

Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: results from multiple mathematical models

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SUMMARY

Background: The COVID-19 epidemic could lead to the disruptions to provision of services for people living with HIV and people at risk of acquiring HIV in sub-Saharan Africa, where UNAIDS estimates that more than two thirds of the 37.9 million people living with HIV reside in 2018. We set out to predict the potential effects of such disruptions on HIV-related deaths and new infections.

Methods: Five well-described models of HIV epidemics were each used to estimate the effect of various potential disruptions to HIV prevention and treatment services on HIV-related deaths and new infections in sub-Saharan Africa over 1- and 5-year periods.

Findings: A six-month interruption of supply of antiretroviral drugs (ARV) across the whole population of people living with HIV on treatment would be expected to lead to an approximately 2-fold (from 1.87- to 2.80-fold across models) increase in HIV-related deaths over a one year period compared to the case with no disruption. In sub-Saharan Africa this amounts to an excess of over 500,000 (471,000 – 673,000) adult HIV deaths should such a high level of disruption occur. There would also be an approximately 2-fold increase in mother to child transmission of HIV. Interruption of ARV supply affecting only a proportion of the population or for a shorter duration would have lesser effects. While an interruption of supply of ARV drug would have by far the largest impact of any potential disruptions, effects of poorer clinical care due to over-stretched health facilities, interruptions of supply of other drugs such as cotrimoxazole and suspension of HIV testing would all have significant population impacts. Interruption to condom supplies and peer education would make populations more vulnerable to increases in HIV incidence, although physical distancing measures could lead to reductions in risky sex.

Interpretation: During the COVID-19 epidemic it is critical that governments, donors, suppliers and communities focus on maintaining the supply of ARVs for people with HIV to avoid additional HIV-related deaths, and the provision of other essential prevention measures to prevent any increase in HIV incidence.

Key words: HIV; COVID-19; modelling; sub-Saharan Africa; treatment interruption.

RESEARCH IN CONTEXT

Evidence before this study

The COVID-19 pandemic could lead to disruptions to provision of services for people with HIV in sub-Saharan Africa. We searched Web of Science on 24 April 2020 using the terms (covid* AND model* AND hiv* AND africa) and found no studies that predict the effects of COVID-19 disruption on HIV outcomes in sub-Saharan Africa.

Added value of this study

We bring together results from five independent HIV models to estimate the magnitude of effects on numbers of HIV-related deaths and new infections resulting from disruptions to antiretroviral treatment (ART) services. We find that if there were to be a six-month interruption of supply of ART affecting all people taking ART this would be predicted to double HIV-related deaths over 1 year. In sub-Saharan Africa as a whole this would amount to an excess of over 500,000 (471,000– 673,000) adult HIV deaths should such a high level of disruption occur.

Implications of all the available evidence

When considering plans to manage negative effects of the COVID-19 epidemic, it is critical that governments, donors, suppliers and communities focus on maintaining the supply of ARVs for people with HIV to avoid additional HIV-related deaths, and the provision of essential prevention services so as to not allow an increase in incidence.

INTRODUCTION

Disruption to delivery of health care in sub-Saharan African settings caused by COVID-19 could lead to adverse consequences for the health of people beyond those from COVID-19 itself [1-3]. Causes of such disruption could include COVID-19 morbidity and mortality itself, clinic closures or reduced services, physical distancing and other measures put in place to combat the virus spread. HIV remains highly prevalent in sub-Saharan Africa with over 25.7 (22.2-29.5) million people estimated to be living with HIV in the region in 2018 [4]. There is concern that possible disruptions in HIV programmes due to COVID-19 [1,2,5] could impact HIV-related mortality and new infections. Negative effects of the COVID-19 epidemic on access to health services have begun to emerge. A recent survey in South Africa found that 13% of people said they did not have access to their chronic medication during lockdown [6]. A rapid assessment in Zimbabwe found 19% of people with diagnosed HIV attempting to get an ARV refill had not been able to, or only able to get a partial refill [7], and a survey in Kenya and Nigeria found 14% of people unable to pick up needed medications [8].

We set out to explore these potential effects using existing mathematical models of HIV epidemiology and intervention programmes in sub-Saharan Africa. In this paper, we consider the predicted effects on HIV mortality and HIV incidence of temporary disruption to different individual HIV services for periods of 3- or 6-months over 1- and 5-year periods. We consider the disruption causing complete interruption of the programme for all affected people to compare potential impacts on different HIV services; we do not intend to convey that we consider necessarily such a level of disruption likely to actually occur.

METHODS

Five well described existing HIV models were used to estimate the impact of different disruptions to HIV prevention and treatment services; Goals [9], Optima HIV [10], HIV Synthesis [11], an Imperial College London Model [12], and EMOD [13]. The features of each model are summarized in Table 1. Important to note from Table 1 are the different model assumptions relating to effects of antiretroviral therapy (ART) interruption, which account for the fact that immune recovery during ART therapy tends to be quite rapidly lost after interruption of treatment. The models handle this in various ways but most attempt to reflect an assumption that immune recovery during ARV therapy would be quite rapidly lost after interruption of treatment, which follows empirical observations that showed a median loss of 187 CD4 cells/mm³ in 2 months and 25% of people experiencing a loss of > 317 cells/mm³ [14,15]. Specific relevant details for the implementation of the disruptions in each model are given below.

All models simulate disruptions caused by COVID-19 that last for 3- or 6-months during 2020 with all persons who would otherwise benefit from a given programme being affected. The potential

disruptions to programmes, broadly grouped as prevention programmes, HIV testing, and treatment and care, are shown in Table 2. Service use is assumed to return to pre-disruption period levels at the end of the disruption period. We consider the impacts on HIV mortality and incidence over 1- and 5- year time periods. We express results as the predicted fold increase in HIV deaths relative to the annual number of such deaths in the relevant time period in which no COVID-19 disruptions or epidemic occur, and similarly for HIV incident cases. We then show results for example countries, focussing on the impact on HIV deaths from interruption of ART, since this disruption has the greatest impact. Relevant details for each model are as follows:

Goals: It is assumed that coverage of all interventions except voluntary medical male circumcision (VMMC) remains at 2019 levels, and VMMC coverage increases according to current trends. The “condom availability interrupted” disruption is modelled as all behavior change interventions being suspended for the 3 or 6 month period, including community mobilization, condom promotion, school-based programs and outreach to key populations. The result is an increase in the number of partners and a reduction in condom use. Modelling reduction in sexual activity means that during the disruption period there is no casual or commercial sex for heterosexuals or men who have sex with men. For disruption of prevention of mother to child transmission (PMTCT) this means no mother to child transmission (MTCT) prophylaxis services are offered during the disruption period.

Optima HIV: The impact of a disruption in HIV services from 1 March-2020 including prevention, testing, and treatment were modelled for 3- and 6-month interruption in 2020 and 2020-2024. The mortality rate for those on ART whose treatment was suspended was applied followed findings from Grund et al. [14]. CD4 cell counts declined rapidly as a result and gradually returned to pre-ART levels after interruption. Once ART resumed, the mortality rate for those on ART by CD4 count was applied. Circumcision rates were held constant over the disruption period, as it was assumed no new VMMC would be performed due to physical distancing concerns. The impact on drug resistance as a result of HIV treatment disruption, behavior change as a result of COVID-19 pandemic lockdown (e.g. changes in numbers sexual acts and receptive needle sharing), and additional COVID-19-related deaths among people living with HIV were not included.

HIV Synthesis model: We generate a range of setting scenarios (n=1500 for each period of disruption) aiming to collectively represent the range of HIV epidemic and program characteristics across and within countries in sub-Saharan Africa (Appendix HIV Synthesis Model Supplementary Table 1). Where there are disruptions, we determine at random which potential program disruption(s) occurs. There is a 50% chance for each disruption and the probabilities of each disruption are sampled independently; several disruptions can occur simultaneously. This is so that we can consider a range of disruptions simultaneously; there is no intention that 50% represents an estimate of the probability that such disruptions will occur. For each setting scenario we calculate the relative increase in HIV mortality (or HIV incidence) over the one-year period, due to the disruption. For the effect of ART interruption, to generate country specific estimates, we considered across setting scenarios the relationship between the proportion of people with HIV who have viral

suppression at the start of 2020 and the relative increase in death rate (see Appendix). To estimate the relative increase in death rate for a given country we referred to the proportion of people with HIV who have viral suppression in the country to generate a country-specific estimate. We then apply these estimated relative risks to the estimated annual number of adult HIV-related deaths from most recent UNAIDS 2018 estimates [4]. Figures are for adult mortality only. Suspension of PMTCT services is not considered separately from interruption of all ART, which has an effect on MTCT. The increase in death rate in people with AIDS diseases due to over-stretched health system is implemented as a two-fold increase in death rate during the 3-month period in which an AIDS disease occurs. The effect of intermittent taking of ARVs due to sporadic drug supply is in the context of an assumed transition to dolutegravir based ART regimens. Estimates of disruption of PrEP programs should be understood in the context of overall only 0.2% of women aged 15-25 being on PrEP so it is not possible to discern clear impact of suspension. Assumptions on CD4 cell count changes during ART interruption lead to a mortality rate of 1.7% in the first 3-month period of interruption due to disruption of ART availability and 5.0% during the second 3-month period.

Imperial Model: The baseline scenario is one in which no COVID-19 disruptions or epidemic occur. For each disruption scenario, we compare outcomes over a 1-year or 5-year period beginning in mid-2020. The assumptions corresponding to the interruption of each service are as follows. VMMC: no new circumcisions occur during the disruption, and when the disruption ceases, circumcisions resume at the pre-disruption rate. Condom availability interrupted: condom use is assumed to be reduced by 50% for the duration of the disruption. Suspension of ART initiation: no new individuals are initiated on ART for the duration of the disruption and scale-up continues at pre-disruption rates after the disruption ends, such that those who would have been initiated on ART during this period of time are allowed to start but may have progressed to a later stage of infection before starting. Viral load testing, enhanced adherence counselling, and switches stopped: an additional 10% of individuals on ART are assumed to have an unsuppressed viral load. Increase in death rate in people with AIDS diseases due to overstretched health system: the death rate for those with AIDS doubles for the duration of the disruption. Break in supply of ARVs leading to ART interruption: 100% of individuals on ART are assumed to stop using ART for the duration of the disruption and are then re-initiated. If the person has progressed to AIDS in the meantime, ART re-initiation is assumed to be too late for the person to recover health. Reduction in sexual contacts: all sexual contacts across all risk groups decrease by 10% for the duration of the disruption, and then return to pre-disruption levels immediately following the disruption.

EMOD Model: The disruption in HIV services including prevention, testing, and treatment were modelled for 3- and 6-month intervals beginning in mid-2020. The scenario of VMMC interruption was assumed to apply only to in-clinic circumcisions provided by HIV prevention programs; traditional male circumcision was assumed to continue at the pre-disruption rate. A disruption in condom availability was assumed to increase per-coital-act transmission probabilities by an average of 54% during the disruption interval, after which transmission probabilities return to their pre-

disruption rates. During suspension HIV testing and of ART initiation, all individuals who would have tested or initiated ART are unable to do so during the disruption, but may re-attempt testing and ART initiation after the disruption period at rates equivalent to pre-disruption rates among ART-naïve individuals. Disruption of viral load testing, enhanced adherence counselling, and switches is assumed to increase the proportion of individuals with unsuppressed viral load to 42.5% during the disruption period [16]. A break in supply of ARVs leading to ART interruption is assumed to interrupt all ART use during the disruption and resume ART use for those who survived the interruption to their ART or attempted to initiate ART during the disruption. Survival during and after the disruption depends on CD4 count and age, with older adults experiencing more rapid CD4 cell count declines and higher risk of mortality. Viral load suppression after ART initiation, including re-initiation after a treatment interruption, is assumed to take an average of three months and up to six months.

RESULTS

Results for predicted effects of disruptions on various HIV services from the five models are shown over 1 (Table 2a) and 5 (Table 2b) years. Not surprisingly, disruptions to aspects of care for people living with HIV are associated with increases in mortality risk, most notably disruption to the supply of ART to people on treatment resulting in discontinuation of ART. Six months of such interruption is predicted to lead to an excess number of HIV deaths comparable to the estimated current number of annual HIV deaths (i.e., an approximate 2-fold increase in mortality risk (from 1.87 to 2.80 across models)). Although the effect in the first year is greatest, there is also a substantial effect in the years following the disruption, such that a six-month period of ART interruption is predicted to lead to excess deaths amounting to around 40% (35% to 41% across models) of the current annual number of deaths on average for each of the next 5 years. A three-month interruption is predicted to lead to approximately half of the excess HIV deaths.

A more sporadic interruption of supply, leading to irregular access to ARVs, would have a lower immediate effect on HIV mortality (a 1.05- and 1.17-fold increase compared with current annual number of deaths over 1 year for a 3- and 6- month disruption, respectively; a 1.00- and 1.03- fold increase over 5 years) but even in the context of largely dolutegravir-based ART [17] would lead to an increase in drug resistance resulting in a 1% lower proportion of people on ART with viral suppression over the next 5 years (HIV Synthesis model). An interruption to supply of cotrimoxazole is predicted to lead to an 8% increase in HIV mortality over one year (HIV Synthesis model).

A disruption of VMMC would be predicted to have only a very small effect on HIV incidence. Disruption to outreach and condom programmes could lead to increases in the number of new infections of up to 25% over one year. If there are also reductions in sex with non-regular partners as a result of physical distancing then the net effect could be reductions in new infections, to the effect of 4% and 7% reductions over 1 years and 1% and 2% reductions over 5 years (for 3- and 6-month disruptions, respectively; Imperial model). Longer term effects on HIV incidence are small.

PrEP programmes are generally small in most settings but a 6-month disruption is predicted to lead to a 1% rise (1.01-fold increase) in HIV incidence over 1 year (HIV Synthesis).

In Table 3 we compare the predicted excess number of HIV deaths across models, in countries and regions of sub-Saharan Africa resulting from a 6-month interruption of ART. This suggests over 500,000 excess HIV deaths in sub-Saharan Africa (range of estimates 471,000 - 673,000). The proportion of such HIV deaths which occur in people aged < 65 is estimated as 95% (HIV Synthesis model).

A cessation of PMTCT activities could lead to significant increases in the number of new child infections (Optima HIV and Goals models): 78% in Malawi, 37% in Mozambique, 104% in Uganda, 78% in Zimbabwe (in Goals model) because PMTCT coverage is quite high in most countries. The HIV Synthesis model identifies an impact on MTCT of interruption of ART, with an excess of 1.67 and 2.07 times more babies born with HIV in 1 year as a result of 3 and 6 months of disruption, respectively.

DISCUSSION

The COVID-19 pandemic presents a formidable challenge to governments and their ministries of health in sub-Saharan Africa. There is a real danger that the COVID-19 epidemic and the public health responses to it could lead to negative effects on health beyond any caused directly by COVID-19 itself, including through impacts on delivery of existing health interventions. While any disruptions to healthcare provision will have a negative health impact on affected individuals, it is helpful to have a clear appraisal of the aspects of existing care provision that are the most critical to preserve. We considered the effects of various disruptions to HIV programmes and, most notably, we find that interruption to ART taking would have particularly serious consequences for the 17 million people on ART in sub-Saharan Africa [4]. A six-month interruption of ART supply would be expected to approximately double HIV-related deaths over one year. In sub-Saharan Africa this amounts to over 500,000 (471,000 – 673,000) excess adult HIV deaths. This relates to the fact that CD4 lymphocyte count recovery that takes years to achieve on ART is rapidly lost after viral replication resumes in the absence of ART. Interruption of ARV supply affecting only a proportion of the population or for a shorter duration would have lesser effects.

While an interruption of ARV drug supply to people would have by far the largest impact of any potential disruptions, effects of lower quality clinical care due to over-stretched health facilities, interruptions of supply of other drugs such as cotrimoxazole, taken to prevent protozoal, bacterial and fungal infections, and suspension of HIV testing, or from reluctance to access care out of concern for becoming exposed to SARS-CoV-2 [18] would all have significant population impacts. Interruption to condom supplies, PrEP, and peer education would make populations more vulnerable to increases in HIV incidence, although physical distancing measures could lead to

reductions in risky sex. A short interruption in VMMC services does not have a significant effect on HIV incidence.

We chose to study the effects of disruptions to entire affected populations. Our results are intended to convey where the greatest vulnerabilities are amongst the various services which form part of HIV programmes and should not be taken as a prediction that disruption will be as extensive as this. Such an extensive disruption to ART access seems unlikely unless, for example, a country's supply of drug is delayed in being dispatched from the factory or in transit. The supply line from manufacturers at this point appears reasonably robust, and some programmes have started multi-month prescriptions and dispensing to reduce vulnerability to interruptions [19,20]. In reality a disruption to a smaller subset of the population is more likely. We did not specifically consider disruptions of services to key populations such as female sex workers or men who have sex with men but given the levels of stigma these could represent populations who are particularly vulnerable to interruptions in services. Condom access and other prevention services outside health facilities might be particularly limited at times when movement is restricted. Some form of disruptions affecting sections of the population could well last longer than 6 months, especially if health systems are severely affected by loss of personnel or fear of returning to health care settings if access to personal protective equipment is limited or not available, and it will be important to monitor such effects.

While there is some uncertainty around the magnitude of the impact that programme disruptions would have on HIV epidemic outcomes, partially reflected in the range of predictions across our five independent models, there is consensus across models that interruption to taking of antiretrovirals represents the greatest threat to HIV outcomes. The differences across models in predicted consequences of ART interruption result largely from differences in how interruptions are modelled, and the consequent death rate assumed (see Appendix). Two of the models (Optima HIV and HIV Synthesis) directly consider the CD4 cell count after interruption, with the latter model assuming generally more rapid and greater declines than the former. In HIV Synthesis, the CD4 cell count declines rapidly towards the pre-ART nadir, hence the impact on death rate is greater for those with a higher CD4 cell count pre-ART. Similarly, in the Optima HIV model, the CD4 cell count declines following Grund et al. findings, resulting in a gradual return to pre-ART CD4 cell counts after interruption [14]. The Goals model assumes an immediate return to pre-ART death rate after interruption, and the Imperial model calculates the death rate based on the mean time to progress to AIDS in the absence of ART. While data are available on changes in CD4 cell count after interruption (e.g. [14]) there are little direct data on death rates as there have not been programmatic situations in which people have been observed longitudinally after interrupting ART, due to the known harmful effects of stopping ART.

Although we have highlighted that the largest effect of disruptions to HIV programmes would occur as a result of ART interruption, it should not be interpreted that effects on prevention, testing and other aspects of treatment and care would not be significant. These programmes have evolved over

several years and are generally highly effective and cost effective, so any loss to their functioning will lead to adverse health consequences for many people. Some short-term changes to HIV programmes, such as reduced use of condoms, are not impactful in terms of the excess number of HIV-related deaths in the medium-term, but we note that new HIV infections would increase and could have further long-term ramifications not represented in the five-year time horizon. Similarly, reductions in peer support may not have short term effects but over time may result in suboptimal treatment adherence and retention in care. Health care provision of all types, for HIV and other diseases and conditions, should be prioritised for maintenance, with modifications if needed, in so far as can be safely attained during the period of threat from COVID-19. Multi-month dispensing for PrEP as well as ART users, and extra emergency provision of supplies is likely required in order to be able to safely provide existing levels of health care at the same time as responding to COVID-19.

Previous evaluations have considered effects on HIV care in other crisis situations such as the post-election unrest in Kenya in 2007 [21,22], during the Ebola epidemic in Guinea in 2014 [23], in acute conflict areas in the Central African Republic and Yemen [24], and as a consequence of food security [25]. All found significant negative effects but also evidence of resilience and ability to successfully deliver ARVs [24,25]. In addition to concern over negative effects of the pandemic, there could be longer term benefits as the crisis has led to simplifications to delivery of care, with multi-month dispensing and less clinic visits per patient, which are less costly and associated with a similar outcome [26].

Our model predictions are inherently limited by the available data to inform them. While there is generally a rich amount of data on HIV and effects of programmes implementing interventions, there are some key uncertainties. One of these is over the magnitude of the impact on death rates of interruption of ART. Important other points or limitations to note include that we do not model any interaction between HIV and COVID-19 infection – that is people with HIV are not assumed to be more or less likely to acquire or die from COVID-19. We also note that there are several models that address excess mortality from disruption of services for HIV and TB, Malaria and other communicable diseases [3,27-29]; all of these models point to similar levels of excess death and we recognize that there can be overlaps in the persons counted as a TB versus an HIV related death. Taken together, however, these models raise the spectre of increased mortality among the most vulnerable and at risk populations in sub-Saharan Africa and can quickly erase years of public health gains if action to mitigate these effects are not swift and coordinated.

In conclusion, when considering plans to manage negative effects of the COVID-19 epidemic, it is critical that governments, donors, suppliers and communities focus on maintaining the supply of ARVs for people with HIV to avoid excess HIV-related deaths and the provision of essential prevention services for key populations to prevent any increase in HIV incidence among the most vulnerable.

AUTHOR CONTRIBUTIONS

Conception of the modelling analyses: all

Model implementation: BLJ, EM, SK, DtB, LB-M, JS, JAS, H-Y K, GM, AP, AB, TH, RM-H

Manuscript drafting and critical review: all

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REFERENCES

1. El-Sadr W, Justman J. Africa in the Path of Covid-19. *N Engl J Med*. 2020. doi: 10.1056/NEJMp2008193
2. Drain PK, Garrett N. SARS-CoV-2 pandemic expanding in sub-Saharan Africa: Considerations for COVID-19 in people living with HIV. *E Clinical Medicine*. 2020; 000: 100342.
3. World Health Organization . The potential impact of health service disruptions on the burden of malaria: a modelling analysis for countries in sub-Saharan Africa. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
4. UNAIDS. UNAIDS Data 2019. https://www.unaids.org/sites/default/files/media_asset/2019-UNAIDS-data_en.pdf
5. Nyoni T, Okumu M. COVID-19-Compliant Strategies for Supporting Treatment Adherence Among People Living with HIV in Sub-Saharan Africa. *AIDS and Behavior* <https://doi.org/10.1007/s10461-020-02888-0>
6. HSRC South Africa. <https://yiba.co.za/hsrc-study-on-covid-19-indicates-overwhelming-compliance-with-the-lock-down/>
7. UNAIDS/ZNNP+/NAC Rapid Assessment survey. Zimbabwe.
8. Finmark Trust. <http://covid19tracker.africa/Download/Survey%20Measuring%20COVID-19%20Impacts.pdf>
9. Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD. What is Required to End the AIDS Epidemic as a Public Health Threat by 2030? The Cost and Impact of the Fast-Track Approach (2016) *PLoS ONE* 11(5):e0154893: doi:10.1371/journal.pone.0154893
10. Kerr CC, Stuart RM, Gray RT, et al. Optima: A Model for HIV Epidemic Analysis, Program Prioritization, and Resource Optimization. *J Acquir Immune Defic Syndr*. 2015;69(3):365-376. [https://doi: 10.1097/QAI.0000000000000605](https://doi:10.1097/QAI.0000000000000605).
11. Phillips AN, et al. Potential Impact and Cost-Effectiveness of Condomless-Sex-Concentrated PrEP in KwaZulu-Natal Accounting for Drug Resistance. *J Infect Dis* 2020.
12. Beacroft L, Smith JA, Hallett TB. What impact could DMPA use have had in South Africa and how might its continued use affect the future of the HIV epidemic? *JIAS* 2019 <https://doi.org/10.1002/jia2.25414>
13. Bershteyn A, Gerardin J, Bridenbecker D, et al. Implementation and applications of EMOD, an individual-based multi-disease modeling platform. *Pathogens and disease* 2018;76(5). <https://academic.oup.com/femspd/article/76/5/fty059/5050059>
14. Grund B, Babiker A, Baxter J, Cohen C, Gatell J, Hoy J, et al. Predictors for the initial CD4+ decline after ART interruption in the SMART Study. THPE144 International AIDS Conference, Toronto 2006.
15. Wit FW, Blanckenberg DH, Brinkman K, Prins JM, van der Ende ME, Schneider MM, Mulder JW, de Wolf F, Lange JM; ATHENA Study Group. Safety of long-term interruption of successful antiretroviral therapy: the ATHENA cohort study. *AIDS*. 2005;19(3):345-8.
16. Jobanputra K, Parker L, Azih C, Okello V, Maphalala G, Jouquet G, Kerschberger B, Mekeidje C, Cyr J, Mafikudze A, Han W, Lujan J, Teck R, Antierens A, van Griensven J, Reid T. Impact and Programmatic Implications of Routine Viral Load Monitoring in Swaziland, *JAIDS* September 1st, 2014 - Volume 67 - Issue 1 - p 45-51 doi: 10.1097/QAI.0000000000000224
17. WHO. Update of recommendations on first- and second-line antiretroviral regimens. Policy brief. <https://www.who.int/hiv/pub/arv/arv-update-2019-policy/en/>

18. Editorial. When pandemics collide. *Lancet HIV*. 2020. [https://doi.org/10.1016/S2352-3018\(20\)30113-2](https://doi.org/10.1016/S2352-3018(20)30113-2).
19. PEPFAR. *PEPFAR Technical Guidance in Context of COVID-19 Pandemic. April 8, 2020 Updates*. 2020[cited 2020 22nd April]; Available from: https://www.state.gov/wp-content/uploads/2020/04/04.08.2020_PEPFAR_Technical_Guidance_During_COVID.pdf.
20. World Health Organisation. *Q&A on COVID-19, HIV and antiretrovirals*. 2020 [cited 2020 22nd April]; Available from: <https://www.who.int/news-room/q-a-detail/q-a-on-covid-19-hiv-and-antiretrovirals>.
21. Mann M, Diero L, Kemboi E, et al. Antiretroviral Treatment Interruptions Induced by the Kenyan Postelection Crisis Are Associated With Virological Failure. *JAIDS* 2013; Volume: 64 Issue: 2 Pages: 220-224
22. Yoder RB, Nyandiko WM, Vreeman RC, Ayaya SO, Gisore PO, Braitstein P, et al. Long-Term Impact of the Kenya Postelection Crisis on Clinic Attendance and Medication Adherence for HIV-Infected Children in Western Kenya. *JAIDS* 2012; 59 Issue: 2 Pages: 199-206 DOI: 10.1097/QAI.0b013e31823b4448
23. Leuenberger D, Hebelamou Jean, Strahm Stefan, et al. leDEA West Africa Study Grp. Impact of the Ebola epidemic on general and HIV care in Macenta, Forest Guinea, 2014. *AIDS* 2015; 29 Issue: 14 Pages: 1883-1887.
24. Ferreyra C, O'Brien Daniel; Alonso B et al. Provision and continuation of antiretroviral therapy during acute conflict: the experience of MSF in Central African Republic and Yemen *CONFLICT AND HEALTH*, Volume: 12, Article Number: 30. Published: Jul 2 2018
25. Young S, Wheeler A, McCoy S, et al. A Review of the Role of Food Insecurity in Adherence to Care and Treatment Among Adult and Pediatric Populations Living with HIV and AIDS. *AIDS AND BEHAVIOR* Volume: 18 Supplement: 5 Pages: S505-S515 Published: OCT 2014
26. Mutasa-Apollo T, Ford N, Wiens W, et al. Effect of frequency of clinic visits and medication pick-up on antiretroviral treatment outcomes: a systematic literature review and meta-analysis. *JIAS* 2017, 20(Suppl 4):21647
27. Hogan AB, Jewell B, Sherrard-Smith E et al. The Potential Impact of the COVID-19 Epidemic on HIV, TB and Malaria in Low- and Middle-Income Countries. Imperial College London (01-05-2020). doi: <https://doi.org/10.25561/78670>.
28. The potential impact of the COVID-19 responses on tuberculosis in high-burden countries: a modelling analysis. http://www.stoptb.org/assets/documents/news/Modeling%20Report_1%20May%202020_FINAL.pdf?utm_source=The+Stop+TB+Partnership+News&utm_campaign=4bee55b759-partner+survey+2019_COPY_01&utm_medium=email&utm_term=0_75a3f23f9f-4bee55b759-190009025
29. Glaziou P. Predicted impact of the COVID-19 pandemic on global tuberculosis deaths in 2020. medRxiv preprint doi: <https://doi.org/10.1101/2020.04.28.20079582>

Table 1. Features of the contributing models.

	Goals	Optima HIV	HIV Synthesis	Imperial model	EMOD
Structure	Compartment model with disaggregation by risk group	Population-based compartment model with sex, age, and risk group disaggregation.	Individual-based stochastic. 3-month time step.	Compartmental model with sex, age, and risk structure.	Individual-based stochastic Simulation. Daily time step
Approach to calibration to data and estimates for specific settings	Epidemiological parameters (probability of transmission per act; variation by stage of infection, presence of other STIs, effectiveness of condoms and ART) are varied to fit the model to prevalence estimates from surveillance and surveys.	Epidemiological parameters (probability of transmission per act, variation by stage of infection (informed by CD4 counts and viral load monitoring), HIV testing rate, mortality rate, presence of other ulcerative STIs and/or tuberculosis, as well as effectiveness of condoms, circumcision, and un/suppressive ART) are varied to fit the model to prevalence estimates from surveillance and surveys.	Parameters relating to population characteristics, sexual behaviour (condomless sex) and age-gender mixing, HIV acquisition, HIV testing, natural history (CD4 count and viral load), ART, risk of AIDS and death varied within plausible bounds to create a range of setting scenarios. Country situations are mimicked by selecting setting scenarios with epidemic and programmatic features consistent with country data.	Epidemiological and HIV intervention parameters (probability of transmission per act, proportion of the population in each risk group, sex- and risk-specific sexual contact rates, risk-specific condom use, amount of risk group mixing, ART and VMMC uptake) are varied to fit the model to country-specific prevalence, incidence, ART and VMMC coverage, and mortality estimates, reported by UNAIDS.	The model is parameterized with epidemiologic data including population size, fertility, mortality, voluntary male circumcision coverage, health seeking and sexual behaviour. South Africa data on age and sex specific HIV prevalence, ART coverage, population size and HIV incidence were used to calibrate the model. Calibration was performed using a parallel simultaneous perturbation optimization (PSPO) algorithm. Roulette resampling in proportion to the likelihood of each simulation was used to select 250 model parameter sets.
Sexual behavior	Behaviors (number of partners, acts per partner, condoms use,	Behaviors (type of partners (regular, casual, or commercial sexual;	Number of short- term condomless sex partners in 3-month period, and	Sexual contact rates differ by risk group (low, medium, high) and by	Four types of sexual partnerships (marital, informal, transitory, and

	needle sharing) differ by risk group: female sex workers, male clients, males and females with non-regular partners, faithful couples, MSM and PWID	injecting), acts per partner, condom use, needle sharing, differ by age and risk group (female sex workers, clients of sex workers, men who have sex with men, and people who inject drugs).	potentially one long term condomless sex partner in period.	age. Condoms are assumed to be used differentially by each risk group.	commercial) are remembered over time and formed according to specifiable partner age patterns.
HIV acquisition determinants (including prevention interventions included)	Acquisition depends on characteristics of the individual (number of partners, circumcision status, PrEP use), the partner population (HIV prevalence, ART use, stage of infection), and the partnerships (acts per partner, prevalence of other STIs, type of sex, condom use)	Acquisition depends on characteristics (type of act (regular, casual, commercial sexual; injecting), number of acts, circumcision and PMTCT status, PrEP and PEP use), and population status (HIV testing, diagnosis, HIV prevalence, un/suppressive ART use, stage of infection), in specified partnerships.	Acquisition risk for each condomless sex partner depends on viral loads of people of (age-mixing relevant) opposite sex. Circumcision and PrEP are modelled.	Acquisition risk for each sex act depends on HIV stage of infection, ART status, circumcision status, PrEP use, and condom use.	Acquisition risk depends on characteristics of an individual which include number of partners, circumcision status (males), condom use, other STIs and coital acts. In addition, characteristics of the partner which include ART use if HIV positive and stage of infection also determine an individual's acquisition risk
HIV natural history	Rate of decline of CD4 count off ART depends on current CD4 count and age, mortality off ART depends on sex, age and CD4 count, mortality on ART depends on CD4 count at initiation, age, sex and duration on ART.	Rate of decline of CD4 count and viral load off ART depends on current CD4 count and viral load. Change in CD4 count on ART depends on current CD4 count and viral suppression of treatment. Mortality both on and off ART depends on current CD4	Viral load, CD4 count decline dependent on viral load. Risk of AIDS and death dependent on current CD4 count, current viral load, age.	Rate of progression through each stage of infection is modeled based on mean duration in each stage. Mortality on ART depends on whether ART was initiated at CD4 ≥ 350 or CD4 < 350 .	HIV prognosis is calculated using a Weibull distribution where the parameters of the distribution are derived from CD4 count and age at the time of infection. CD4 count decreases from the time of infection. CD4 count increases if an individual enrolls for ART. New

		count and ART status (un/suppressive).			prognosis is calculated for ART dropouts.
HIV testing / diagnosis	Testing is by type of test and population group and determines knowledge of status, but this is not linked to transmission since ART coverage is direct input.	Testing is by population group and year, which determines knowledge of status, which allows linkage to care and initiation on ART based on coverage level.	Whether tested or not in each period. Testing indicated in antenatal clinic, for symptoms potentially of HIV, general testing with various degrees of targeting at people with higher probability of infection.	HIV testing/diagnosis is not explicitly represented but is considered a prerequisite for any initiation of treatment.	HIV testing/diagnosis occurs voluntarily, at antenatal visits, or once symptomatic
ART	Risk of mortality while on ART is determined by age, sex, CD4 count at treatment initiation and duration on treatment.	Risk of mortality while on ART is determined by dynamically changing CD4 count over the course of treatment.	Specific drugs and their current level of activity given drug resistance, and current ART adherence. Being currently on ART has a small independent effect on risk of AIDS and HIV death over and above these.	Risk of mortality while on ART is specific to whether ART was initiated early (CD4 \geq 350) or late (CD4 <350).	Risk of mortality while on ART is determined by age, sex, CD4 count at treatment initiation and duration on treatment.
ART interruption	Immediate return to CD4 count at time of treatment initiation. Survival progression identical to those who are treatment naïve.	Substantial initial decline in CD4 count towards pre-ART nadir (consistent with Grund et al. 2006) and gradual return post-interruption. Viral load return is dependent on viral load monitoring.	Immediate viral load return to pre-ART level, substantial initial decline in CD4 count towards pre-ART nadir (consistent with Grund et al.).	Mean survival time of 14 years after stopping ART, exponentially distributed, based on the survival time for HIV-positive persons who have never been on ART (consistent with Todd <i>et al.</i> AIDS 2007). A sensitivity analysis is also modelled using mean survival time of 32 years (Grund et al.) and 8 years after stopping ART (a	CD4 count decreases following dropout from ART. Prognosis is recalculated based on the age and CD4 count at the time of dropping off ART. Computation of ART prognosis after re-enrolling is identical to the initial enrollment with prognosis parameters corresponding to the age

				hypothetical worst-case scenario). Immediate return to pre-interruption ART on resumption of services with no effect on survival, except if individuals have already progressed to AIDS.	and CD4 count at re-enrollment.
Mother to child transmission and its prevention	Depends on CD4 count of the mother if no prophylaxis, or prophylaxis regimen; retention on prophylaxis at delivery, duration of breastfeeding, drop out of prophylaxis during breastfeeding	Depends on CD4 count of the mother if no MTCT and breastfeeding practice.	Dependent on viral load in the mother at birth.	Mother to child transmission and PMTCT are not explicitly modelled.	Depends on CD4 count of the mother if no prophylaxis, or prophylaxis regimen; retention on prophylaxis at delivery
Other specific features		Timestep 0.1 of a year. This was customized and is 0.2 by default.	Transmission of drug resistance.		

Table 2a. Predicted average relative excess in HIV-related deaths and new HIV infections in 1 year in over 2020 in countries in sub-Saharan Africa that would result from a **3- / 6-months** disruption of specific HIV services.

HIV service disruption	Relative increase in HIV mortality in 1 year over 2020-2021 from a 3- / 6-months disruption of services					Relative increase in HIV incidence in 1 year over 2020-2021 from a 3- / 6-months disruption of services				
	Goals	Optima HIV	HIV Synthesis*	Imperial Model	EMOD	Goals	Optima HIV	HIV Synthesis	Imperial Model	EMOD
Suspension of VMMC services	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.01	1.003 / 1.006	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00
Condom availability interrupted	1.001 / 1.003	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.01	1.06 / 1.12	1.07 / 1.11	1.05 / 1.10	1.12 / 1.25	1.16 / 1.28
Suspension of HIV testing	-----	1.01 / 1.02	1.00 / 1.00	-----	1.00* / 1.00*	-----	1.00 / 1.01	1.00 / 1.00	-----	1.01 / 1.01
No new ART initiation	-----	1.03 / 1.05	1.00 / 1.00	1.03 / 1.06	1.01 / 1.02	-----	1.02 / 1.04	-----	1.02 / 1.04	1.01 / 1.05
Suspension of PMTCT	1.05 / 1.10	1.06 / 1.12	-----	-----	-----	1.04 / 1.08	1.03 / 1.09	-----	-----	-----
Viral load testing, enhanced adherence counselling and drug regimen switches stopped	-----	1.11 / 1.23	1.00 / 1.00	1.00 / 1.00	1.02 / 1.05	-----	1.04 / 1.09	-----	1.03 / 1.07	1.02 / 1.01
Increase in death rate in people with AIDS diseases due to over-stretched health system	-----	-----	1.05 / 1.07	1.08 / 1.16	-----	-----	-----	1.00 / 1.00	1.00 / 0.99	-----
ART interruption	1.43 / 2.12	1.35 (1.13 – 1.61) / 1.87 (1.20 – 2.49)	1.88 / 2.80	1.72 (1.25 – 2.34) / 2.28 (1.44 – 3.36)	2.31 / 2.74	1.10 / 1.28	1.11 / 1.23	-----	1.17 (1.16 – 1.20) / 1.32 (1.30 – 1.36)	2.72 / 3.45

Table 2b. Predicted average relative excess in HIV-related deaths and new HIV infections per year for 5 years over 2020-2024 in countries in sub-Saharan Africa that would result from **3- / 6-months** disruption of specific HIV services.

HIV service disruption	Relative increase in HIV mortality in 5 years over 2020-2024 from a 3- / 6-months disruption of services					Relative increase in HIV incidence in 5 years over 2020-2024 from a 3- / 6-months disruption of services				
	Goals	Optima HIV	HIV Synthesis	Imperial Model	EMOD	Goals	Optima HIV	HIV Synthesis	Imperial Model	EMOD
Suspension of VMMC services	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.003/1.006	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00
Condom availability interrupted	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.00	1.00 / 1.01	1.01 / 1.02	1.02 / 1.03	1.02 / 1.02	1.02 / 1.05	1.03 / 1.06
Suspension of HIV testing	-----	1.01 / 1.02	1.00 / 1.00	-----	1.00 / 1.01		1.00 / 1.01	1.00 / 1.00	-----	1.01 / 1.01
No new ART initiation	-----	1.01 / 1.01	1.00 / 1.00	1.01 / 1.02	1.00 / 1.02		1.00 / 1.00	-----	1.01 / 1.01	1.00 / 1.02
Suspension of PMTCT	1.02 / 1.04	1.03 / 1.06	-----	-----	-----	1.01 / 1.02	1.01 / 1.02	-----	-----	-----
Viral load testing, enhanced adherence counselling and drug regimen switches stopped	-----	1.03 / 1.07	1.00 / 1.00	1.00 / 1.00	1.02 / 1.03		1.01 / 1.03	-----	1.01 / 1.02	1.02 / 1.03
Increase in death rate in people with AIDS diseases due to over-stretched health system	-----	-----	1.00 / 1.00	1.00 / 1.00	-----		-----	1.00 / 1.00	1.00 / 1.00	-----
ART interruption	1.20 / 1.40	1.20 / 1.35	1.23 / 1.41	1.24 (1.10 – 1.39) / 1.46 (1.18 – 1.80)	1.27 / 1.46	1.02 / 1.09	1.06 / 1.11	-----	1.05 (1.05 – 1.05) / 1.08 (1.08 – 1.10)	1.33 / 1.49

Footnotes to Table 2:

Optima HIV: Values in the table are for all ages. Interruptions commence on 1 March 2020. Numbers of circumcisions are held constant over the disruption period, as it was assumed no new circumcisions would be performed due to physical distancing concerns. Changes in sexual contacts due lockdowns could be assumed as an increase in acts between regular partners and a decrease between casual and commercial partners; however, since there is uncertainty around the common change across all countries modeled no behaviour were modeled.

HIV Synthesis: Values of 1.00 indicate estimate is not discernibly different from 1.00 given stochastic variation. Figures in the Table are for adults only and are for 4 three-month periods 2020.25-2021.00, or 20 periods 2020.25-2025. Suspension of PMTCT is not considered separately from interruption of all ART, which has an effect on MTCT. Estimates of disruption of PrEP programs should be understood in the context of overall only 0.2% of women aged 15-25 being on PrEP so it is not possible to discern clear impact of suspension. There is an impact on MTCT of interruption of ART, with an excess of 1.67 / 2.07 times more babies born with HIV in 1 year as a result of 3 / 6 months of disruption.

Imperial model: Interruptions begin from 2020.5 and last for three months or six months, with outcomes determined over one or five years following the beginning of the interruption. Figures in the table are an average of three countries in sub-Saharan Africa (Malawi, South Africa, and Zimbabwe) and are for adult mortality and new infections only. Numbers in parentheses are confidence intervals for survival estimates of individuals who have stopped ART (point estimate = mean survival time off of ART of 14 years, lower bound = mean survival time off of ART of 32 years, upper bound = mean survival time off of ART of 8 years), with more details provided in the Appendix. Each scenario is modelled independently of other scenarios.

EMOD: Values with 1.00* in the table indicate that differences in estimates were non-significant given the stochastic variation. Interruptions commenced on 1 July 2020 to 31 October 2020 and 31 December 2020 for 3- and 6-months disruption, respectively. To estimate the impact of condom availability interruption, transmission probability per coital act was increased by an average of 54% during the disruption interval. Transmission risk factor returns to default values after the disruption period.

Table 3. Predicted excess deaths over 1 year due to 6 months interruption of ART

Country	Estimated HIV-related deaths in 2018*	Excess HIV-related deaths over 1 year				
		GOALS	Optima HIV	HIV Synthesis	Imperial Model**	EMOD
South Africa	71,000	110,000	84,000	83,800	81,100 (25,300 - 161,500)	140,900
Malawi	13,000	34,000	18,000	24,100	13,300 (4,400 – 26,200)	23,400
Mozambique	54,000	92,000	54,000	58,500	69,100 (23,800 – 127,400) [†]	-----
Zimbabwe	22,000	48,000	21,000	28,000	21,300 (7,000 – 42,000)	33,400
Eswatini	2,400	6,100	4,700	9,200	3,100 (1,100 – 5,700) [†]	5,800
Lesotho	6,000	14,000		7,600	7,700 (2,600 – 14,200) [†]	6,600
Uganda	23,000	52,000	43,000	48,600	29,400 (14,200 – 54,300) [†]	30,400
Kenya	25,000	58,000	38,000	46,200	32,000 (11,000 - 59,000) [†]	38,800
Botswana	4,800		9,500	19,350	6,100 (2,100 – 11,300) [†]	10,200
Tanzania	25,000	48,000	24,000	31,600	32,000 (11,000-59,000) [†]	33,600
Eastern & Southern Africa	310,000		380,000	465,000	397,000 (136,000 – 732,000) [†]	404,900
Cameroon	17,000	18,000	15,000	18,600	21,800	14,500

					(7,500 – 40,100) [†]	
Cote d'Ivoire	16,000	13,000	12,000	17,800	20,500 (7,000 – 37,800) [†]	6400
Nigeria	53,000	65,000	52,000	52,500	67,800 (23,300 – 125,100) [†]	27,000
Western & Central Africa	160,000		140,000	208,000	205,000 (70,000 – 378,000) [†]	66,100
Sub-Saharan Africa	470,000		520,000	673,000	602,000 (207,000 – 1,109,000) [†]	471,000

* UNAIDS Data 2019 [4]. ** Imperial Model: Numbers in parentheses are confidence intervals for survival estimates of individuals who have stopped ART as described in Table 1. [†]Figures are estimated by applying the relative increase in HIV mortality over 1 year from Table 2a to estimated HIV-related deaths in 2018 by country. In EMOD, the number of deaths during an ART interruption in each setting is assumed to be proportional to the number on ART with viral load suppression at the time of the interruption

