5 years of age receiving a full round of treatment in the counterfactual no COVID-19 scenario (and 35% coverage in the mitigated and well-managed COVID-19 suppression simulations). The treatment of clinical cases with recommended first-line drugs is likely to be impeded when the health system is

at capacity as facilities close. Therefore, we assume that the proportion of those receiving appropriate prompt treatment remains at 2017 levels unless the Health System is in a period of High Demand, when that proportion is reduced by 50%. It is assumed that no clinical cases of malaria are treated when there is 'Extremely High Demand' on the health system or during the un-managed COVID-19 suppression scenario.

COVID-19 Model

Potential COVID-19 trajectories were produced using an adapted age-structured SEIR model of transmission of SARS-2-Cov virus that has been expanded to explicitly capture the progression of disease within the hospital [1, 26]. The model incorporates age-specific disease severity using age-dependent probabilities for the proportion of infections that result in disease requiring hospitalisation (and hence the need for treatment with high-pressure oxygen), the proportion developing severe pneumonia disease and hence requiring intensive care (for whom ~80% require mechanical ventilation) and the risk of mortality. Model parameters for transmission and disease progression are based on analysis of data from China and the UK [1, 26]. To produce simulations representative of the LMIC settings considered here the model was calibrated to typical social contact patterns observed within surveys in sub-Saharan Africa (here we used a survey from Zimbabwe) which show less substantial declines in contact rates by age compared to the UK; and used the demographic schedules of Nigeria [27]. Life-years lost were calculated under this demography using the corresponding life tables.

To capture the likely constraints within a health system we contrasted this demand for healthcare with a representative level of supply using the median estimated provision of hospital beds and intensive care units for a low-income country [1, 26]. This threshold was chosen on the basis that, although many countries in sub-Saharan Africa are lower-middle-income and therefore likely to have a higher total number of hospital beds and intensive care units, access to high pressure oxygen and mechanical ventilation within hospitals is lower than within equivalent high-income settings. During the course of a projected scenario, as healthcare capacity is exceeded, individuals requiring either mechanical ventilation or high-pressure oxygen who are not able to receive these interventions are then subject to a substantially higher degree of mortality, leading to excess mortality during time-periods in which health systems are overwhelmed. See [26] for full details, code and parameterisation.

Representative scenarios were simulated using a basic reproduction number of 3 representing a 3.5 day doubling time in cases and deaths, which is thought to be reflective of many trajectories currently observed globally [28]. Once a threshold of 0.1 deaths per million (approximately reflecting the COVID-19 level of mortality observed in many countries in Africa to date) is exceeded, the pandemic trajectory follows four potential scenarios:

- *"No action".* Here no direct action is taken but contact rates are reduced by 20% relative to baseline according to assumed behaviour change in the face of the pandemic even in the absence of specific, coordinated public health interventions.
- *"Mitigation".* Here through combinations of isolation and social distancing contact rates are reduced by 45% for a period of 6 months after which infections fall to low levels and contact

rates return to pre-pandemic levels. This scenario approximates the maximum reduction in the final size of the epidemic that can be achieved whilst generating sufficient levels of immunity capable of preventing a second wave once measures are lifted (assuming infection leads to high levels of immunity from reinfection) and thus produces the lowest final numbers of COVID-19 infections of the three strategies that do not involve indefinite suppression.

- *"Suppression":* Here stringent suppression-targeting interventions are implemented to reduce contact rates by 75% and these are maintained indefinitely in the hope that a pharmaceutical intervention (e.g. effective vaccine) can be developed and deployed. We run this scenario for 12 months but note that at the end of this period lifting suppression, in the absence of such a pharmaceutical intervention, would lead to a second wave of equivalent size as in the "*Suppression and lift scenario*".
- *"Suppression-Lift":* Here the stringent 'lockdown' type interventions implemented by many countries are represented by a reduction in contact rates of 75%. This reduction is maintained for two months at which point it is lifted and contact rates return to 80% of their pre-pandemic levels (i.e. the levels simulated within our 'No Action' scenario) for the remainder of the epidemic.

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