Mathematical modelling tools in the response to the HIV epidemic in Zimbabwe

Manicaland HIV/STD Prevention Project

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July, 2008

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Acknowledgements

This report was written by members of *The Manicaland HIV/STD Prevention Project.* The work was funded by the Centers for Disease Control and Prevention. The findings and conclusions presented in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

The Manicaland HIV/STD Prevention Project would like to extend its gratitude to all organizations and individuals who have devoted their time and effort towards the successful conduct of the workshops, collecting data and preparation of this report. In particular, to Sabada Dube, Timothy Hallett, Marie-Claude Boily, Geoff Garnett (Imperial College London) and Simon Gregson (Imperial College London and Biomedical Research and Training Institute, Harare, Zimbabwe) for preparing this report; to Anastasia Said (Partnership for Child Development) and Kim Marsh (Imperial College London) for providing editorial assistance to this report; to Stacie Greby, Shannon Hader and Mike St. Louis (Centers for Disease Control and Prevention) for coordinating the workshops; to Christine Chakanuka, Frank Chikhata, Elisabeth Gonese, Agnes Mahomva, Owen Mugurungi, and Getrude Ncube (National AIDS and Tuberculosis Unit, Ministry of Health and Child Welfare) for technical support; and to Florence Mutevedzi (Biomedical Research and Training Institute, Harare, Zimbabwe) for logistical support. *The Manicaland HIV/STD prevention project* is grateful to the Partnership for Child Development (http://www.child-development.org/) for funding support and assistance in the preparation of this report.

The following partners have also made valuable contributions to this project; Peter Illif (Zimbabwe Vitamin A for Mother and Babies Project); Sostan Moyo and Felix Tarwireyi (Zimbabwe AIDS Prevention Project); Choice Makufa, Sazilinah Makumbe and Melody Manyasha (Pact-Zimbabwe); Karin Hartzold and Noah Taruberekera (Population Services International); E. Chidombwe (Zimbabwe AIDS Prevention and Support Organization); and D. Musekwa (National University of Science and Technology).

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Cover image: Prevention of mother-to-child transmission intervention launch in Mutasa District, Eastern Zimbabwe. Photo by Sabada Dube.

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Executive summary

In 2002, the Centers for Disease Control and Prevention (Atlanta, USA) funded *The Manicaland HIV/STD Prevention Project* to work in collaboration with the National AIDS and Tuberculosis Unit at the Ministry of Health and Child Welfare in Zimbabwe to promote the development and use of mathematical models to increase awareness of such tools and to strengthen local capacity. A series of workshops were planned that fostered collaboration between infectious disease epidemiologists, policymakers and programme implementers, based in Zimbabwe and London.

At the first workshop, held in 2003 at the Centre for the Evaluation of Public Health Interventions (CEPHI), Harare, Zimbabwe, a variety of modelling approaches were introduced and participants gave recommendations on topics as priorities for investigation using mathematical models. Four subsequent workshops focused on these topics in turn:

(1) In 2004, prevention of mother-to-child transmission (PMTCT);
(2) in 2005, voluntary counselling and testing (VCT);
(3) in 2006, strategies for delivering antiretroviral therapy (ART); and
(4) in 2007, the potential impact of circumcision interventions.

Key findings from each of these four workshops are presented in brief below and in-depth within this report. Although quantitative estimates and projections are specific to Zimbabwe, we expect that the qualitative findings will be applicable to other settings experiencing mature generalized HIV&AIDS epidemics.

Assessment of the impact of interventions to prevent mother-to-child transmission

- Since the beginning of the epidemic, approximately 500,000 children have been infected with HIV from mother-to-child transmission.
- Existing interventions averted 4,600 infections between 2002 and 2005, mostly in urban areas – far below the United Nations General Assembly Special Session (UNGASS) targets.
- Coverage and acceptance must increase for PMTCT to have a greater impact; to achieve the 20% reduction in mother-to-child transmission (2005 UNGASS target) using the existing Nevirapine regimen, programme coverage would have to be increased to 80%, and acceptance would have to increase to 95%.
- Switching to a new regimen (Nevirapine and Zidovadine) could substantially increase the impact of programmes: to reduce transmission by 50% (2010 UNGASS target), the national programme in Zimbabwe will have to increase PMTCT coverage to 90%, and increase acceptance of both VCT and ART to 100%, and use a regimen with at least 60% efficacy.
- Long-term breastfeeding leads to mother-to-child transmission, but also confers substantial benefits for infant survival. The recommended strategy should be exclusive breastfeeding for the first 6 months, followed by replacement feeding.

Predicting the impact of voluntary counselling and testing and how to optimize programmes

- If VCT programmes generate the same behavioural changes seen in some scientific trials, 80% coverage of services could lead to as little as 3% fewer infections over the next 25 years.
- Within the same time period, 23% (667,000) of infections could be averted if higher quality behaviour change services are promoting long-lasting changes.

- This reduction in incidence could lead to fewer individuals acquiring HIV and 1.8 million fewer individuals needing ART over the next 50 years.
- The impact of VCT in Zimbabwe depends on reaching as many individuals as possible and in providing sufficient counselling that allows individuals to adopt and maintain safe sexual behaviour. For example, two-fold increases in condom use could lead to 2% fewer infections if the change in behaviour lasts for 1 year, but 12% fewer infections if the change in behaviour is permanent.
- Twice as many infections could be averted if counselling services are focused on young men and women.
- Services focused on older individuals or those with serious illnesses though will not have a substantial impact on preventing infection but could allow more individuals to receive treatment.

Estimating the resources required in the roll-out of antiretroviral therapy

- Around 480,000 to 780,000 individuals in Zimbabwe could receive antiretroviral treatment by 2030 if universal access to the treatment is provided from 2010.
- To achieve this, doctors will have to initiate treatment for approximately 20 patients each month. In 2010, nurses will have to make almost 40 extra appointments each month to assess patients'need for treatment and to monitor those already on treatment. By 2030, this is expected to increase to 110 appointments.
- Given that the number of monitoring appointments with nurses will increase rapidly after the treatment programme has scaled up, allowing nurses to initiate patients should not be a long-term strategy for alleviating the case-load for doctors.
- The impact of ART programmes is limited by infected patients not entering care or entering care too late. Increased uptake of testing and referral from other health care services could improve the impact of ART programmes; if 70% of individuals test for HIV before they develop symptoms, 60% more life-years could be saved compared to if current testing rates do not increase.
- Frequently monitoring patients and using CD4 cell counts increases the chance of treatment starting at the right time; 70% more life-years are saved if patients are initiated using CD4 cell counts than on the basis of symptoms alone, and life-expectancy at HIV infection is increased by up to 35% if individuals are monitored every 3 months instead of every 24 months.

The potential impact of male circumcision to prevent HIV transmission

- HIV incidence could be reduced by 25% to 30% if around 50% of men are circumcised after approximately 20 years.
- Even with 100% coverage and acceptance of circumcision, the intervention, on its own, is not expected to lead to the terminal decline of the HIV epidemic in Zimbabwe.
- Circumcision interventions, however, operate synergistically with other types of prevention interventions; thus circumcision services should be accompanied by a renewed and vigorous focus on promoting reductions in sexual risk behaviour.

- The impact of circumcision interventions is expected to develop slowly over several decades and is therefore not expected to contribute substantially to progress towards short-term national targets for reduced HIV prevalence among young men and women.

- Over the first 30 years of an intervention, circumcising men aged between 20 to 29 years could lead to a greater reduction in HIV incidence. Although, In the long-term, circumcising infants or boys (younger than 19 years of age) could lead to greater reductions in incidence; however, no impact would be detected for the first 20 years of an intervention.

- Men being circumcised should be encouraged to test for HIV infection – but there would not be substantial dangers of increased incidence if infected men are circumcised.

Introduction

Mathematical models have been used extensively to understand how epidemics of infectious diseases, such as HIV, occur and how they can be reduced and their impact mitigated. Models are most useful when they have been developed in collaboration between epidemiologists, programme implementers and decision-makers so that they are able to capture the important local aspects of the epidemic and can provide meaningful answers to relevant strategic questions.

The Centers for Disease Control and Prevention in Zimbabwe identified a need to strengthen local capacity in using mathematical models and to develop and apply new models to understand how existing and planned interventions could be optimized. To this end, a series of workshops were held in Zimbabwe with researchers, programme implementers and decision-makers from Zimbabwe and Imperial College London. The first workshop (2003) introduced fundamental modelling concepts and techniques to participants, who also made recommendations for topics to study in future workshops. In 2004, an interactive computer-based workshop was held that focused on the prevention of mother-to-child transmission. Participants were able to manipulate the model and refine its structure and parameters to fit better with local conditions. Three further workshops held between 2005 and 2007 focused on voluntary counselling and testing (VCT), delivering antiretroviral therapy (ART) and male circumcision. These workshops made use of more complex models. On the first day of the workshops, a preliminary version of the model was presented and participants were invited to pose questions to be addressed. Over the following 3 to 4 days, the model was redeveloped by the computer programmers in line with suggestions and re-parameterized if further data became available from the Ministry of Health and Child Welfare, the Central Statistical Office or from other sources. At the end of the workshops, results were presented to policymakers, and round-table discussions were used to formulate policy implications and to identify future areas of research. Finalized models were distributed to participants as stand alone spreadsheet or Windows-based applications.

A computer-lab workshop at CEPHI.

Scientific reports of the workshops, the models and the results have been presented at international conferences and written up for publication in scientific journals. This report is a non-technical summary that compiles the key findings from all the workshops. References are therefore, not specifically cited within this report, but provided as a guide for further reading in the Bibliography. Technical details of the models have been published in scientific journals and can also be obtained from *The Manicaland HIV/STD Prevention Project.*

HIV&AIDS epidemic in Zimbabwe and the public health response

Orientation

Zimbabwe is a Southern African country with a population, in 2002, of approximately 12 million. Around 58% of the population live in rural areas, 32% in urban areas and 10% in 'other' areas, such as peri-urban settlements, mines and commercial estates.

The HIV epidemic

The HIV epidemic in Zimbabwe began in the early 1980s, with the first confirmed diagnosis in 1985. Early HIV screening by the Zimbabwe Blood Transfusion Services indicated that HIV prevalence was between 2% and 3% by the mid 1980s. By 1998, the national prevalence was estimated to be between 25% and 30% (see Figure 1).

Urban and peri-urban regions have experienced the worst epidemics, but, unlike many other African countries, a considerable rural epidemic has also been detected. The early socio-demographic impact of HIV in rural Zimbabwe was first described by Gregson *et al* (see Bibliography)[1], who reported that prevalence in the general population exceeded 20%. Women, working men, divorcees and widows were among the groups most likely to be infected. Prevalence among young women was found to be much higher than prevalence among young men; which may be partly due to women forming sexual partnerships with older men.

Monitoring the epidemic

National trends in HIV prevalence are estimated using a standard modelling tool designed by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and measurements of prevalence among women attending antenatal clinics. The national HIV surveillance system of antenatal clinics was first established in 1990, but was revised and standardized in 2000. Further details are given in the 2006 National Estimates Report (see Bibliography).

Recent downturn in the epidemic

The most recent national estimates of HIV prevalence (since 2000) have shown substantial declines (see Figure 1). Although it may be expected that prevalence declines in a mature epidemic due to increasing AIDS-related mortality, there are reasons to believe this trend is partly attributable to changes in sexual behaviour leading to reduced incidence rates. First, the prevalence decline is seen among young women (aged 15 to 24 years), among whom AIDS-mortality is low. Second, declines in prevalence have also been observed in longitudinal studies of women in Harare and of communities in rural Eastern Zimbabwe, where it is certain that trends could not be generated through shifting biases in fertility or representativeness of the antenatal clinic surveillance system. Measurements of HIV incidence in this period, although not directly comparable because they were from different samples, show declines. Third, reports of sexual behaviour in national and regional surveys indicate reductions in sexual risk behaviour, especially among men, forming fewer casual sexual partnerships and visiting commercial sex workers less frequently. The most recent estimate of HIV prevalence in Zimbabwe (2006) is 15%.

[1] Throughout this report references are not cited but provided in the Bibliography as a guide for further reading.

Public health response

From an early stage in the epidemic, Zimbabwe was one of the few sub-Saharan African countries that took steps to initiate interventions aimed at preventing HIV from spreading. Donated blood was screened for HIV, and condom distribution programmes were scaled up, treatment services for sexually transmitted infections (which can increase the likelihood of HIV spread) were improved and counselling and testing services were made available. A national tax the – AIDS levy – was introduced to finance HIV prevention, mitigation and treatment services through the National AIDS Council. The National AIDS Council also developed implementation structures at the provincial and district levels.

Celebrating the opening of an HIV prevention initiative in Eastern Zimbabwe.

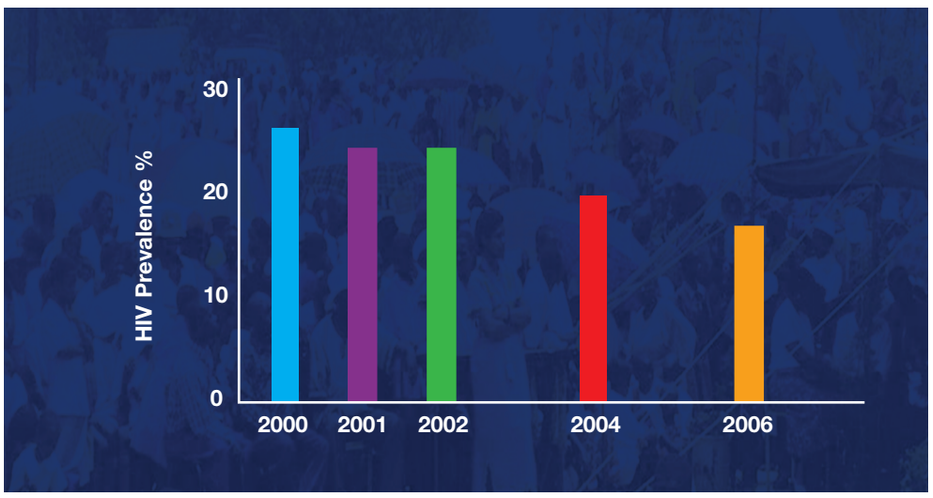


Figure 1: HIV prevalence in Zimbabwe, 2000 to 2006. Data for 2002, 2004 and 2006 use the parallel testing algorithm. Data for 2000 and 2001 were collected using an alternative testing algorithm, but the values presented here are corrected for any systematic differences between the two tests.

Assessment of the impact of interventions to prevent mother-to-child transmission

Key findings

- Since the beginning of the epidemic, approximately 500,000 children have been infected with HIV from mother-to-child transmission.
- Existing interventions averted 4,600 infections between 2002 and 2005, mostly in urban areas – far below the UNGASS targets.
- Coverage and acceptance must increase for PMTCT to have a greater impact; to achieve the 20% reduction in mother-to-child transmission (2005 UNGASS target) using the existing Nevirapine regimen, programme coverage would have to be increased to 80%, and acceptance would have to increase to 95%.
- Switching to a new regimen (Nevirapine and Zidovadine) could substantially increase the impact of programmes: to reduce transmission by 50% (2010 UNGASS target), the national programme in Zimbabwe will have to increase PMTCT coverage to 90%, and increase acceptance of both VCT and ART to 100%, and use a regimen with at least 60% efficacy.
- Long-term breastfeeding leads to mother-to-child transmission, but also confers substantial benefits for infant survival. The recommended strategy should be exclusive breastfeeding for the first 6 months, followed by replacement feeding.

Orientation

In recognition of the high HIV prevalence among pregnant women attending antenatal clinics in Zimbabwe, and following the UNGASS Declaration of Commitment on HIV&AIDS, the Zimbabwe Ministry of Health and Child Welfare, National AIDS and Tuberculosis Unit, in 2001, designed and implemented a PMTCT programme based on the provision of single-dose Nevirapine to pregnant women and their infants.

Between 2002 and 2005, the programme was scaled up with increasing numbers of health facilities registered and equipped to provide PMTCT services. In 2002, around 46,000 women sought antenatal care at clinics offering PMTCT services. This figure increased to 98,000 in 2003, 116,000 in 2004, and 196,000 in 2005, indicating that approximately 50% of all pregnant women in 2005 had access to PMTCT services. However, acceptance of HIV testing and ART remained low; in 2005, only 65% of women accepted HIV testing, and of those who tested positive, only half took up treatment.

Estimated rates of mother-to-child transmission

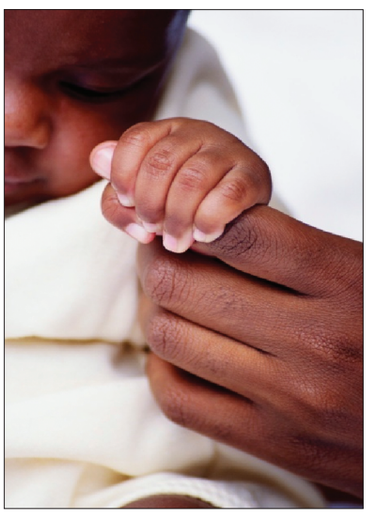
Models of fertility, mother-to-child transmission and the impact of treatment to prevent transmission were developed that allowed estimation of the number of infants that were infected with HIV (see Figure 2). As some important parameters could not be specified precisely, the model was also used to quantify the range of plausible projections.

In total, we estimated that between 1987 and 2005 approximately 504,000 (range 362,000-666,000) infants were vertically infected with HIV. The fraction of infants infected with HIV was below 1% before 1987, but quickly rose to almost 10% (range 7.4%-12.1%) in the early 1990s as more women became infected. Following trends in HIV infection in adults, infections in infants subsequently declined to approximately 8% (range 6.0%-10.7%) in 2000 and 6.2% (range 4.9%-8.9%) in 2005.

Following the earlier spread of the HIV epidemic in urban areas, infant infections in urban areas peaked, at approximately 12%, in the mid 1990s. The rate of infant infections in rural areas and 'other' areas peaked at 12% in the late 1990s. We estimated that, in 2005, 7.2% (range 5.1%-9.3%), 5.1% (range 3.7%-6.5%) and 8.1% (range 6%-10.4%) of infants born in urban, rural and 'other' areas, respectively, were vertically infected with HIV. In 2005, infants born in 'other' areas were estimated to be at higher risk of infection compared to those born in rural or urban areas because of higher HIV prevalence in 'other' areas. Although a higher percentage of children born in 'other' areas are at higher risk of mother-to-child transmission, this represents a small total number of infections compared to those in rural or urban areas.

The impact of breastfeeding and HIV on infant survival

In the absence of PMTCT programmes, the model indicates that 32% (range 25%-44%) of infants infected with HIV could have been infected through breastfeeding. This figure is expected to increase as availability of PMTCT programmes increases. For example, if 50% of women had access to PMTCT services, around 35% to 42% of paediatric infections could be attributable to breastfeeding.



A newborn reaches for her mother's finger.

The chance of mother-to-child transmission through breastfeeding is closely linked to the duration of breastfeeding. At birth, 4.3% (range 3.2%-5.3%) of infants born in Zimbabwe are estimated to be vertically infected; if breastfeeding on average lasts for: 60 days, the cumulative proportion of infected infants increases to 4.8%; if breastfeeding lasts for 12 months, the figure increases to 5.9%, and if breastfeeding lasts for 24 months, the figure increases to 6.6%.

Although breastfeeding increases the chances of an infant being infected with HIV, avoiding breastfeeding could have serious consequences for infant survival. If the PMTCT programme reached 50% of pregnant women, infant mortality could be reduced by 5.7% and under-five mortality could be reduced by 3.3%, compared to if there was no intervention. Under these same assumptions, if HIV infected women did not breastfeed at all, infant and under-five mortality could substantially increase – by up to 24% and 16%, respectively. However, if babies of infected women are breastfed for the first 6 months and then weaned, infant and under-five mortality could be reduced by 14% and 10%, respectively, substantially enhancing the impact of the PMTCT programme.

The impact of PMTCT interventions in Zimbabwe

The impact of interventions on PMTCT is estimated in the model by comparing scenarios which incorporate the effect of the intervention with those that assume that there is no intervention. Overall, we found that the implementation of the PMTCT programme resulted in relatively modest declines in mother-to-child transmission (see Figure 3). Between 2002 and 2005, a total of 4,600 (range 3,900-7,800) infant infections were averted. In 2005, the number of infections among infants was reduced by approximately 9%. This implies that the PMTCT programme in Zimbabwe was not able to achieve the UNGASS target of reducing mother-to-child transmission by 20% by the end of 2005.

Cumulatively, between 2002 and 2005, half of the infections averted were in urban areas. The impact of PMTCT programmes in 2005 was also greatest in urban areas, where 14% of infections were averted, compared to 9% in rural and 'other' areas.

How to improve the impact of PMTCT interventions

With the same intervention coverage and acceptance levels, the number of infections averted could have been doubled if the more efficacious Nevirapine and Zidovadine (NVP+ZDV) regimen had been used. If programme coverage was increased from 50% to 100% and acceptance increased from 65% to 100%, we estimate that, by 2010, the current single-dose Nevirapine programme could prevent a cumulative 16,300 infections, compared to the 35,200 expected infections averted if a NVP+ZDV regimen had been used from the start. In contrast, there is negligible difference in impact if alternative regimens of short-course Zidovadine or short-course Zidovadine and Lamivudine/3TC were used instead.

The fraction of vertical transmission averted by the current programme is limited by a combination of low programme coverage and acceptance. Given the current low levels of programme acceptance, expanding the programme to maximum coverage could have little impact if acceptance is not increased simultaneously, even if a more efficacious regimen, such as NVP+ZDV, was used. Indeed, programme impact is less sensitive to increases in regimen efficacy when coverage and acceptance levels are low. However, regimen efficacy becomes much more important as coverage and acceptance increases.

Based on current prevalence levels, in order to achieve the 20% reduction in mother-to-child transmission (2005 UNGASS target) using the existing Nevirapine regimen, programme coverage would have to be increased to 80%, and acceptance would have to be increased to 95%. Furthermore, to reduce mother-to-child transmission by 50% (2010 UNGASS target), the national programme in Zimbabwe will have to increase PMTCT coverage to 90%, and increase acceptance of both VCT and ART to 100%, and use a regimen with at least 60% efficacy.

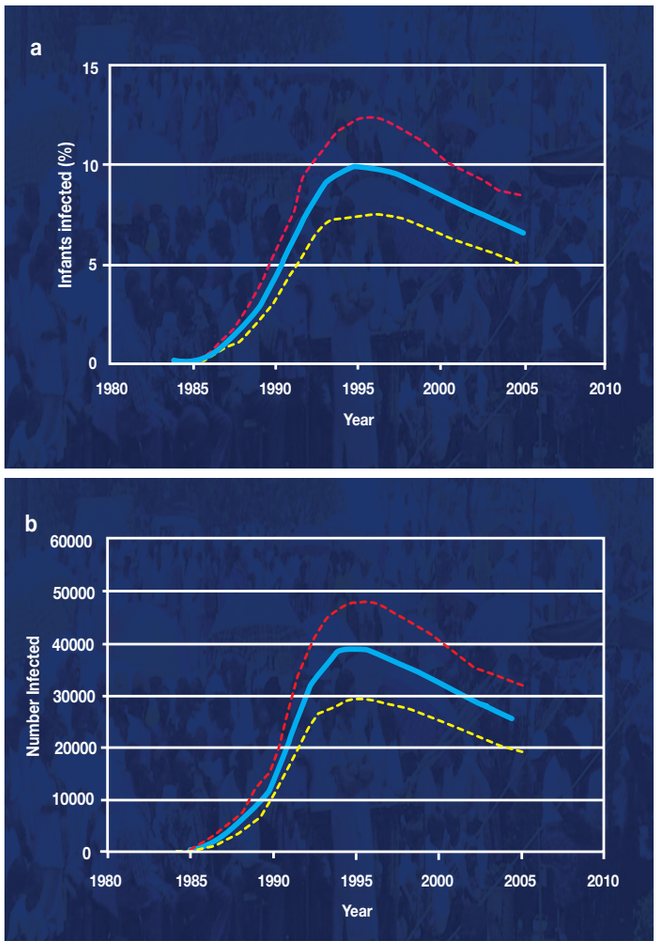


Figure 2: Proportion (a) and Number (b) of infants infected with HIV through mother-to-child transmission per year (1980 to 2005). Dashed lines indicate range of credible values.

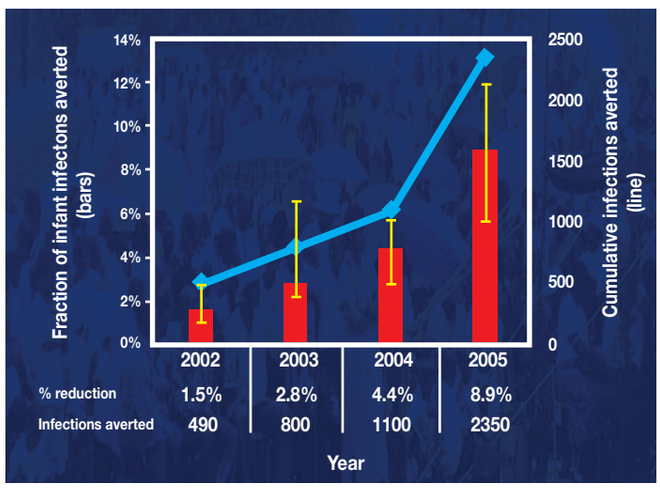


Figure 3: Fraction of infant infections averted (bars) and cumulative number of infections averted (lines) between 2002 and 2005.

Predicting the impact of voluntary counselling and testing and how to optimize programmes

Key findings

- If VCT programmes generate the same behavioural changes seen in some scientific trials, 80% coverage of services could lead to as little as 3% fewer infections over the next 25 years.
- Within the same time period, 23% (667,000) of infections could be averted if higher quality behaviour change services are promoting long-lasting changes.
- This reduction in incidence could lead to fewer individuals acquiring HIV and 1.8 million fewer individuals needing ART over the next 50 years.
- The impact of VCT in Zimbabwe depends on reaching as many individuals as possible and in providing sufficient counselling that allows individuals to adopt and maintain safe sexual behaviour. For example, two-fold increases in condom use could lead to 2% fewer infections if the change in behaviour lasts for 1 year, but 12% fewer infections if the change in behaviour is permanent.
- Twice as many infections could be averted if counselling services are focused on young men and women.
- Services focused on older individuals or those with serious illnesses though will not have a substantial impact on preventing infection could however, allow more individuals to receive treatment.

Orientation

VCT for HIV infection first became available in Zimbabwe in the late 1980s with the establishment of routine procedures for screening blood donors by the Zimbabwe Blood Transfusion Service. In 1996, the Matebeleland AIDS Council opened the first VCT centre in Zimbabwe. The Zimbabwe AIDS Prevention and Support Organization (ZAPSO) opened the first centre in Harare in 1997 and began to roll-out services to other parts of the country. In 1998, Population Services International (PSI) opened their first socially-marketed VCT centre in Harare, branded “New Start”. These centres have now been established around the country and include both free-standing (stand alone) centres and centres integrated within hospitals and other health care facilities. In addition, the Family AIDS Caring Trust (FACT) established a free-standing VCT service in Mutare, the provincial capital of Manicaland. From 2003, the Zimbabwe Association of Church-related Hospitals (ZACH) began to establish integrated VCT services in mission hospitals in rural areas through the Care for HIV/AIDS Prevention and Positive Living (CHAPPL) Network. Other hospitals have established similar services with support from agencies such as Pact and Médecins du Monde. Some of these centres also operate mobile VCT services that extend into the more remote rural areas.

To strengthen the VCT strategy, Zimbabwe’s National Policy on HIV&AIDS (1999) encouraged the establishment of VCT services which are available, accessible, and affordable throughout the country. The policy also advocated mainstreaming of VCT in the public and private sectors and inclusion of VCT as part of a standard care plan in antenatal care, treatment for tuberculosis and sexually transmitted infections, and for all in- and out-patient services.

The records from the Ministry of Health and Child Welfare, National AIDS and Tuberculosis Unit, indicate that a total of 292,941 clients (approximately 5% of the adult population) received HIV testing in 2004; the majority (57%) received VCT from PSI. However, these figures do not include those tested in research programmes.

VCT interventions are beset by problems of low coverage, low acceptability and stigma. Due to the costs involved in setting up and running a VCT centre, coverage of VCT services in many developing countries including Zimbabwe are low but rapidly increasing. To increase intervention coverage and acceptability, a range of innovative service delivery approaches can be applied depending on the context. These approaches include integration within the existing health facilities, free-standing and mobile services. In scaling up VCT, a coordinated response by all stakeholders, including partnerships between donors, government and non-governmental organizations is crucial to ensure a standardization of services in terms of quality of care and support offered to clients and to avoid duplication of services within regions.

The VCT services currently available in Zimbabwe (excluding private doctors and research programmes) can be categorized into four approaches according to their organization with respect to other services as:

(1) *Hospital associated:* Integration of VCT into general health care facilities;
(2) *PMTCT:* Integration of VCT into antenatal clinics;
(3) *Stand alone:* Centre established for predominantly providing VCT; and
(4) *Outreach:* Mobile outreach to populations.

Modelling the impact of voluntary counselling and testing

The epidemiological impact of any HIV intervention depends upon the prevailing patterns of risk within the population. The distribution of number of sexual partners and the extent of unprotected sex within each partnership are proximate determinants of the spread of HIV and it is these variables that must be changed to influence the epidemic. This must be represented in models, but although the currently observed risk patterns are the background against which interventions must act, they are probably not the patterns of behaviour which generated the initial high spread of HIV. There is growing evidence that across Zimbabwe behaviour change occurred in the second half of the 1990s, presumably in response to AIDS-related deaths and HIV control programmes. Evidence from surveys in Harare suggests that condom use by 2000 was already high, with 80% of individuals reporting condom use at last sex with a casual partner, although condom use in regular partnerships is less likely. In our simulation of the observed HIV epidemic, both increases in condom use and reductions in numbers of partners were assumed.

Against this background simulated epidemic, we explored the impact of increased VCT coverage on the HIV epidemic. In the following projections, we assume that the fraction that can access VCT increases steadily to 80% over 10 years (2005 to 2015), and that service is of sufficient capacity that 40% of those in the catchment can receive VCT in the first year.

Three alternative scenarios for the behaviour changes associated with VCT are simulated. These were:

(1) Observed behaviour changes in a large efficacy trial in low-income settings.

(2) Behaviour changes associated with VCT delivered in a cohort study in Eastern Zimbabwe – *Manicaland HIV/STD Prevention Project* – indicate modest levels of protective behaviour change.

(3) A more optimistic set of assumptions which reflects efficacy comparable to the most successful studies of VCT in Africa and America.

It is not clear how long behavioural changes are sustained after receiving VCT (the studies in each scenario have only run for a few years), so two versions of each scenario are simulated, where the mean duration of the behaviour change is 2 years or 8 years.

Projections of the prevalence trend between 1980 and 2030 are shown in Figure 4. The model projects that there is expected to be ~2.9 million new infections among adults over 20 years (2005 to 2025) without further intervention. If the behavioural changes following VCT are similar to those observed in a large efficacy trial in low-income settings (scenario 1) and last for 2 years on average, then 4% of expected HIV infections could be averted over 20 years (116,000 infections). If the changes last for 8 years instead, almost twice as many infections could be averted (218,000). Alternatively, if the behavioural changes observed in the rural Zimbabwean cohort (scenario 2) are repeated at the national level and last for 2 years, then the rapid expansion of VCT across the country could avert less than 3% of infections over 20 years (84,000). However, with the greater levels of protective behaviour change – including among uninfected individuals – generated by high quality HIV prevention counselling that are indicated in other studies (scenario 3), the model predicts that there could be 12%-23% (348,000-667,000) fewer infections over a 20 year period.

(Recent estimate of incidence are approximately 0.4%). The continuing relatively high HIV incidence rate in Zimbabwe means that it is important to scale up high quality VCT quickly. Assuming that these optimistic behavioural changes last 8 years, the model projects that if VCT is scaled up to 80% of the population over 5 years instead of 10 years, ~200,000 more infections could be averted.

Opportunities for care and treatment

An important goal of testing is to identify those who can benefit from treatment, but, with a focus on promoting behaviour change, VCT could lead to reduced need for treatment in the future. Without any VCT programme, the model projects that the total number of individuals that will be indicated for ART in Zimbabwe over 50 years will be 6.8 million. With high quality HIV prevention counselling, protective behaviour change could lead to fewer people acquiring HIV and 1.8 million fewer individuals would need to start ART. The difference in the number needing ART between the three alternative scenarios increases over time as the epidemic is set to reach more and more people if services are not optimized, but could be sent into decline if high quality VCT is implemented.

Context of VCT: Geographic and programmatic issues

We explored the impact of increasing coverage of populations in urban, rural and 'other' areas. Since knowledge of infection in those infected is a direct consequence of testing, there is a simple relationship between the proportion who know their status and the coverage which is independent of HIV prevalence. Thus, the proportion of HIV-positive individuals that are aware of their infection is identical to populations in urban, rural and 'other' areas. In contrast, the number identified who could benefit from treatment is a function of the number of individuals infected in the urban, rural and 'other' areas, which is the product of HIV prevalence and the denominator population size.

Despite HIV prevalence being lowest in rural communities, the greater number of individuals resident in these areas means that more people who need treatment are to be found in rural areas than in urban or 'other' areas. Per person tested, the number identified will be less but rural areas have to be included in VCT programmes if those who need care are to be equitably identified.

The situation for infections and deaths averted is different, with the greatest reductions in HIV incidence across the whole population achieved through screening urban populations. The relative impact of behaviour change will depend upon the distribution of risks of acquiring and transmitting infection, and while HIV prevalence is higher in urban communities, the virus is likely to spread through a wide number of people with moderate risk whose contribution to HIV infection can be readily reduced. The higher prevalence in 'other' communities can also be reduced significantly, but these communities represent a smaller proportion of the Zimbabwean population.

A similar analysis of infections and deaths averted was undertaken for an expansion of each of the four VCT service approaches: hospital associated; PMTCT; stand alone; and outreach. There is no clear distinction between these four approaches, presumably because there is relatively little difference in clients between the types of service. The obvious conclusion is, that it does not matter which service model is chosen for scaling up. However, this ignores the costs of the different approaches and their relative abilities to reach particular geographic sections of the population.

How to optimize interventions

In studies of VCT, behaviour change has been greatest among infected individuals. In the model, behaviour change among those infected has a greater effect in reducing HIV incidence than the same changes among those not infected, because those infected are more likely to be part of ongoing HIV transmission. However, for a given number of individuals counselled, the population level impact of VCT is greater when uninfected individuals change their behaviour instead. This is simply because the majority of clients will be uninfected. Therefore, the impact of VCT programmes that do not motivate behaviour change among uninfected individuals will fall very short of their potential.

Maintaining behaviour change is crucial to the impact of the intervention. For example, in the model, a 20% to 30% increase in condom use that is maintained permanently is equivalent in terms of infections averted over 20 years to a three-fold increase in condom use that lasts for only 1 year. The maintenance of behaviour change is especially important for young clients who are at greatest risk of infection and play a crucial role in onward transmission.

The emphasis in VCT programmes should be placed on reaching more people rather than repeat testing those already within a programme. Here, repeat testing is defined as testing people with a negative result after several months or years (rather than re-testing within a few weeks to confirm a negative result). Repeat testing can: identify individuals with highly infectious incident infections; allow prevention messages to be reinforced and prevent false complacency in individuals who test negative but continue high risk behaviour; and can be most productive in groups with high incidence. However, the population level benefits of using limited resources for repeat testing are outweighed by the lost opportunity to test more people once. For the same number of tests and counselling sessions, more infections and AIDS-deaths are averted if priority is given to testing more people once rather than fewer people many times.

Provided individuals are willing to disclose their HIV status, increased testing creates the opportunity for couples to alter behaviour according to the status of both partners,

or for partner choice to depend, in part, on HIV status. High levels of condom use have been observed in discordant couples aware of their HIV status and our model suggests that when knowledge and disclosure of HIV status is high, consistent condom use in such partnerships could generate a greater reduction in HIV incidence than smaller increases in condom use by infected individuals in all partnerships or casual partnerships.

The impact of sero-sorting, where individuals tend to form sexual partnerships preferentially with individuals of the same HIV status as themselves, is weak unless unrealistically large proportions of partnerships are sero-sorted and individuals frequently return for testing. Without frequent testing, individuals can incorrectly think they are uninfected (having been infected since their last test) and will preferentially form sero-discordant partnerships. However, repeat testing fails to outweigh the benefit of testing more people once when sero-sorting is up to the extreme level of 95%.

Resource constraints will be the major determinant of VCT implementation, but the ideal distribution of clients can be explored in the model to help guide policy. In the model, we keep the number of people receiving VCT constant whilst adjusting the relative probability that an individual is tested according to their age, gender, sexual behaviour and disease symptoms. The optimal target population depends greatly on the primary role of VCT. To maximize the identification of those that will require ART, VCT should focus on those groups in the population with the highest HIV prevalence, i.e. individuals at most risk of infection, older individuals and those with symptoms of immune-suppression. In addition, targeting women could increase uptake of measures to prevent mother-to-child transmission, and therefore avert more child deaths. To promote behaviour change using high quality HIV prevention counselling, more infections are averted if those at highest risk and younger individuals are targeted because these groups contribute disproportionately to the spread of infection. Targeting individuals with symptoms is not an effective way to avert more infections, despite these individuals being more infectious, because they will form fewer new sexual partnerships in the following years. Therefore, to increase the number of people in care and to prevent AIDS deaths, the recommended strategy is to target testing of older people, those experiencing symptoms of immune-suppression and women. However, to optimize prevention through behaviour change and to substantially decrease AIDS deaths in the future, providing VCT to the young should be the priority. Provider-initiated testing in health settings may be less suitable for delivering this service than fully trained counsellors working in dedicated facilities.

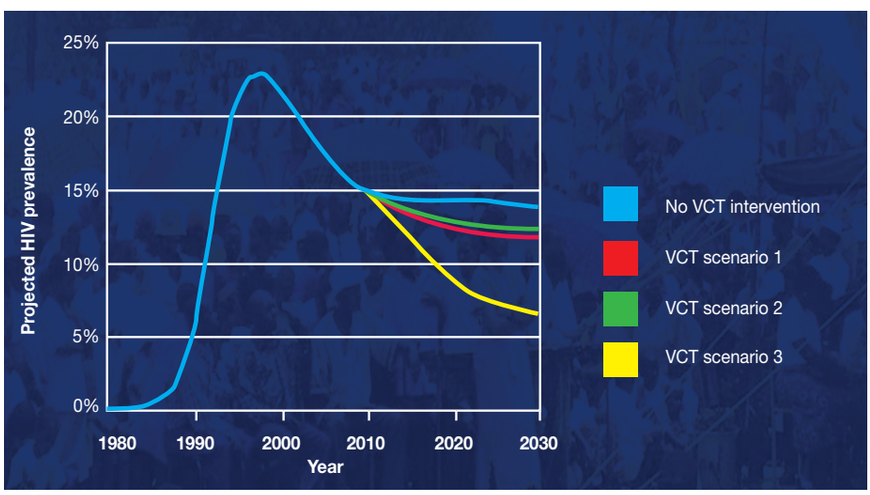


Figure 4: HIV prevalence between 1980 to 2030 with and without VCT scale up and with different behaviour changes following VCT. It is assumed that behaviour changes last for 8 years. Scenario 1: Behaviour change as observed in a trial in low-income settings; Scenario 2: Behaviour change as observed in a Zimbabwean cohort study; Scenario 3: Optimistic behavioural changes based on findings in VCT trials from Africa and America.

Estimating the resources required in the roll-out of antiretroviral therapy

Key findings

- Around 480,000 to 780,000 individuals in Zimbabwe could receive antiretroviral treatment by 2030 if universal access to the treatment is provided from 2010.
- To achieve this, doctors will have to initiate treatment for approximately 20 patients each month. In 2010, nurses will have to make almost 40 extra appointments each month to assess patients' need for treatment and to monitor those already on treatment. By 2030, this is expected to increase to 110 appointments.
- Given that the number of monitoring appointments with nurses will increase rapidly after the treatment programme has scaled up, allowing nurses to initiate patients should not be a long-term strategy for alleviating the case-load for doctors.
- The impact of ART programmes is limited by infected patients not entering care or entering care too late. Increased uptake of testing and referral from other health care services could improve the impact of ART programmes; if 70% of individuals test for HIV before they develop symptoms, 60% more life-years could be saved compared to if current testing rates do not increase.
- Frequently monitoring patients and using CD4 cell counts increases the chance of treatment starting at the right time; 70% more life-years are saved if patients are initiated using CD4 cell counts than on the basis of symptoms alone, and life-expectancy at HIV infection is increased by up to 35% if individuals are monitored every 3 months instead of every 24 months.

Orientation

With funding from 'The Global Fund to Fight AIDS, Tuberculosis and Malaria' and investments from other bilateral agencies, the Zimbabwe Ministry of Health designed a national strategy to deliver life-saving ART. The strategy involves building up treatment capacity, starting with four major central hospitals and then expanding to provincial and district facilities. Between 2002 and 2005, services for treating opportunistic infections were also substantially improved. In collaboration with the Ministry of Health and Child Welfare, UNAIDS proposed a comprehensive district level hospital roll-out programme accompanied by continual Ministry assessment activities. In addition to public health efforts, private doctors also provide AIDS treatment services. In total, by the end of 2005, approximately 36,524 patients were on ART, including 6,000 private patients. Currently, activities are in place to increase ART coverage following the national ART strategy.

How to make projections for ART delivery programmes

Providing ART is a long-term intervention that imposes a great burden on the already fragile health care systems. Projections of the costs and benefits of providing ART relative to other types of interventions have been influential in setting international public health priorities and mobilizing resources. However, it has not been clear how long-term impacts are linked to prevailing conditions and programme strategy, although understanding this relationship is essential for optimizing current practices and for making adequate provisions for the future.

Two of the main resources required in ART programmes are the therapy itself (drugs and other associated materials) and the time given by doctors and nurses in monitoring patients and initiating therapy. These costs will approximately scale with the number on ART and the number of appointments with doctors and nurses. UNAIDS and the World Health Organization (WHO) have calculated the number in need of ART as the sum of individuals in need in therapy (within 2 years of death in the absence of the therapy) and the number that have already started ART after a 10% yearly attrition rate. While this method has provided useful guideline estimates, it is also important to understand how the epidemiological context and properties of the ART programme determine such quantities. ART programmes in different countries will manage patients and initiate ART in alternative ways and the pattern of ART uptake may change over time. Similarly, the total resources required under alternative patient management strategies can be found by considering the range of disease states in the standard population, but this does not consider how monitoring efforts or the method of ART initiation is linked to survival outcomes and years spent on ART. Previous analyses that have examined the relative resource-requirements of different initiation strategies have not represented practicalities in ART delivery, such as errors in CD4 counts, non-continuous monitoring of individuals or possible changes in the profile of those entering care. Therefore, it is important to explore how these epidemiological and programmatic factors could modify projections for the burden of providing ART. We have developed a model that tracks the numbers infected with HIV in Zimbabwe, how their condition deteriorates and when they seek treatment. This allows us to make projections for ART need and required appointments with doctors and nurses over time and to examine how this is related to current programmatic policy.

The model projections for Zimbabwe

The overall estimate for the number of appointments required and the number on ART in Zimbabwe between 2000 and 2030 is shown in Figure 5. Approximately 3,500 patients are initiated on ART each month during this period. The monitoring case-load (of patients found to be infected but not yet on ART) increases over time when ART becomes available, up to 80,000 appointments each month in 2030. If patients receiving ART are seen every 6 months, by 2030 there could be 100,000 such appointments each month.

If the ART programme is scaled up, universal access in 2010 is expected to equate to ~110,000 individuals receiving therapy. Sustaining universal access could lead to between 480,000 and 780,000 individuals receiving ART in 2030, depending on the assumptions made about survival on ART.

Besides survival, the long-term (2030) estimates are most sensitive to changes in incidence over time and patterns of antenatal clinic referral and VCT uptake. Monitoring individuals from early on in their infection allows more individuals to enter care and for ART to be initiated at the right time. Currently, VCT uptake is low in Zimbabwe but if 70% of the infected individuals receive VCT sometime before they develop symptoms and 90% of pregnant women are referred from antenatal clinics, then 200,000 (30%) more individuals could be on ART by 2030 and 64,000 more life-years could be saved each year between 2005 and 2030.

The ART programme in Zimbabwe is already benefiting from the behavioural changes in the late 1990s, which may have reduced by 38,000 (26%) the number of individuals expected to be receiving ART in 2010. High impact prevention interventions (including VCT) scaled up between 2005 and 2010 will not affect the short-term projections, but could lead to ~310,000 fewer people receiving ART in 2030 – a 46% reduction that could increase further over time.

In the model, monitoring patients every 12 months instead of every 6 months leads to ~37% fewer appointments with health care workers but this means that ART cannot always be started at the right time, so that fewer start ART and fewer life-years are saved. Monitoring every 3 months leads to ~78% more appointments but this increases the chance that ART is initiated at the right time: life-expectancy at HIV infection is increased by up to 35% if individuals are monitored every 3 months instead of every 24 months. The clinical advantage of frequent monitoring depends on the initiation rule: with 'symptomatic initiation' (using only patients' symptoms to decide when to start treatment) 160,000 more life-years are saved by 2030, but with 'CD4 initiation' (measuring CD4 cell counts and using this to inform clinical decision-making) 520,000 more life-years are saved.

Ethiopian Pharmaceuticals Manufacturing Factory (EPHARM), Addis Ababa, Ethiopia.

Taking these factors together, for the same 'universal access' scenario and roughly stable incidence, the model predicts that as few as 160,000 or as many as 2 million could be receiving therapy in 2030 - more than a ten-fold difference. With the same assumptions about survival on ART and incidence (but all other parameters varied), in 2030 there could be between 180,000 and 500,000 on ART – a three-fold difference.

In Zimbabwe, in 2006, monitoring and follow-up appointments could be with nurses but ART had to be initiated by a doctor. Data from the Ministry of Health and Child Welfare in Zimbabwe (December 2006) showed that 174 doctors had been trained to initiate ART, and 1,530 nurses had been trained to monitor those not yet on ART and care for those already receiving ART. Assuming the number of doctors and nurses trained remains constant, the model suggests that, if the current ART strategy continues, in 2010, nurses will have to meet ~27 pre-ART monitoring appointments and ~12 follow-up appointments each month. Doctors will have to meet ~22 patients to initiate ART each month (see Figure 6 – 'Current'). Anticipated changes, such as increased referral from VCT, initiation with CD4 counts and more frequent monitoring, could save 50% more life-years but will require ~70 additional appointments for nurses and ~20 additional appointments for doctors (see Figure 6 – 'Optimal'). By 2030, the follow-up case-load will have substantially increased. Reductions in HIV incidence following VCT and other types of prevention interventions could reduce the monitoring load for nurses and initiation load for doctors by 2030, but the follow-up load for nurses will remain very high (see Figure 6 - 'Optimal + VCT').

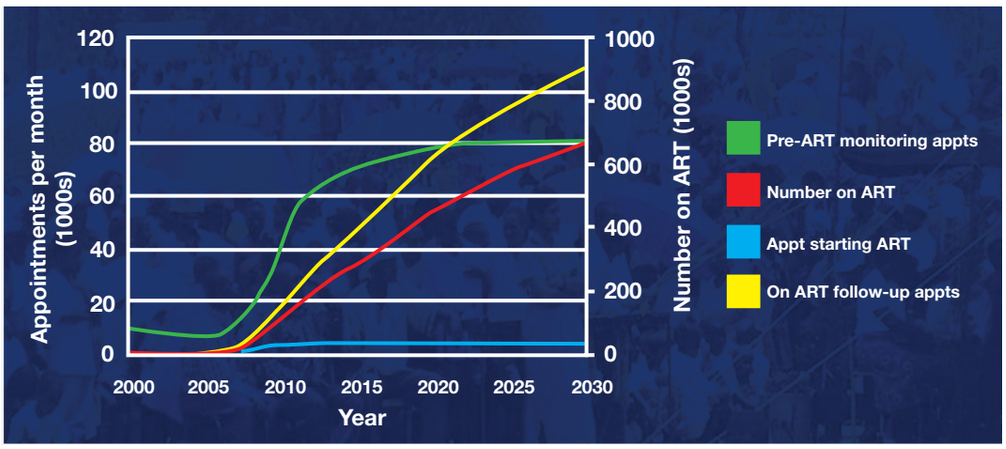


Figure 5: Projected numbers on ART and health care requirements in Zimbabwe.

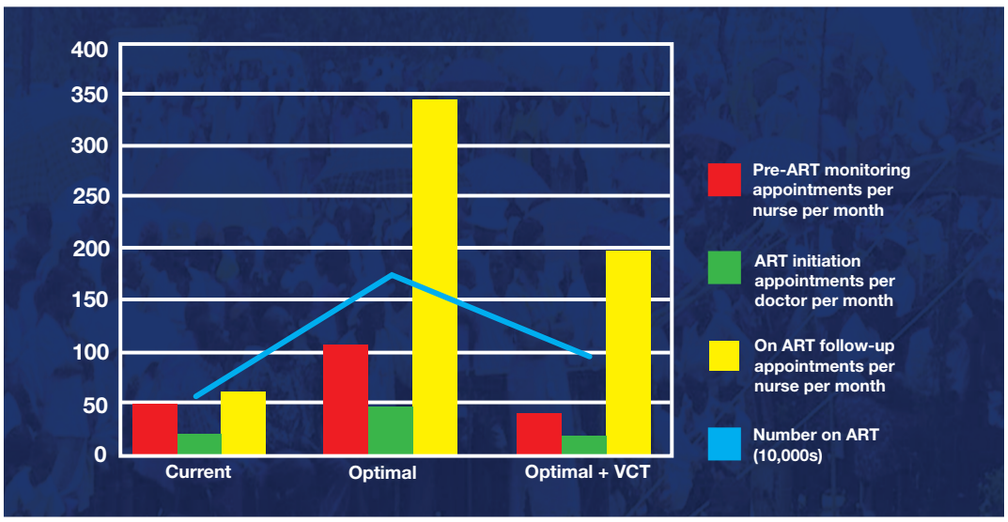


Figure 6: Projections of resource required in 2030 assuming either continuation of current practices ('Current'), a switch to CD4 initiation and more intensive patient monitoring ('Optimal'), or the switch to CD4 initiation and more intensive patient monitoring accompanied by an expanded VCT intervention leading to widespread reductions in sexual risk behaviour ('Optimal + VCT').

The potential impact of male circumcision to prevent HIV transmission

Key findings

- HIV incidence could be reduced by 25% to 30% if around 50% of men are circumcised after approximately 20 years.
- Even with 100% coverage and acceptance of circumcision, the intervention, on its own, is not expected to lead to the terminal decline of the HIV epidemic in Zimbabwe.
- Circumcision interventions however, can operate synergistically with other types of prevention interventions; though circumcision services should be accompanied by a renewed and vigorous focus on promoting reductions in sexual risk behaviour.
- The impact of circumcision interventions is expected to develop slowly over several decades and is therefore not expected to contribute substantially to progress towards short-term national targets for reduced HIV prevalence among young men and women.
- Over the first 30 years of an intervention, circumcising men aged between 20 to 29 years could lead to a greater reduction in HIV incidence. Although, in the long-term, circumcising infants or boys (younger than 19 years of age) could lead to greater reductions in incidence; however, no impact would be detected for the first 20 years of an intervention.
- Men being circumcised should be encouraged to test for HIV infection, but there would not be substantial dangers of increased incidence if infected men are circumcised.

Orientation

Recently, three clinical trials in Kenya, South Africa and Uganda have shown that male circumcision can reduce the chance that men are infected with HIV by approximately 60%. WHO and UNAIDS now recommend that male circumcision should be considered as part of a comprehensive HIV prevention package. The Zimbabwe Government and local stakeholders began consultation meetings on the feasibility and acceptability of male circumcisions in 2007.

The impact of potential circumcision interventions at the population level to reduce HIV incidence is determined by many other factors besides the biological effect on female-to-male transmission, including the existing patterns of sexual risk behaviour in Zimbabwe. We constructed a model of HIV transmission and explored the impact of alternative types of circumcision interventions, targeting men and boys of different ages. We also analyzed how potential interventions could contribute in progress towards national targets for reducing HIV prevalence among young men and women, and act together with existing programmes. Lastly, we sought to investigate the importance of avoiding circumcising HIV-infected men, in the light of some findings that the chance of transmission from men can be elevated if they have sex before the circumcision wound has healed completely.

The impact of targeting different age-groups

The age-distribution of men being circumcised is determined primarily by acceptability of circumcisions by men of different ages, local cost and logistical issues. However, in models, it is possible to explore the epidemiological implications of circumcisions among different age-groups. Two factors that determine the impact of circumcision in a particular age-group are: the risk of infection that men face at that age (determined by sexual behaviour); and the risk that men of that age pose to others (determined by their HIV prevalence and sexual behaviour). Typically, the ages when men are most at risk of infection and when they are most likely to transmit infection are temporally distinct, with young men suffering higher rates of HIV incidence and older men being more likely to transfer infection to younger women.

Model simulations are run where circumcisions only occur within a particular age-group (see Figure 7). In each simulation, it is assumed that men are 60% less likely to be infected with HIV when they are exposed if they are circumcised (based on evidence from clinical trials mentioned earlier). In one set of runs, it is assumed that circumcision has no influence on the chance of male-to-female transmission. In an alternative set of runs, it is assumed that circumcised men are 30% less likely to transmit the infections than uncircumcised men.

The model results indicate that the impact of circumcisions among different age-groups operates over different time scales. Circumcising young boys has no effect on incidence in the population for the first 10 years after the intervention starts because they are not initially at risk of infection. However, in the long-term, circumcising young boys is likely to have the greatest effect because they will be partially protected from infection for their entire sexual lifetime. In contrast, circumcisions among older men have an immediate effect on incidence in the population but the long-term impact of circumcising older men is smaller. Circumcisions among the oldest age-group considered i.e. between 40 to 49 year olds have very little impact, even in the short-term, because the men that remain uninfected in this age-group are no longer at high risk of infection.

In the medium-term (20 to 30 years after the intervention starts), circumcising men aged between 20 to 29 years leads to the greatest reduction in incidence. In the long-term, circumcising infants or boys (younger than 19 years of age) leads to the greatest reductions in incidence.

If it is assumed that circumcision leads to a lower chance of male-to-female transmission, the overall impact of the same type of intervention is expected to be much greater and the relative impact of circumcising middle-aged men (aged between 30 to 39 years) is increased. This is because these men are the most likely to cause new infections among women, as a large proportion of these men are infected and are likely to form several casual partnerships, particularly with younger women. The main conclusion - that circumcisions among men aged between 20 to 29 years could lead to greater reductions of incidence in the first 20 to 30 years after the intervention - remains valid.

Another important consideration in designing programmes, however, is the achievable level of uptake in different ages, which primarily will be determined by the fraction of men that find circumcision acceptable. Promisingly high levels of acceptability have been reported, although it is not thought likely that all men will want to be circumcised and this will probably vary by age. These factors were not included in the simulations presented in Figure 8 but are the subject of investigation here.

It is expected that acceptability of circumcision will be greater among young boys (as their mothers may be able to provide informed consent on their behalf) but acceptability is lower among adults. The previous results have highlighted the particular advantage in achieving higher levels of uptake among young adults and it is thought that carefully constructed campaigns and public information could increase acceptability in this age-group. Therefore, optimistic scenarios were constructed that assumed that 80% of young boys (under 5 years), 40% of young men (aged 20 to 29 years), and 20% of men of other ages (30 years and older) would agree to be circumcised if a programme was made available.

Such an intervention could be expected to avert approximately 20% of infections between 2007 and 2050, if circumcision only protected men from infection. Over the first 5 years of the intervention, the reduction in incidence in the population will be mostly generated by circumcisions among young men (aged 20 to 29 years). This is due to a combination of the high risk of infection that these men face, the sexual behaviour of these men exposing younger women to infection, and the high levels of uptake that it is assumed could be achieved in this age-group. In the medium-term (after 20 to 30 years), the impact of circumcisions among adolescents (between 13 to 19 year olds) is greatest.

A related consideration is the impact of circumcisions among different age-groups on the number of infections averted per 1,000 operations. This can be thought of as a measure of “efficiency” - a higher value indicates a more effective intervention for the same number of operations, and therefore cost. The model shows that over the first 5 years of the intervention, efficiency is low with <10 infections averted per 1,000 infections, because coverage is low, and there has not been time for the indirect effects of the intervention (reductions in incidence among women, because prevalence among men has declined) to develop. However, efficiency increases over time and over 10 years there are up to 20 infections averted per 1,000 operations, and over 45 years there could be more than 40 infections averted per 1,000 operations.

In the first 5 years of the intervention, the efficiency of circumcisions among young men aged between 20 to 29 years is greatest. This is because men at this age are at risk of infection and likely to transmit infection to women. If the intervention is maintained, over time, circumcisions among younger age groups become more efficient. Although the rate of incidence in the population after 45 years is lower if only boys aged between 0 to 5 years are circumcised, this is not the most efficient strategy, because it requires many more operations.

Can timely circumcision interventions contribute to the national targets for HIV prevalence?

The National Strategic Plan for 2006 to 2010 in Zimbabwe aims to reduce prevalence to 10% among young women aged between 15 to 24 years of age, and to reduce prevalence among young men aged between 20 to 29 years of age to below 2.5%. The 2005/06 Demographic and Health Survey indicates that the target for young women has nearly been reached, with the prevalence estimated to be almost 11%. The prevalence among men, however, is near 4%. Using these baseline values, a circumcision intervention was simulated that started in 2007. The levels of acceptability assumed were set optimistically higher than in previous simulations, with 60% of 20 to 29 year old men and 40% of other aged men (30 years and older) agreeing to be circumcised. It was further assumed that an intervention could take 2 years to reach full scale, when as many as 1 million operations could be performed each year. It should be noted that this represents a very optimistic prediction, probably

exceeding the speed of scale up and intensity that an actual intervention could achieve.

Despite the high levels of coverage and speed of service scale up, the impact of the intervention is not expected to be substantial before 2010. The gradual reduction in incidence and the long duration of HIV infection leads to slow changes in prevalence, even if the intervention is highly effective. Therefore, it is not likely that a scale up of circumcision services could meaningfully contribute to reaching the targets for prevalence among young people in the National Strategic Plan. Nonetheless, as discussed above, the impact of the intervention in the long-term is considerable.

If, in addition to a circumcision intervention, other behavioural changes develop over the next few years (including reductions in partner numbers and increased condom use), then the impact of circumcision could be much greater. Interventions to prevent transmission tend to operate synergistically, and with sufficient behavioural change, the epidemic could even be driven to extinct (see Figure 8).

The epidemiological consequences of circumcising infected men

Data from some observational studies have indicated that circumcised men infected with HIV are less likely to transmit infection than uncircumcised men. However, this has not been found in other studies and a trial in Uganda was halted because there was a danger that sexual activity among infected men, before the circumcision had healed, might be associated with increased risk of transmission.

The model was used to evaluate male circumcision under three alternative scenarios to capture the range of uncertainty around the possible effects of circumcision on HIV transmission. These were:

(1) Circumcision has no effect on the chance of male-to-female HIV transmission.

(2) Infected men are more likely to transmit HIV in the 6 week healing period after circumcision. After the healing period, they have the same chance of transmitting HIV as uncircumcised men.

(3) Same as for (2), but after the healing period, circumcised men are 30% less likely to transmit HIV.

In all these simulations, it is assumed that infected men are equally likely to be circumcised as uninfected men.

Our findings show that HIV incidence among circumcised men could be reduced by about the same amount under all three scenarios. This is because it assumed that circumcised men are directly protected and this does not strongly depend on the way HIV influences male-to-female transmission. HIV incidence among women is expected to be reduced with the first scenario, when circumcision does not have an effect on the chance of HIV transmission. The magnitude of the reduction grows over time because prevalence among males declines. If the chance of transmission of HIV is higher from circumcised men during the healing period (second scenario), then incidence among women could very slightly increase during the first years of the intervention. However, over time, the indirect protection for women counterbalances this effect and, after 10 years of the intervention, the model predicts that women are also at less risk of HIV infection. In scenario three, when HIV transmission from circumcised men is higher during the healing period and lowers afterwards, the reduction in incidence among women is greater than if circumcision had no effect on transmission rates at all. Given the conflicting evidence on the benefits of circumcising infected men, including the chance that transmission is increased if men resume sex before the wound has healed, it is recommended that infected men are not targeted by interventions. However, modelling does not support infected men being denied circumcision on the grounds of a potential adverse effect at the population level.

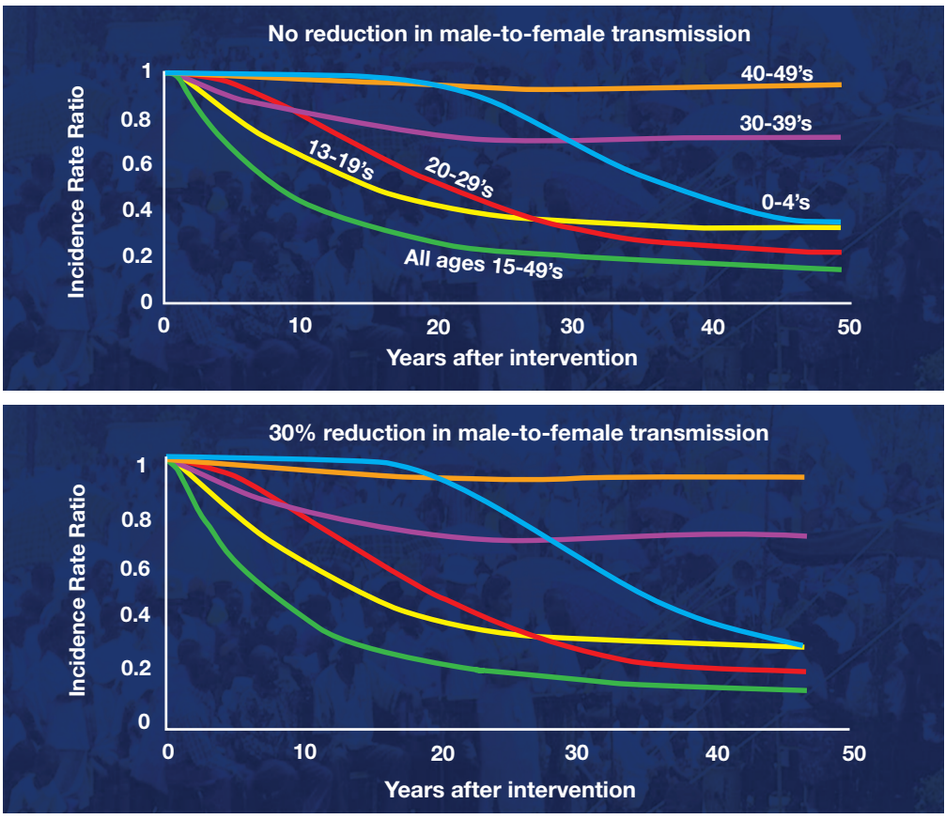


Figure 7: The theoretical impact of targeting different age groups for circumcision. The different coloured lines show predicted HIV incidence over time relative to if there is no circumcision intervention, assuming men in different age groups are circumcised. In these simulations, it is assumed that all men in the population are eligible and willing to be circumcised. In the upper panel, no effect of circumcision on the chance of male-to-female transmission is assumed. In the lower panel, it is assumed that circumcised men are 30% less likely to transmit HIV in each sexual act with women than uncircumcised men.

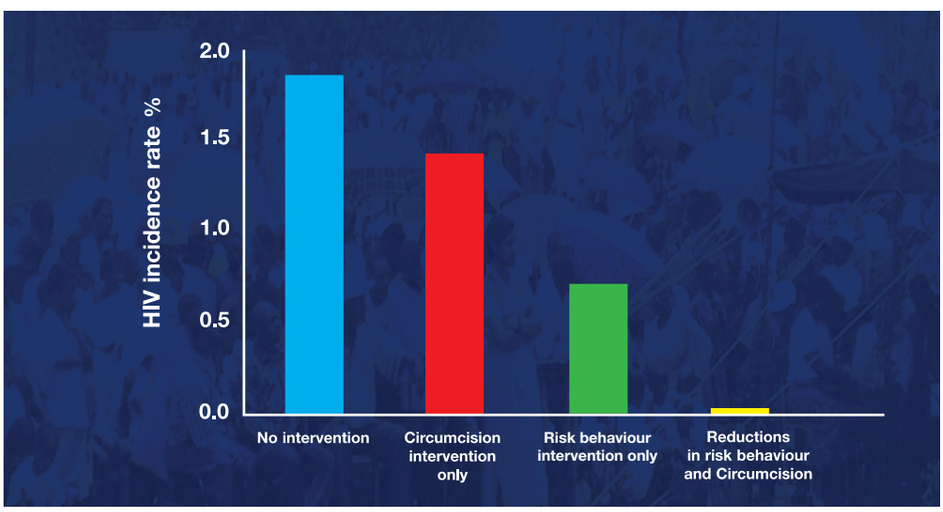


Figure 8: Interaction of circumcision interventions with existing behaviour change programmes. Four epidemic projections show: (i) No intervention; (ii) Circumcision intervention only with 90% coverage; (iii) Reductions in risk behaviour intervention that leads to an average 30% reduction in partner change rate and 30% increase in condom with casual partners; and (iv) Both interventions: reductions in risk behaviour and circumcision. The output for all four epidemic projections is HIV incidence per 100 person-years at risk. Note that the 'no intervention' scenario' reflects the epidemic conditions in Zimbabwe before the recent changes in risk behaviour that contributed to the observed decline in prevalence and incidence.

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