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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 pandemic could lead to disruptions to provision of HIV services for people living with HIV and those at risk of acquiring HIV in sub-Saharan Africa, where UNAIDS estimated that more than two-thirds of the approximately 38 million people living with HIV resided in 2018. We aimed to predict the potential effects of such disruptions on HIV-related deaths and new infections in sub-Saharan Africa.

Methods

In this modelling study, we used five well described models of HIV epidemics (Goals, Optima HIV, HIV Synthesis, an Imperial College London model, and Epidemiological MODeling software [EMOD]) to estimate the effect of various potential disruptions to HIV prevention, testing, and treatment services on HIV-related deaths and new infections in sub-Saharan Africa lasting 6 months over 1 year from April 1, 2020. We considered scenarios in which disruptions affected 20%, 50%, and 100% of the population.

Findings

A 6-month interruption of supply of antiretroviral therapy (ART) drugs across 50% of the population of people living with HIV who are on treatment would be expected to lead to a 1·63 times (median across models; range 1·39–1·87) increase in HIV-related deaths over a 1-year period compared with no disruption. In sub-Saharan Africa, this increase amounts to a median excess of HIV deaths, across all model estimates, of 296 000 (range 229 023–420 000) if such a high level of disruption occurred. Interruption of ART would increase mother-to-child transmission of HIV by approximately 1·6 times. Although an interruption in the supply of ART drugs would have the largest impact of any potential disruptions, effects of poorer clinical care due to overstretched health facilities, interruptions of supply of other drugs such as co-trimoxazole, and suspension of HIV testing would all have a substantial effect on population-level mortality (up to a 1·06 times increase in HIV-related deaths over a 1-year period due to disruptions affecting 50% of the population compared with no disruption). Interruption to condom supplies and peer education would make populations more susceptible to increases in HIV incidence, although physical distancing measures could lead to reductions in risky sexual behaviour (up to 1·19 times increase in new HIV infections over a 1-year period if 50% of people are affected).

Interpretation

During the COVID-19 pandemic, the primary priority for governments, donors, suppliers, and communities should focus on maintaining uninterrupted supply of ART drugs for people with HIV to avoid additional HIV-related deaths. The provision of other HIV prevention measures is also important to prevent any increase in HIV incidence.

Funding

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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, 2, 3] Causes of such disruption could include COVID-19-related morbidity and mortality, clinic closures or reduced service availability, and 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 million (uncertainty range 22·2–29·5) people estimated to be living with HIV in the region in 2018.[4] Concern exists that possible disruptions in HIV programmes due to COVID-19[1, 2, 5] could affect HIV-related mortality and new infections. Negative effects of the COVID-19 epidemic on access to health services have begun to emerge. A survey of people living with HIV run by the Human Sciences Research Council in South Africa via a social media platform found that 13% of people said they did not have access to their chronic medication during lockdown,[6] with some reports in the area as of May, 2020, show-

ing that only 30–50% of patients were collecting their medication.[7] A rapid survey assessment in Zimbabwe in April, 2020, found 19% of people with HIV attempting to get a refill of an antiretroviral drug had not been able to, or were only able to get a partial refill,[8] while a telephone-based survey in Kenya and Nigeria run by the Finmark Trust in April, 2020, found 14% of people were unable to collect needed medications.[9] In a May, 2020, WHO survey in five of 13 countries in sub-Saharan Africa, antiretroviral therapy (ART) stock availability for major first-line drugs was reported to be 3 months or less, with reasons including failure of suppliers to deliver on time (Low-Beer D, WHO, Geneva, Switzerland, personal communication).

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, but the relative consequences for HIV mortality and incidence of disruptions of different activities is not widely appreciated, and neither is the potential absolute magnitude of impact. We searched Web of Science on April 24, 2020, with no date or language restrictions, using the terms (COVID* AND model* AND HIV* AND Africa) and found no studies that predict the effects of disruption due to COVID-19 on HIV outcomes in sub-Saharan Africa.

Added value of this study

Our study provides a robust assessment of the potential effects of HIV service disruptions in sub-Saharan Africa resulting from COVID-19 and informs those organising programmes of the area of greatest priority, which is to maintain the supply of antiretroviral drugs for people with HIV. The consistency of the main findings across multiple models adds weight to the findings.

Implications of all the available evidence

During the COVID-19 pandemic, the primary priorities for governments, donors, suppliers, and communities to avoid additional HIV-related deaths and HIV incidence should be to maintain constant supply of antiretroviral drugs for people living with HIV. Provision of other HIV prevention interventions should also be carefully maintained to prevent an increase in HIV incidence.

We aimed to explore the effects of HIV service disruptions using existing mathematical models of HIV epidemiology and intervention programmes in sub-Saharan Africa. In this Article, we consider the predicted effects of temporary disruption to different individual HIV services for periods of 3

or 6 months over 1-year and 5-year periods on HIV mortality and incidence. We also considered disruptions that affect 20%, 50%, or 100% of the population. The primary analysis considered effects over 1 year of a 6-month disruption for 50% of the population.

Methods

Study design

In this modelling study, we used five well described existing HIV models to estimate the impact of different disruptions to HIV prevention and treatment services as a result of the COVID-19 pandemic on HIV-related mortality and incidence. These models were Goals,[10] Optima HIV,[11] HIV Synthesis,[12] an Imperial College London Model,[13] and Epidemiological MODeling software (EMOD).[14] This study arose from discussions within an ad hoc group composed of the authors and other individuals (listed in the Acknowledgments).

Models and data sources

The features of each model are summarised in table 1. Each model is based on information provided by a wide array of previous studies, as has been described previously.[10, 11, 12, 13, 14] Importantly, the models make assumptions relating to effects of ART interruption that account for the fact that immune recovery during ART tends to be lost quite rapidly after interruption of treatment. These assumptions are based on, for example, empirical observations[15, 17] that showed a median loss of 187 CD4 cells per μL after ART interruption and 25% of people have a loss of more than 317 cells per μL in 2 months.

Table 1

Characteristics of the contributing models

	Goals	Optima HIV	HIV Synthesis	Imperial College London model	EMOD
Structure	Compartment model with disaggregation by risk group	Population-based compartment model with sex, age, and risk group disaggregation; 1-month time step	Individual-based stochastic model; 3-month time step	Compartmental model with sex, age, and risk structure	Individual-based stochastic simulation; daily time step; network model
Approach to calibration of data and estimates for specific settings	Epidemiological parameters (probability of transmission per sex act; variation by stage of infection, presence of other STIs, and effectiveness of condoms and ART) are varied to fit the model to prevalence estimates from surveillance and surveys	Epidemiological parameters (probability of transmission per sex act, variation by stage of infection [informed by CD4 cell counts and viral load monitoring], HIV testing rate, mortality rate, presence of other ulcerative STIs or tuberculosis, or both, and effectiveness of condoms, circumcision, and unsuppressive or suppressive	Parameters relating to population characteristics, sexual behaviour (condomless sex), age-gender mixing (ie, distribution of ages of male sexual partners of women of a given age and vice versa), HIV acquisition, HIV testing, natural history (CD4 cell count and viral load), ART, and risk of AIDS and death varied within plausible	Epidemiological and HIV intervention parameters (probability of transmission per sex act, proportion of the population in each risk group, sex-specific and risk-specific sexual contact rates, risk-specific condom use, amount of mixing of at-risk groups, ART and VMMC uptake) are varied to fit the model to country-specific prevalence, incidence, ART	Parameterised with epidemiological data including population size, fertility, mortality, VMMC coverage, and health-seeking and sexual behaviour; data from South Africa on age-specific and sex-specific HIV prevalence, ART coverage, population size, and HIV incidence were used to calibrate the model; calibration was

Data are for adults and children, unless otherwise stated. ART=antiretroviral therapy. EMOD=Epidemiological MODeling software. MSM=men who have sex with men. MTCT=mother-to-child transmission. PEP=post-exposure prophylaxis. PMTCT=prevention of mother-to-child transmission. PrEP=pre-exposure prophylaxis. PWID=people

who inject drugs. STI=sexually transmissible infection. VMMC=voluntary medical male circumcision.

Each model is based on many data sources; for instance, over 100 citations were used in the construction of the HIV Synthesis model. More details on the data used for each model are in the previous publications.[10, 11, 12, 13, 14]

Analytical approach

All models simulate disruptions that last for 3 or 6 months starting from April 1, 2020, with 20%, 50%, or 100% of people who would otherwise benefit from a given service being affected, with our primary focus being on the 50% scenario. The potential disruptions to services are broadly grouped as prevention programmes, HIV testing, and treatment and care (table 2). At the end of the disruption period, service use is assumed to return to levels during the pre-disruption period. We considered the impacts on HIV mortality and incidence over 1-year and 5-year periods (table 2; appendix pp 4–5). We express results as the relative change in HIV deaths over the period of interest due to service disruption relative to the predicted annual number of such deaths in the relevant time period if no COVID-19 disruption or epidemic occurred. We used similar methods to describe the relative change in incidence of new HIV infections. We also considered the possibility that sexual activity will be decreased during the disruption period due to physical distancing measures (appendix pp 2–7). Using the results on the relative change in mortality due to interruption of ART, we calculated the predicted excess number of HIV deaths over 1 year in various example countries and sub-Saharan Africa as a whole.

Table 2

Predicted average relative change in HIV mortality and incidence over 1 year from April 1, 2020, due to a 6-month disruption of specific HIV services for 20%, 50%, and 100% of the population in countries in sub-Saharan Africa

	Relative increase in HIV mortality					Relative increase in HIV inciden			
	Goals	Optima HIV	HIV Synthesis	Imperial College London Model	EMOD	Goals	Optima HIV	HIV Synthesis	Im Col Lo Mo
Prevention programmes									
Suspension of VMMC services									
20% disruption	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·99–1·01)	1·00 (1·00–1·00)	1·00 (1·00–1·10)*	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·99–1·01)	1·0 (1· 1·0
50% disruption	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·97–1·03)	1·00 (1·00–1·00)	1·00 (1·00–1·08)	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·97–1·03)	1·0 (1· 1·0
100% disruption	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·95–1·07)	1·00 (1·00–1·00)	1·00 (1·00–1·07)*	1·01 (1·00–1·01)	1·00 (1·00–1·00)	1·00 (0·94–1·07)	1·0 (1· 1·0
Condom availability interrupted									
20% disruption	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·99–1·01)	1·00 (1·00–1·00)	1·00 (1·00–1·07)*	1·07 (1·03–1·12)	1·02 (1·00–1·04)	1·01 (0·99–1·05)†	1·0 (1· 1·0
50% disruption	1·00 (1·00–1·00)	1·00 (1·00–1·00)	1·00 (0·97–1·03)	1·00 (1·00–1·00)	1·00 (1·00–1·08)*	1·19 (1·07–1·30)	1·06 (1·01–1·10)	1·03 (0·99–1·13)†	1·1 (1· 1·1
100% disruption	1·01 (1·00–1·01)	1·00 (1·00–1·00)	1·00 (0·95–1·06)	1·00 (1·00–1·00)	1·00 (1·00–1·07)	1·38 (1·15–1·62)	1·12 (1·02–1·20)	1·07 (0·98–1·28)†	1·2 (1· 1·2
Suspension of PMTCT									
20% disruption	1·01 (1·00–1·02)	1·00 (1·00–1·01)	..	..	..	1·02 (1·00–1·05)	1·01 (1·00–1·02)	..	..
50% disruption	1·03 (1·01–	1·01 (1·00–	..	..	..	1·05 (1·00–	1·02 (1·01–	..	..

Data are relative changes in estimates, with 95% uncertainty intervals in parentheses. For the Goals model, values are weighted averages of 13 countries in sub-Saharan Africa (South Africa, Malawi, Mozambique, Zimbabwe, eSwatini, Lesotho, Uganda, Kenya, Botswana, Tanzania, Cameroon, Côte d'Ivoire, and Nigeria). We assumed constant condom use rates and PMTCT coverage; historical rates of growth in VMMC; and adult and paediatric ART coverage increasing from 2019 levels to UNAIDS fast-track targets of 81% of all people who live with HIV on ART by 2025 for countries that are below those targets now or 90% if current coverage exceeds 81%.[10] The VMMC, testing, and no new ART initiation disruptions affect the growth in the base case. For the increase in AIDS mortality due to overstretched health systems, we assumed that survival would be 2 years shorter with a complete failure of the health system and adjusted the age-specific, sex-specific, and CD4 cell count-specific survival rates accordingly to reflect the 6-month disruption affecting 20%, 50%, or 100% of the population. We assumed no change in sexual behaviour during the service disruption period. All estimates for this model are for adults and children, as relevant. For the Optima HIV model, all values are for all ages and are an average of 12 countries in sub-Saharan Africa (Botswana, Cameroon, Côte d'Ivoire, eSwatini, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, and Zimbabwe). Numbers of circumcisions are held constant over the disruption period because we assumed no new circumcisions would be done due to physical distancing concerns due to the COVID-19 pandemic. For the HIV Synthesis model, deaths and new HIV infections apply to adults only. 95% uncertainty intervals are the 2·5% and 97·5% percentiles of the distribution across setting scenarios and thus reflect uncertainty and intersetting variability. Suspension of PMTCT is not considered separately from interruption of all ART, which has an effect on MTCT. Estimates of disruption of PrEP programmes should be understood in the context that overall only 0·2% of women aged 15–25 years are on PrEP. An effect is seen on MTCT of interruption of ART, with an excess of 2·69 times more babies born with HIV in 1 year as a result of 6 months of disruption in 50% of people. For the Imperial College London model, 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. For survival estimates of individuals who have stopped ART (average monthly mortality risk of 0·24%, lower bound of average monthly mortality risk of 0·10%, and upper bound of 0·44%) more details are in the appendix (pp 17–18). Each scenario is modelled independently of other scenarios. For the EMOD model, to estimate the impact of condom availability interruption, transmission probability per sex act was increased during the disruption interval in proportion to the level of service disruption. Transmission risk factor returns to default values after the disruption period. ART=antiretroviral therapy. EMOD=Epidemiological MODeling software. MTCT=mother-to-child transmission. PMTCT=prevention of mother-to-child transmission. PrEP=pre-exposure prophylaxis. VMMC=voluntary medical male circumcision.

*Differences in estimates were non-significant given the stochastic variation.

†Data are significantly different from 1 —ie, no stochastic variability.

A summary of key aspects of each model is shown in table 1. Additional details on the approach we took for this analysis by each model are as follows. In the Goals model, coverage of all interventions except voluntary medical male circumcision (VMMC) were assumed to remain at 2019 levels, and VMMC coverage to increase according to current trends in recent years. Interruption of condom availability is modelled like all other behaviour change interventions, being suspended for the 3-month or 6-month periods, including community mobilisation, condom promotion, school-based programmes, and outreach services to key populations. The result is an increase in the number of sexual partners and a reduction in condom use. Modelling a reduction in sexual activity, as in the sensitivity analysis (appendix p 6), means that during the disruption period no casual

or commercial sex occurs between heterosexual individuals or men who have sex with men (MSM). For suspension of prevention of mother-to-child transmission (PMTCT), the disruption means no mother-to-child transmission (MTCT) prophylaxis services are offered during the disruption period.

In the Optima HIV model, new VMMCs were assumed to stop over the disruption period. Change in sexual behaviour was represented by a 50% reduction in casual and commercial sexual contacts for applicable risk groups for the duration of the disruption, which return to pre-disruption levels immediately after the disruption period ends. Average values include results for 12 countries in sub-Saharan Africa (Botswana, Cameroon, Cote d'Ivoire, eSwatini, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, and Zimbabwe). Regional values are sums of country values located in the given region. The mortality rate for those on ART whose treatment is suspended was applied on the basis of data from Grund and colleagues.[15] As a result, CD4 cell counts decrease rapidly and then gradually return to pre-ART levels after interruption ends. Once ART is resumed, the mortality rate for those on ART by CD4 cell count was applied. The impact on ART drug resistance as a result of disruption of HIV treatment and additional COVID-19-related deaths among people living with HIV were not included.

We used the HIV Synthesis model to generate a range of setting scenarios (n=300), with an aim to collectively represent the diversity of HIV epidemic and programme characteristics across and within countries in sub-Saharan Africa (appendix pp 11–12). For the effect of ART interruption, to generate country-specific estimates, we considered the association between the proportion of people with HIV who have viral suppression at the start of 2020 and the relative increase in death rate across setting scenarios. For this model, we present data for adult mortality only. Suspension of PMTCT services is not considered separately from interruption of all ART, which affects MTCT. We implemented the increase in the death rate among people with AIDS-defining illnesses due to overstretched health systems as a doubling in the death rate during the 3-month period in which an AIDS-defining illness occurs. Estimates of disruption of pre-exposure prophylaxis (PrEP) programmes are in the context of only 0·2% of women aged 15–25 years overall being on PrEP in the model. The assumptions in the model on changes in CD4 cell count during ART interruption result in 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. This model included effects of co-trimoxazole use for prevention of opportunistic infections, in addition to antiretroviral drugs. We also present the age breakdown of HIV deaths from this model.

To estimate the relative increase in death rate for a country, we referred to the proportion of people with HIV who have a suppressed viral load in the country to generate a country-specific estimate and applied the relative risk estimate to the annual number of adult HIV-related deaths from most recent UNAIDS 2018 estimates (appendix pp 13–15).[4]

The Imperial College London Model assumes that no new VMMCs occur during the disruption period, and that when the disruption ceases, circumcisions resume at the pre-disruption rate. For interruption of condom availability, condom use is assumed to be reduced by 50% for the duration of the disruption. ART initiation is assumed to be suspended such that no new individuals are initiated on ART for the duration of the disruption period and scale-up continues at pre-disruption

rates after the disruption period ends, such that those who would have been initiated on ART during this period are allowed to start but might have progressed to a later stage of infection before starting. Viral load testing, enhanced adherence counselling, and switches are assumed to stop, and an additional 10% of individuals on ART are assumed to have an unsuppressed viral load. The death rate among people with AIDS-defining illnesses is assumed to increase due to overstretched health systems, such that the death rate for those with AIDS doubles for the duration of the disruption. A break in the supply of ART drugs, leading to ART interruption, is assumed to happen for 100% of individuals on ART, hence they stop using ART for the duration of the disruption period and are then re-initiated. If an individual has progressed to AIDS during this interruption, ART re-initiation is assumed to be too late for them to recover. Reduction in sexual contacts is assumed such that all sexual contacts across all risk groups decrease by 10% for the duration of the disruption period, and then return to pre-disruption levels immediately after the disruption period.

In the EMOD model, the scenario of VMMC interruption was assumed to apply only to in-clinic circumcisions provided by HIV prevention programmes; 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, and after the disruption period transmission probabilities were assumed to return to their pre-disruption rates. A proportion of individuals who would have tested or initiated ART during the disruption period are unable to do so but might re-attempt testing and ART initiation after the disruption period ends at rates equivalent to pre-disruption rates among ART-naive individuals. Disruption of viral load testing, enhanced adherence counselling, and switches are assumed to increase the proportion of individuals with unsuppressed viral load during the disruption period.[18] A break in supply of ART drugs leading to ART interruption is assumed to interrupt a proportion of ART use during the disruption period and resume ART use for those who survived the interruption to their ART or attempted to initiate ART during the disruption period. Survival during and after the disruption period depends on CD4 cell count and age, with older adults having more rapid decreases in CD4 cell count and increased risk of mortality. Viral load suppression after ART initiation, including re-initiation after a treatment interruption, is assumed to take an average of 3 months and up to 6 months. For scenarios with reduction in risky sexual behaviour during the service disruption period, we assumed a 50% reduction in risky sexual behaviour for commercial, informal, and transitory sexual contacts.

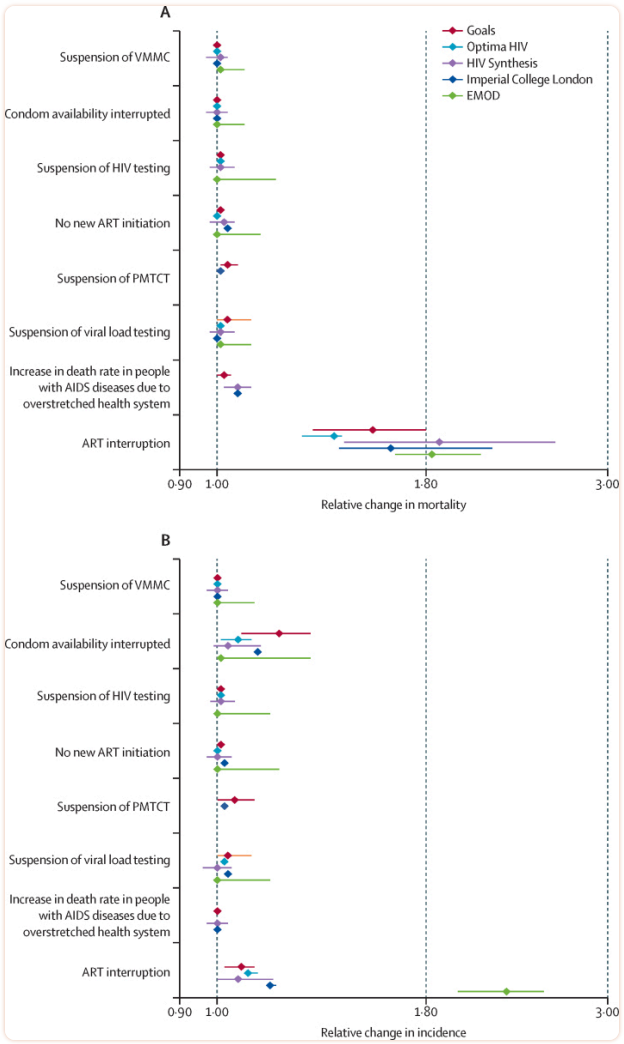
Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Results for predicted effects of disruptions on various HIV services from the five models are shown in table 2 for 20%, 50%, and 100% of people being affected by the disruption, and predicted effects for the 50% scenario are shown in the figure. Disruptions to care and treatment services for people living with HIV are associated with increases in mortality risk, most notably dis-

ruption to the supply of ART drugs to people already on treatment resulting in discontinuation of ART. 6 months of such interruption to 50% of people is expected to lead to a 1·63 times (median over models; with the lowest estimate predicted using the Optima HIV model [1·39] and the highest by the HIV Synthesis model [1·87]) increase in HIV-related deaths over a 1-year period compared with no disruption. Although the effect in the first year is greatest, a substantial effect was also seen up to 5 years after the start of the disruption, such that a 6-month period of ART interruption for 50% of people is predicted to lead to an increase of 1·15–1·29 times the current annual number of deaths for each of the next 5 years (appendix pp 4–5). A 3-month interruption is predicted to lead to approximately half the excess HIV deaths estimated for the 6-month period (appendix pp 2–3). Although an interruption in the supply of ART drugs would have the largest impact of any potential disruptions, effects of poorer clinical care due to overstretched health facilities, interruptions of supply of other drugs such as co-trimoxazole, and suspension of HIV testing would all have a substantial effect on population-level mortality, with an up to a 1·06 times increase in HIV-related deaths over a 1-year period due to disruptions affecting 50% of the population compared with no disruption (table 2).



Figure

Predicted relative change in HIV mortality (A) and incidence (B) in 1 year from April 1, 2020, from a 6-month disruption of specific HIV services in sub-Saharan Africa, for 50% of the population

Datapoints are point estimates with 95% uncertainty intervals indicated by whiskers. ART=antiretroviral therapy. EMOD=Epidemiological MODeling software. PMTCT=prevention of mother-to-child transmission. VMMC=voluntary medical male circumcision.

A disruption in VMMC programmes is predicted to have only a very small effect on HIV incidence (table 2). Disruption to outreach and condom programmes for 50% of people could lead to increases in the number of new infections of up to 1·19 times over 1 year. If reductions in sex with non-regular partners also occurred as a result of physical distancing, then the net effect could be a reduction in new infections (appendix pp 6–7). Longer-term effects over 5 years on HIV incidence are small (appendix pp 4–5). PrEP programmes are generally small in most settings, but a 6-month disruption in 50% of people is predicted to lead to a 1·005 times relative change in HIV incidence over 1 year (HIV Synthesis model; data not shown).

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 for 20%, 50%, and 100% of people on ART. For a 50% disruption, the median number of excess deaths in sub-Saharan Africa, across models, is estimated to be 296 000 (range 229 023–420 000). The proportion of such HIV deaths that occur in people younger than 65 years is estimated to be 95% (HIV Synthesis model; data not shown).

Table 3

Predicted excess HIV-related deaths over 1 year from April 1, 2020, due to a 6-month interruption of ART for 20%, 50%, and 100% of the population in countries in sub-Saharan Africa

	Estimated HIV-related deaths in 2018*	Excess HIV-related deaths over 1 year: 2020–21				
		Goals	Optima HIV	HIV Synthesis	Imperial College London Model†	EMOD
South Africa	71 000 (52 000–91 000)	..	..	..	..	..
20% disruption	..	35 000 (27 000–34 000)	19 000 (15 000–24 000)	14 500 (10 600–20 500)	16 000 (5000–32 000)	27 614 (26 000–29 228)
50% disruption	..	100 000 (80 000–130 000)	45 000 (36 000–57 000)	42 200 (30 400–64 000)	40 100 (12 500–80 000)	68 519 (66 600–70 500)
100% disruption	..	230 000 (170 000–280 000)	84 000 (66 000–107 000)	112 000 (74 600–190 000)	80 400 (25 000–160 300)	138 126 (135 400–140 900)
Malawi	13 000 (11 000–16 000)	..	..	..	..	..
20% disruption	..	4800 (3800–5700)	3800 (3700–4000)	3200 (1800–4200)	2600 (900–5200)	4582 (3900–5500)‡
50% disruption	..	14 000 (11 000–17 000)	9300 (8900–9900)	9900 (6100–14 000)	6600 (2200–12 900)	11 370 (9600–13 600)‡
100% disruption	..	32 000 (25 000–38 000)	18 000 (17 000–19 000)	29 200 (12 900–46 700)	13 200 (4300–25 900)	22 921 (19 400–27 400)‡
Mozambique	54 000 (39 000–73 000)	..	..	..	..	..
20% disruption	..	11 000 (6500–16	12 000 (9700–16	9500 (5900–14 000)	13 500 (4900–25	..

Data are estimates with 95% uncertainty intervals. Data are for adults and children, unless otherwise stated, and analyses assume no change in sexual behaviour associated with the period of disruption. In the EMOD model, the number of deaths during an ART interruption in each setting is assumed to be proportional to the number of individuals on ART with viral load suppression at the time of the interruption. In the HIV Synthesis model, values are for adults only (aged ≥15 years). ART=antiretroviral therapy. EMOD=Epidemiological MODeling software.

*UNAIDS estimates for 2019.[4]

†Numbers in parentheses are 95% uncertainty intervals for survival estimates of individuals who have stopped ART as described in table 1.

‡Estimated by applying the relative increase in HIV mortality over 1 year from table 2 to estimated HIV-related deaths in 2018 by country.

A suspension of PMTCT activities for 3 months could lead to large increases in the number of new child infections according to the Optima HIV and Goals models. For example, in the Goals model, suspension of these activities leads to relative increases in child infections of 1·81 times in Malawi, 1·41 times in Mozambique, 1·70 times in Uganda, and 1·53 times in Zimbabwe because PMTCT coverage is quite high in most countries. The HIV Synthesis model identified the impact on MTCT of interruption of ART, with 1·64 times more babies born with HIV in 1 year as a result of a 6-month disruption in 50% of people.

Discussion

A 6-month interruption in ART supplies for 50% of people would be expected to lead to an approximately 1·63 times (range 1·39–1·87) increase in HIV-related deaths over 1 year. In sub-Saharan Africa, this increase amounts to a median of 296 000 (range 229 023–420 000) excess HIV deaths over this period. This substantial number of excess deaths can be explained by the fact that CD4 lymphocyte cell count recovery, which takes years to achieve on ART, is rapidly lost after viral replication resumes in the absence of ART.

Although an interruption in ART drug supply would have by far the largest impact of any potential disruption, effects of lower quality clinical care due to overstretched health facilities, interruption of supply of other drugs (eg, co-trimoxazole, which is taken to prevent protozoal, bacterial, and fungal infections), and suspension of HIV testing, or due to reluctance among patients to access care because of concerns about exposure to severe acute respiratory syndrome coronavirus 2[19] would all have substantial population-level effects. Interruption to condom supplies, PrEP, and peer education would make populations more susceptible to increases in HIV incidence, although physical distancing measures could lead to reductions in risky sexual behaviour.

We chose to study the effects of disruptions to 50% of affected populations. We aimed to show the areas that are most susceptible to disruption among the various services that form part of most countries' national HIV responses and our results should not be taken as a prediction that disruption will be as extensive as estimated here. Such an extensive disruption to ART access as estimated here seems unlikely unless, for example, a country's supply of ART drugs is delayed in be-

ing dispatched from the factory or in transit. On July 6, 2020, WHO announced that 73 countries have warned that they are at risk of stock-outs of antiretroviral medicines as a result of the COVID-19 pandemic.[20] As of July 29, 2020, The President's Emergency Plan for AIDS Relief reported that the median delay in reciving ART drugs is 35 days for adults and 29 days for children.[21] Deliveries of orders for antiretrovirals are delayed because most manufacturers are based in India (which has been under lockdown in response to COVID-19) and transport challenges. Incoming raw materials from China to India have also been reported to be affected by logistical constraints. Anecdotal evidence from Malawi shows relaxation of eligibility criteria for multi-month dispensing of ART drugs, with around 30–40% of people who live with HIV on ART being on a 6-month refill compared with 10% during the pre-COVID-19 era (Chagoma N, unpublished). We did not specifically consider disruptions of services to key populations, such as female sex workers or homosexual men and other MSM but, given the levels of stigma around these populations, they could be particularly susceptible to interruptions in services. Condom access and other prevention services outside health facilities might be particularly affected at times when movement is restricted. Some form of disruptions affecting sections of the population could 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 personal protective equipment is not available or access is restricted, and monitoring such effects will be important.

While some uncertainty exists around the magnitude of the effect that programme disruptions would have on the HIV epidemic, which is reflected in the range of predictions across the models, interruption of ART is generally agreed to be the greatest threat to HIV mortality and incidence. 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. Two of the models (Optima HIV and HIV Synthesis) directly consider the CD4 cell count decrease after interruption. The Goals model assumes an immediate return to the pre-ART death rate after interruption, and the Imperial College London model calculates the death rate on the basis of the mean time to progress to AIDS in the absence of ART. Although data are available on changes in CD4 cell count after interruption,[15] little direct data exist on death rates because no large scale studies of effects of complete interruption of ART for substantial periods have been done in which people have been observed longitudinally after interruption of ART because of the known harmful effects of stopping ART. All the models predict that ART interruption, in the absence of changes in sexual behaviour, will lead to increases in HIV incidence. The EMOD model predicts that this increase would be particularly large, perhaps due to transmission during acute HIV infection causing a synchronous wave of secondary spread, which might be more pronounced in a network model.

Although the largest effect of disruptions to HIV programmes would occur as a result of ART interruption, effects on prevention, testing, and other aspects of treatment and care could be clinically significant. These programmes 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 could have further long-term ramifications not represented in the 5-year timeline. For example, reductions in peer support might result in suboptimal treatment adherence and retention in care. Health-care provisions 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 and ART users and extra emergency provision of supplies are probably required to safely provide existing levels of health care at the same time as responding to COVID-19.

Previous assessments have considered effects on HIV care in other crisis situations such as the post-election unrest in Kenya in 2007,[22, 23] during the Ebola epidemic in Guinea in 2014,[24] in acute conflict areas in the Central African Republic and Yemen,[25] and as a consequence of food insecurity.[26] All assessments found substantial negative effects but also evidence of resilience and ability to successfully ensure access to ART drugs.[25, 26] By contrast with concern over negative effects of the COVID-19 pandemic, longer-term benefits might be seen because the crisis has led to simplifications to delivery of care, with multi-month dispensing and fewer clinic visits required per patient than previously, which in turn reduces costs and results in a similar health outcome.[27]

Our model predictions are inherently limited by the available data to inform them. Although data on HIV and effects of programmes implementing interventions are available, some key uncertainties exist. One of these uncertainties is the magnitude of the effect of interruption of ART on death rates. Other uncertainties that might also be important include that we did not model any interaction between HIV and COVID-19—eg, that people with HIV were not assumed to be more or less likely to acquire or die from COVID-19, although any excess COVID-19 risk is likely to be small in absolute terms compared with risk of death directly due to HIV. We also note that several models address excess mortality due to disruption of services for HIV and tuberculosis, malaria, and other communicable diseases[3, 28, 29, 30] and all of these models point to similar levels of excess death and we recognise that overlaps can exist in people counted as having died separately of tuberculosis and HIV. However, taken together, our models highlight the real risk of substantially increased mortality among the most susceptible and at-risk populations in sub-Saharan Africa and could quickly erase years of public health gains if action to mitigate these effects are not swift and coordinated.

In summary, during the COVID-19 pandemic the primary priorities for governments, donors, suppliers, and communities to avoid additional HIV-related deaths should focus on maintaining an uninterrupted supply of ART drugs for people with HIV. The provision of other HIV prevention measures is also important to prevent any increase in HIV incidence.

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Contributors

All authors contributed to the conception and design of the modelling analyses. BLJ, EM, SLK, DtB, LB-M, JS, JAS, SGM, ANP, AB, TBH, IT, NC, RG, YT, and RM-H contributed to model implementation. All authors contributed to manuscript drafting and critical review.

Declaration of interests

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Supplementary Material

Supplementary appendix:

Click here to view.(775K, pdf)

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