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No. 2019/1

A Sensitivity Analysis of Parameters Used in Spectrum's Aids Impact Model: The Role of the Sex Ratio of HIV Incidence and Adult Treatment on Mortality Levels and Trends

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A Sensitivity Analysis of Parameters Used in Spectrum’s Aids Impact Model: The Role of the Sex Ratio of HIV Incidence and Adult Treatment on Mortality Levels and Trends

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PREFACE

Within the framework of the biennial publication World Population Prospects, the United Nations Population Division has been generating estimates and projections of mortality indicators for several decades using standard approaches for all countries of the world. Upon the onset of the HIV/AIDS epidemic, new approaches were adopted to measure mortality within a number of countries highly affected by this epidemic. In the *2017 Revision* of the World Population Prospects and for countries most highly affected by the HIV/AIDS epidemic, mortality levels were estimated and projected by modelling explicitly the course of the epidemic and projecting the yearly incidence of HIV infection, while adding the AIDS related deaths to those from the no-AIDS scenario. The Spectrum software and AIM module (Aids Impact Model) were used to estimate the demographic impact of the HIV/AIDS epidemic in selected countries.

This technical paper presents selected results from a sensitivity analysis of parameters used in Spectrum's AIM module on mortality levels and trends. It illustrates how modifications in time-series of selected input parameters or values used in the AIM module may influence the estimated and projected levels and trends of all-cause mortality, using as examples modifications that have been made in a few countries affected by the HIV/AIDS epidemic, namely Gabon, Malawi and Zimbabwe. The analysis focusses on the role of the sex ratio of HIV incidence and "adult treatment" on mortality levels and trends, using selected mortality indicators.

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CONTENTS

PREFACE iii
1. INTRODUCTION 1
2. OVERALL SETTING OF THE SENSITIVITY ANALYSIS 3
3. RESULTS 4
4. DISCUSSION AND RECOMMENDATIONS 16
REFERENCES 18

FIGURES

Figure 1. Sex ratios of HIV incidence: original and modified patterns, Malawi, 1980-2030 5
Figure 2. Life expectancy at birth for males and females: No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1980-2030 6
Figure 3. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1980-2030 6
Figure 4. Adult mortality estimates (45q15) for males and females: No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1995-2015 7
Figure 5. Sex ratios of HIV incidence: original, modified and lower patterns, Gabon, 1980-2030 8
Figure 6. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with original, modified and lower sex ratios of HIV incidence, Gabon, 1980-2030 9
Figure 7. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and modified sex ratios of HIV incidence, Gabon, 1995-2015 10
Figure 8. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and lower sex ratios of HIV incidence, Gabon, 1995-2015 10
Figure 9. Sex ratios of HIV incidence: original and modified patterns, Zimbabwe, 1980-2030 11
Figure 10. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and modified sex ratios of HIV incidence, Zimbabwe, 1995-2015 12
Figure 11. Estimates and projections of the percentage of HIV-positive adult men and women who are in need of receiving ART, 2000-2030, Zimbabwe 13
Figure 12. Life expectancy at birth for males and females: AIDS scenarios with and without adult treatment, Zimbabwe, 1980-2030 13
Figure 13. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with and without adult treatment, Zimbabwe, 1980-2030 14
Figure 14. Estimates and projections of the percentage of HIV-positive adult men and women who are in need of receiving ART, with fluctuating and smoothed adult treatment levels, 2000-2020 15
Figure 15. Adult mortality estimates (45q15) for both sexes combined: AIDS scenarios with fluctuating and smoothed adult treatment levels, 2000-2020 15

ANNEX TABLES

Figure A. 1. Sex ratios of HIV incidence, original patterns, selected countries, 1980-2014 19

Figure A. 2. Estimates of the percentage of HIV-positive adult men (A) and women (B) who are in need of receiving ART, selected countries, 2000-2015 20

Figure A. 3. Adult mortality estimates (35q15) for males and females based on Demographic Health Surveys - Gabon, Malawi and Zimbabwe- for selected periods 22

A SENSITIVITY ANALYSIS OF PARAMETERS USED IN SPECTRUM'S AIDS IMPACT MODEL ON MORTALITY LEVELS AND TRENDS

1. INTRODUCTION

Within the framework of the biennial publication World Population Prospects, the United Nations Population Division has been generating estimates and projections of mortality indicators for several decades using standard approaches for all countries of the world. Upon the onset of the HIV/AIDS epidemic, new approaches were adopted to measure mortality within a number of countries highly affected by this epidemic. The general approach for deriving estimates and projections of mortality was not appropriate for countries whose recent mortality patterns had been significantly affected by this epidemic. The particular dynamic of HIV/AIDS and the severity of its outcome require explicit modelling of the epidemic. Unlike other infectious diseases, HIV/AIDS has a very long incubation period during which an infected person is mostly symptom-free but already infectious. Also, unlike many other infectious diseases, individuals do not develop immunity, but, in the absence of treatment, almost always die as a consequence of their compromised immune system. Another reason for an explicit modelling of the HIV/AIDS is the avalanche-like process of the infection spreading through a population and the particular age pattern of infection exhibited by HIV/AIDS. The additional deaths due to HIV/AIDS, predominantly occurring among adults in their reproductive age, consequently distort the usual U-shaped age profile of mortality; this distorted atypical pattern cannot be found in the model life tables that are available to demographers (Heuveline, 2003). In more recent years, the availability and use of antiretroviral therapy (ART) has also modified substantially the survival prospects of people affected by this epidemic.

As a consequence, instead of an overall mortality process that can be captured by standard age patterns of mortality and smooth trends of changing life expectancy, for countries highly affected by HIV/AIDS, two separate mortality processes have been modelled: the mortality due to the HIV/AIDS epidemic itself and the mortality that prevails among the non-infected population. The latter is often called the level of "background mortality" and has often been reported as the no-AIDS scenario.

In the *2017 Revision* of the World Population Prospects (WPP 2017) and for countries most highly affected by the HIV/AIDS epidemic, mortality levels were estimated and projected by modelling explicitly the course of the epidemic and projecting the yearly incidence of HIV infection, while adding the AIDS related deaths to those from the no-AIDS scenario (United Nations, 2017[1]). The Spectrum[2] software and AIM module (Aids Impact Model) were used to estimate the demographic impact of the HIV/AIDS epidemic in selected countries. The model was developed by the UNAIDS Reference Group on Estimates, Modelling and Projections (Stanecki, Garnett, and Ghys, 2012; Stover, Brown, and Marston, 2012), and epidemiological parameters used by UNAIDS were made available to the Population Division in 2016. Most of these were used by the Population Division to estimate the mortality impact of the HIV/AIDS epidemic while some were adjusted, most importantly the sex ratio of HIV incidence. extracted

The Spectrum software is also used by national programmes and the Joint United Nations Programme on HIV/AIDS (UNAIDS) "to prepare estimates of trends and current values of key HIV indicators for 161 countries. The model uses country-specific HIV surveillance, national surveys, case reports, and vital registration data to determine trends in HIV prevalence and incidence. These are combined with country-specific data on program outputs…and global/regional epidemiological patterns…to produce estimates of

[1] "Country files" used in updating the World Population Prospects were utilized to conduct portions of this analysis though some mortality indicators were recomputed based on annual data in the Spectrum files (5-year averages may differ slightly from official estimates). Non-published data from the no-AIDS scenario and times-series of selected parameters were taken from the "country files".

[2] For accessing the official versions of Spectrum, please see: www.avenirhealth.org/software-spectrum.php. A special release of Spectrum (UNPOP100, December 2014), specifically extended to handle higher life expectancy projections up to age 100 was used for the *2017 Revision*. The same version (v.5.45 beta 10) was used to generate the simulations in the current sensitivity analysis and for updating the countries for which explicit modelling of HIV/AIDS was employed in the *2017 Revision*. Spectrum is an analytical tool developed to support policy decisions concerning public health. Spectrum includes modules for examining health intervention impact and costing along with underlying demographics.

key indicators…" (Stover and others, 2017, p. S5-6). AIM, a module within Spectrum, "is a computer program for projecting the impact of the HIV/AIDS epidemic. It can be used to estimate the number of people infected with HIV, the number of new infections, the need for treatment….and many other indicators of interest." (Avenir Health, 2019, p. 89). "AIM requires that a demographic projection first be prepared…" (ibid, p. 94). Among other inputs, AIM requires an assumption about the past and future course of adult HIV incidence and treatment coverage. In a nutshell, several input parameters are used to generate specific epidemiological patterns which are then combined into a cohort component demographic model.

The Population Division has been incorporating the impact of the HIV/AIDS epidemic on its mortality estimates for some time, either by relying on Spectrum/AIM in more recent years or other software with similar approaches in previous years. When this overall modelling exercise was initiated in the 1990s, for many of the countries highly affect by the HIV/AIDS epidemic, limited data, especially on adult mortality, had been made available or had been thoroughly investigated, not allowing for a systematic comparison between the modelled estimates and other empirical evidence. In more recent years, and with an increase in the availability and analysis of empirical mortality estimates, such comparisons have been made and have led to some questioning or reviewing of the modelled estimates. In that regard and in order to address concerns related to the sex ratio of all-cause mortality in specific age groups, the ratios of female to male HIV incidence for ages 15-49 (or sex ratio of HIV incidence) were adjusted for a number of countries within the *2017 Revision* in order to yield modelled estimates that are more consistent with observed mortality estimates.

Considering that Spectrum/AIM is used by many national programmes, national and international organizations, academics, etc., to measure the demographic impact of the HIV/AIDS epidemic, among other things, it was considered important to further explore the role of specific input parameters within the module on the generated mortality outputs.

The purpose of this technical paper is to illustrate how modifications in time-series of selected input parameters or values used in the AIM module of Spectrum may influence the estimated and projected levels and trends of all-cause mortality.

Within this analysis, the focus is on the following input variables:

1) The sex ratio of HIV incidence (F/M), described as the ratio of female to male incidence in ages 15-49;

2) The percentage of HIV-positive adult men and women who are in need of receiving antiretroviral therapy[3] (ART), also referred to as "adult treatment".

The mortality indicators that are analysed are as follow:

1) Life expectancy at birth by sex;

2) The sex ratio of life expectancy at birth (F/M; female to male ratio);

3) The estimates of adult mortality by sex, described as the probability of dying between ages 15 and 60 (45q15).

[3] Refers to the adults receiving ART plus those eligible but not receiving treatment. Estimates of the need of receiving ART are based on those who are eligible according to CD4 count criteria (Avenir Health, 2019)

2. Overall setting of the sensitivity analysis

The starting point of this analysis are the results from the *2017 Revision* of the World Population Prospects, using selected country examples. The *2017 Revision* made explicit modelling assumptions to incorporate the demographic impact of the HIV/AIDS epidemic for 18 countries where HIV prevalence among persons aged 15 to 49 was ever equal to or greater than 5 per cent between 1980 and 2015. Using as examples modifications that have been made in certain inputs values for a few countries, namely Gabon, Malawi and Zimbabwe, for which the AIDS mortality was modelled using the AIM module, we illustrate how these changes influence the all-cause mortality levels and trends. The analysis focusses on the impact of the sex ratio of HIV incidence and the "adult treatment" on mortality levels and trends. A brief illustration of the role of fluctuating vs. smoothed proportions of HIV-positive adults in need of receiving treatment on mortality trends is also presented.

A. Sex ratio of HIV incidence

At a given HIV incidence rate for the population of both women and men combined, the sex ratio of HIV incidence determines its distribution by sex[4]. A ratio above one implies that the incidence rate is higher for women than men, and, a ratio below one, that the incidence rate is higher for men than women, having implications on their respective simulated survival prospects in subsequent years. Within Spectrum, adult HIV incidence is basically disaggregated into female and male incidence by specifying the ratio of new female infections to new male infections. For countries with "generalized epidemics" where HIV is firmly established in the general population[5], it is generally assumed that the ratio is less than one at the beginning of the epidemic and then increases to greater than one about 10 years into the epidemic. Based on available data, a ratio of 1.38 was assumed in several countries with generalized epidemics (Avenir Health, 2019). When comparing the time-series of the "original" sex ratios of HIV incidence by country, as provided by UNAIDS for the production of the *2017 Revision*, out of 18 countries, 9 countries had the same sex ratios in the year 2000 (with a value of 1.38, roughly implying that 138 women are being infected for each 100 men) and by 2010, that same value was encountered in 13 countries (see annex figure A.1). Furthermore, the Central African Republic, Equatorial Guinea, Malawi and the United Republic of Tanzania had the exact same time-series from 1980 to 2014. A few more countries had a similar pattern as those countries though with different values as start off points in 1980 (Cameroun, South Africa, Uganda, Zimbabwe). Therefore, for most of these countries, the time-series are not country specific estimates and they have been derived from data collected in sentinel surveillance sites such as Rakai, Uganda[6]. On the other hand, estimates for Gabon were partly derived from data collected in the 2012 Gabon Demographic Household Survey[6] (DHS), with an estimated peak value of 2.41; this value implies that substantially more women are being infected as compared to men. It should be noted that within Spectrum, for countries that have information on prevalence by age and sex, the "Incidence Rate Ratios" can be calculated by using survey data (Avenir Health, 2019).

As stated above, in the *2017 Revision*, in order to address concerns related to the sex ratio of all-cause mortality in specific age groups, the sex ratios of HIV incidence were modified for a number of countries in the process of estimating the demographic impact of the HIV/AIDS epidemic. The ratios were modified in the countries that had a prevalence of 8 per cent or more between 1980 and 2015, namely Botswana, the Central African Republic, Kenya, Lesotho, Malawi, Namibia, South Africa, Swaziland, Uganda, the United Republic of Tanzania, Zambia, and Zimbabwe, using lower levels in line with those estimated for Mozambique. The ratios in Congo, Gabon and Rwanda were also modified though assumed to be higher than the pattern used in Mozambique. Overall, in doing these different changes, it was still assumed that more women than men were being infected by HIV, but to a lesser degree than implied with the original

[4] A similar approach is used to distribute the HIV incidence rate by age for each sex. Though not addressed in this technical paper, further analysis on the role of the age pattern of HIV incidence on mortality pattern by age may be worth investigating.
[5] All countries listed in this analysis are considered to have generalized epidemics.
[6] Based on communication with Mr. John Stover from Avenir Health.

time-series included in the Spectrum files, as provided by UNAIDS[7]. These changes had implications for the all-cause mortality levels for both men and women. Generally, it implied higher mortality levels for men and lower ones for women, which, on the whole, is more consistent with empirical evidence regarding the sex differentials in mortality (to be further discussed).

B. Adult treatment

Considering the important role that treatment may have on survival prospects of HIV-positive adults, it was decided to further explore the relations between these variables within a modelled framework. Proportions of HIV-positive adults in need of receiving treatment in each country, for both men and women from 1980 to 2015, were for the most part estimated or calculated based on information provided by UNAIDS[8]. For a few countries, national estimates were derived from sub-regional series, which required further calculations; in some series, point estimates with atypical values were also adjusted. The proportions of HIV-positive adults in need of receiving treatment were then projected to reach 90 per cent in 2050 if it was below 85 per cent in 2015 or to reach 95 per cent if it was above 85 per cent in 2015; it remained constant thereafter until 2100. These values were used to derive the number of adults receiving ART. As observed in annex figure A.2, time-series of “adult treatment” can be quite volatile and these fluctuations may have an impact on the estimated mortality levels. It should also be noted that measuring adequately time-series of adult treatment is not an easy task and that progress has been made in recent years in deriving more reliable estimates.

3. RESULTS

Before embarking on the sensitivity analysis about how modifications in time-series of the sex ratios of HIV incidence may influence the estimated and projected levels and trends of all-cause mortality in selected countries, it was deemed important to briefly review the mortality patterns by sex based on empirical estimates. Annex figure A.3 depicts adult mortality estimates between ages 15 and 50 (35q15[9]) for both males and females as reported in different Demographic Health Surveys for the three countries under analysis in this section (Gabon, Malawi and Zimbabwe). It can be observed that in all three countries, male adult mortality levels are systematically higher than female adult mortality across the observed periods. In the case of Zimbabwe, it could be argued that the sex differential in mortality between gender (male over female: M/F) is reduced overtime though still present. This pattern has also been observed in other countries affected by the HIV/AIDS epidemic (data not shown[10]). Considering that parts of the upcoming analysis will be focussed on adult mortality between ages 15 and 60 (45q15), it is important to point out that in most countries male excess mortality between ages 50 to 60 is usually more pronounced and therefore, one could anticipate larger sex differentials (M/F) in mortality with the 45q15s than with the 35q15s.

A. Malawi

As a first step, and while only modifying the time-series of the sex ratios of HIV incidence in the “country file” of Malawi, a brief description of the changes in the estimated and projected levels of life expectancy at birth by sex, the sex ratios of life expectancy at birth and the adult mortality estimates by sex are provided below.

[7] The time-series of the sex ratios of HIV incidence that were used in the World Population Prospects should not be interpreted as the definitive ones for each country but as alternatives to address mortality estimation matters.
[8] Official estimates from UNAIDS may differ.
[9] The comparison of adult mortality estimates is based on 35q15 estimates since Demographic Health Surveys do not report 45q15 estimates.
[10] Furthermore, Masquelier and others (2017; p. S80) indicated that in selected countries “there was no distinct reduction of the women advantage in adult mortality as the share of AIDS-related deaths increased”.

Figure 1 shows the original and modified time-series of the sex ratios of HIV incidence from 1980 to 2030. In the original series, the start off point in 1980 was estimated at 1 increasing to a value of 1.38 by 1992 and remaining constant thereafter till 2014. Values from 2015 till 2030 are projections on the basis of a linear interpolation, assuming it will reach 1.1 by 2050. The modified series starts with a substantially lower sex ratio in 1980, set at 0.36, implying that many more men are being infected at the onset of the epidemic and increasing rapidly thereafter to reach a value of 1.26 by 2004; thereafter, it remains constant till 2014. As mentioned above, this still assumes that more women than men are being infected by HIV, but to a lesser degree than implied with the original time-series included in the Spectrum files.

Figure 1. Sex ratios of HIV incidence: original and modified patterns, Malawi, 1980-2030

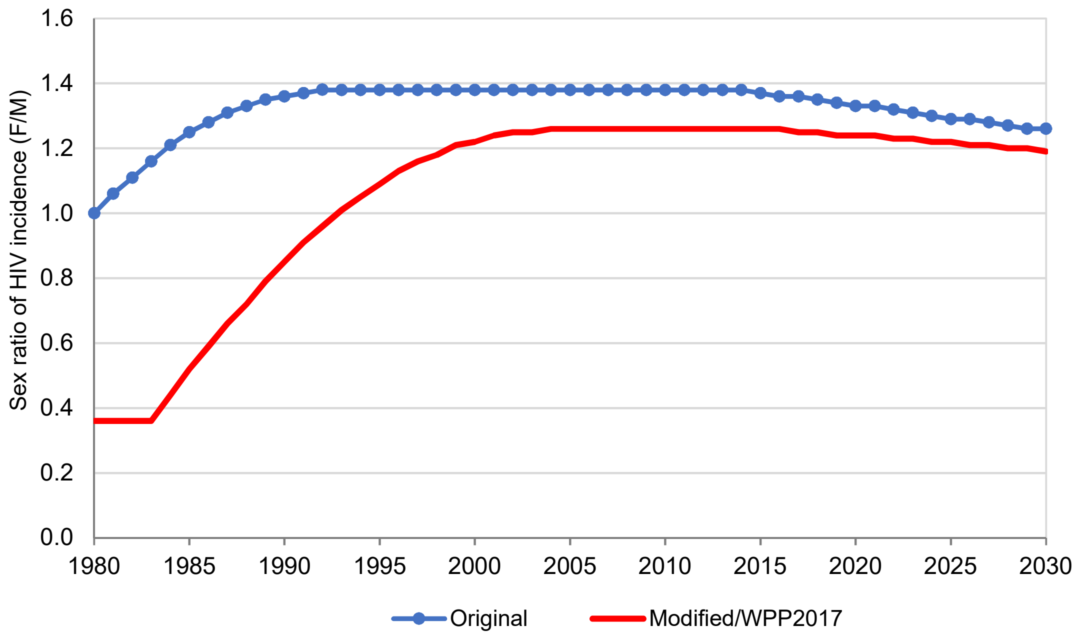


Figure 2 shows the life expectancy estimates by sex from 1980 to 2030 for the "no-AIDS scenario" and the "AIDS scenarios" with the original and modified sex ratios of HIV incidence; figure 3 shows the corresponding trends in the sex ratios of life expectancy at birth (female over male: F/M). With the no-AIDS scenarios, life expectancy increases quite rapidly for both men and women until reaching levels between 65 and 70 years, at which point the pace of increment starts to slow down. Overall, the sex gap in survival prospects favours women and increases from a sex ratio of about 1.04 to 1.06 between 1980 and 2005. With the "AIDS impact", regardless of the scenario, life expectancy levels for both men and women tend to plateau between 1990 and 2005. However, the sex ratio of life expectancy changes dramatically during that period across scenarios. With the original time-series, male survival prospects even surpass that of women in the early 2000s, since it is assumed that relatively more women are contracting HIV. In the modified scenario, the sex ratio increases between 1980 and 1995 and thereafter declines as relatively more women are dying from AIDS related causes. In both scenarios, access to treatment contributes to a recovery in survival prospects. Sex differentials in treatment levels also influences the pace of recovery by sex, in favour of women (to be further explored with other examples below). In the end, the sex ratios of HIV incidence in the original time-series seem to distort the "inherent" sex differential in survival prospects and the derived mortality estimates are less in line with some observed values [11]. As shown in annex figure A.3, adult mortality estimates between the ages of 15 and 50 (35q15) based on survey data are higher for men than women in Malawi (as well as in Gabon and Zimbabwe).

[11] Based on the 2000, 2004 and 2010 Malawi DHSs, adult mortality estimates between ages 15 and 50 (35q15) are higher for men than for women in the 7-year periods prior to each survey (National Statistical Office (NSO) [Malawi] and ICF, 2017).

Figure 2. Life expectancy at birth for males and females: No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1980-2030

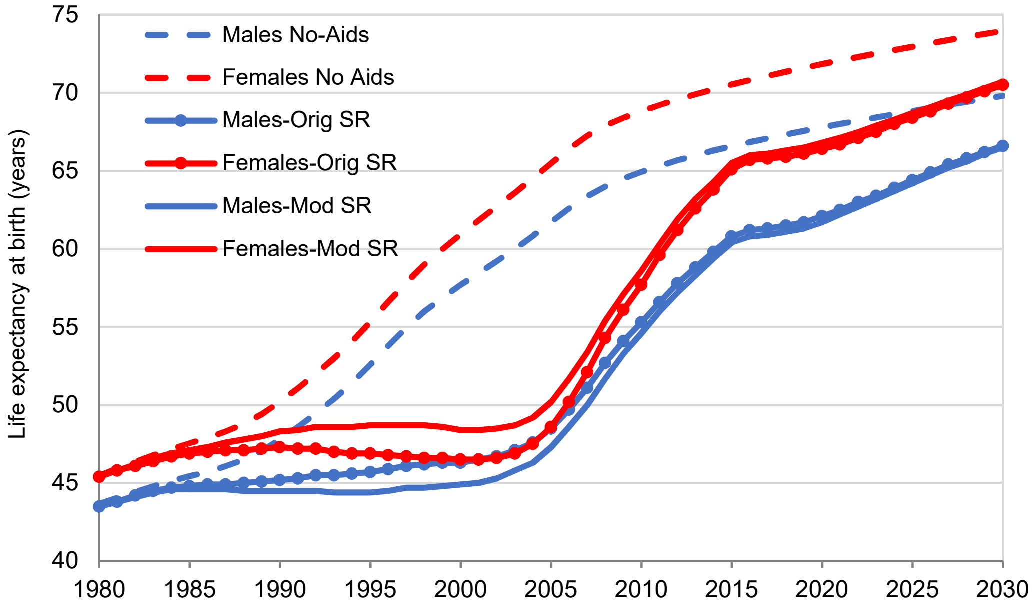
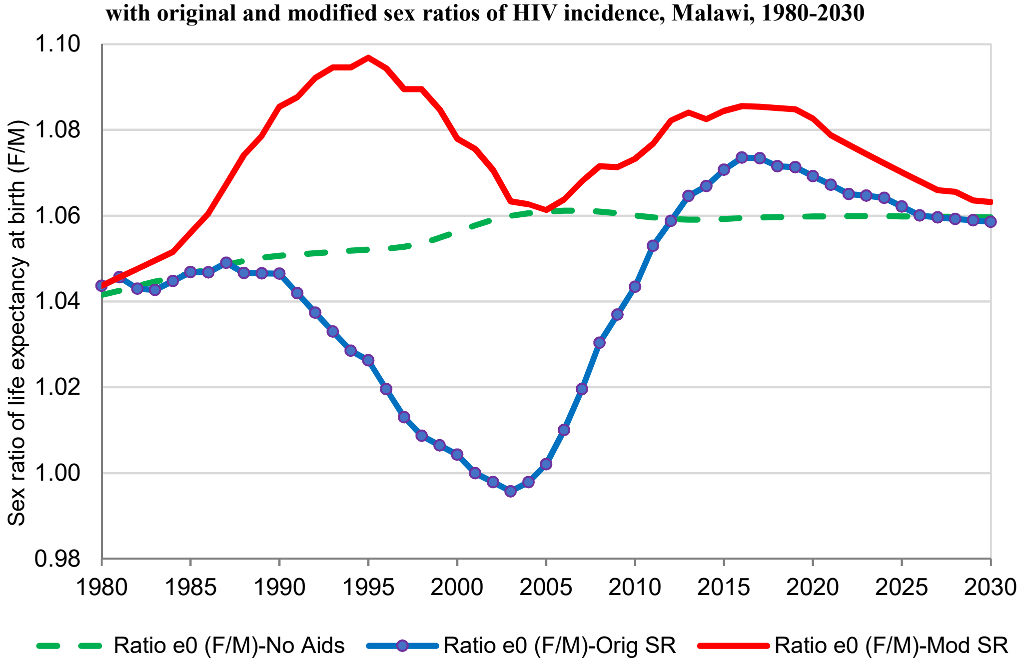
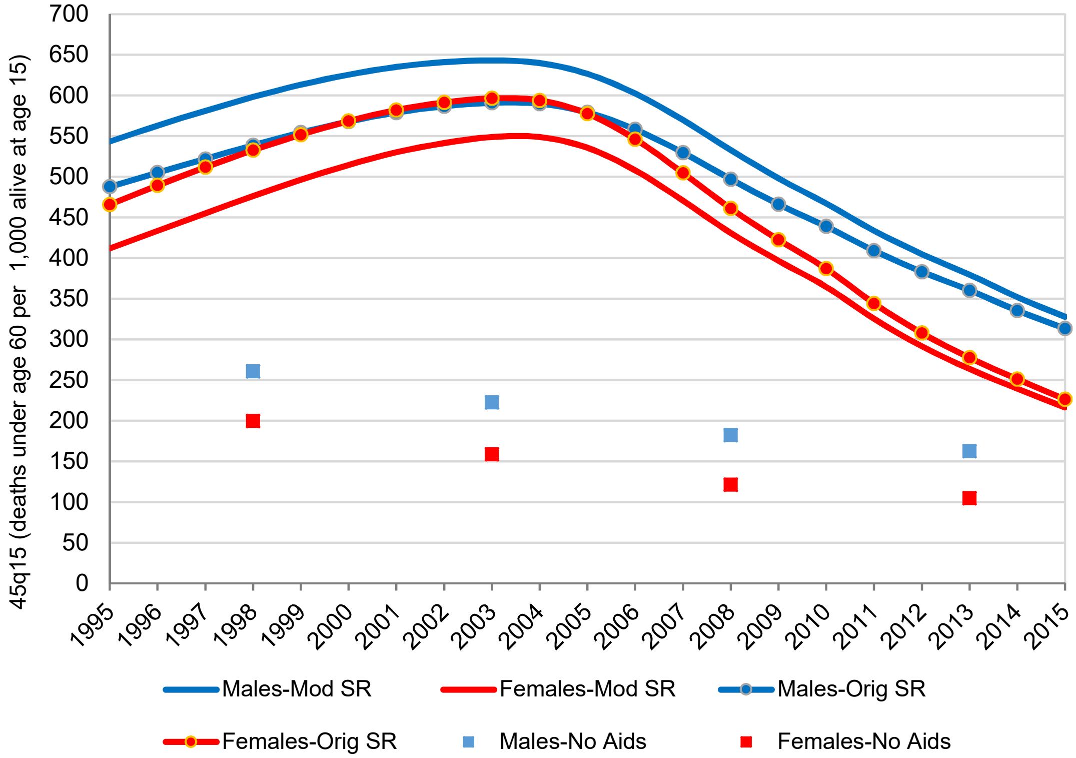


Figure 3. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1980-2030



Considering that AIDS related mortality is concentrated in adult ages, variations in adult mortality estimates (45q15) across scenarios were inspected more closely. Figure 4 shows the adult mortality estimates by sex from 1995 to 2015 for the no-AIDS scenario and the AIDS scenarios with the original and modified sex ratios of HIV incidence. In this figure, it was also decided to include the no-AIDS estimates, which are five-year averages (e.g. 1998 refers to the period 1995-2000); this comparison illustrates that adult mortality estimates excluding AIDS deaths can be relatively low and, in some periods, represent about a third of all-cause mortality (to be further discussed in section 4 below).

Figure 4. Adult mortality estimates (45q15) for males and females: No-AIDS scenario and AIDS scenarios with original and modified sex ratios of HIV incidence, Malawi, 1995-2015

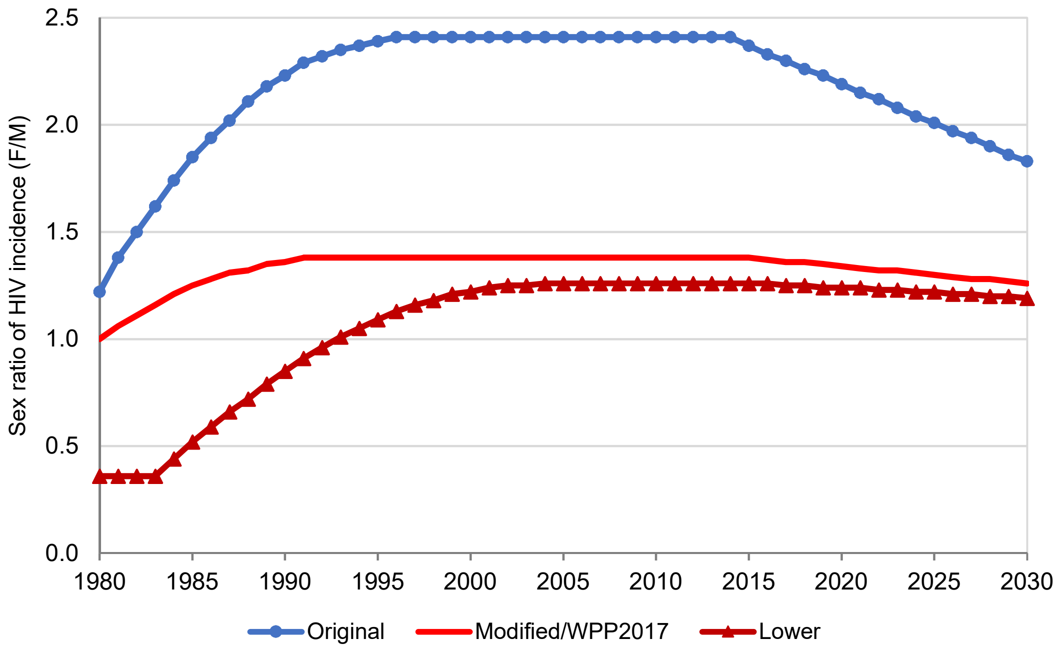


When comparing the 45q15s by sex in the original AIDS scenario, it can be observed that male and female mortality levels are quite similar from about 1996 to 2006, implying a stronger relative change in female survival prospects as compared to the no-AIDS mortality levels by sex. Afterwards, and partly because of the increase in treatment levels which seem to favour women, the sex gap widens. Overall, the sex gap in mortality is more stable during the 20-year span within the modified AIDS scenario, and more in line with observed mortality indicators as indicated above (also see annex figure A.3).

B. Gabon

The situation of Gabon is slightly different from other countries in the sense that the time-series of the sex ratios of HIV incidence were partly derived from data collected in the 2012 DHS of Gabon and that it was decided, as part of this sensitivity exercise, to simulate a “lower” pattern. Figure 5 shows the original, modified and a “lower” time-series of sex ratios of HIV incidence from 1980 to 2030. The estimated peak sex ratio value of 2.41 was used in the original time-series from 1996 to 2014 and implies that many more women than men are being infected by HIV (see blue line, labelled Original). This sex ratio level has important implications on the modelled survival prospects by sex. Within the *2017 Revision*, and as an intermediate approach, it was decided to use the time-series that had been provided by UNAIDS for several other countries[12], starting with a value of 1 in 1980 and a peak value of 1.38 (see red line below, labelled Modified/WPP2017). After careful review of the derived mortality estimates, it probably would have been better to use the lower values as those used in countries such as Malawi (see dark red line, labelled Lower).

Figure 5. Sex ratios of HIV incidence: original, modified and lower patterns, Gabon, 1980-2030



Without showcasing the estimated levels of life expectancy at birth by sex derived for the three different incidence patterns described above, figure 6 illustrates the important variations in the sex ratios of life expectancy at birth across the different "scenarios". While using the original time-series with a peak value of 2.41, female life expectancy estimates are lower and even lower than that of males for several years (see ratios with a value below one), which is not corroborated by empirical mortality estimates[13]. It could be argued that by increasing the sex differential in life expectancy at birth in the no-AIDS scenario, one could simulate all-cause mortality sex ratios (F/M) that are higher. However, that would imply extremely high excess male mortality in the absence of AIDS. As stated above, in the *2017 Revision*, it was decided to use the pattern with values ranging from 1 in 1980 to a peak of 1.38, which yielded somewhat more "reasonable" life expectancy estimates by sex, with the sex ratio of life expectancy (F/M) plateauing at just under 1.02 from about 2005 to 2010 (the sex ratio should be above 1). However, with the use of the "lower" sex ratio of HIV incidence time-series, the sex ratios of life expectancy are somewhat higher overall, which is in better alignment to the levels implied by using empirical data on adult mortality (see figure annex A.3).

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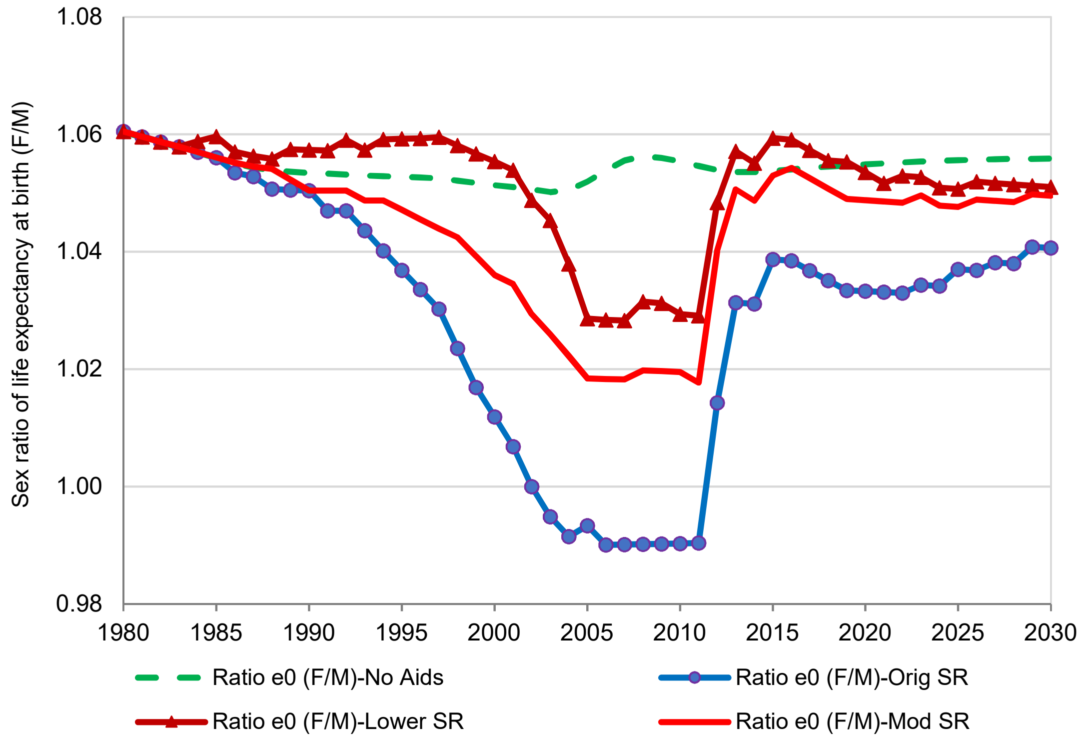
[12] In the original time-series provided by UNAIDS, the Central African Republic, Equatorial Guinea, Malawi and the United Republic of Tanzania were all identical (starting with 1 in 1980 and with a peak value of 1.38). This series implied higher sex ratios of HIV incidence than the one used in most countries and was used in Congo, Gabon and Rwanda; the default time-series reached even higher levels.

[13] Based on the 2000 and 2012 Gabon DHSs, adult mortality estimates between ages 15 and 50 (35q15) are higher for men than for women in the 7-year periods prior to both surveys (Direction Générale de la Statistique (DGS) et ICF International, 2013).

Figure 6. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with original, modified and lower sex ratios of HIV incidence, Gabon, 1980-2030



The concerns that have been raised with regards to the mortality levels by sex depending which time-series of sex ratios of HIV incidence is used are more apparent when looking at the levels and trends of adult mortality estimates. Figures 7 and 8 provide a comparison of adult mortality estimates (45q15) for both males and females based on different scenarios. Figure 7 shows that with the original ratios, adult mortality is substantially higher for females than for males, mainly for the period 2000-2010, with estimates ranging from about 340 for women and 280 for men around 2007. With the modified scenario, the differences are smaller though female mortality is still higher mainly during the period 2005-2010. In figure 8, it can be observed that by using the "lower" scenario, male adult mortality levels are always higher than that of females, though mortality levels by sex do converge in the mid-2000s. The swift changes in mortality levels by sex after 2010 in the different scenarios are partly related to the access of antiretroviral therapy, which prevalence levels are estimated, on the whole, to be higher for women. Lastly, it should be noted that when looking at modelled estimates of adult mortality between the ages 15 and 50 (35q15), the inconsistencies with mortality levels by sex are even more accentuated (data not shown[14]). This could also be partially related to the age pattern of HIV incidence, for which the distribution or median age is younger for women (as mentioned earlier, this aspect is not investigated in this paper).

[14] As mentioned earlier, because male mortality is generally higher than female mortality between ages 50 to 60, one could anticipate larger sex differentials (M/F) with the 45q15s than with 35q15s.

Figure 7. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and modified sex ratios of HIV incidence, Gabon, 1995-2015

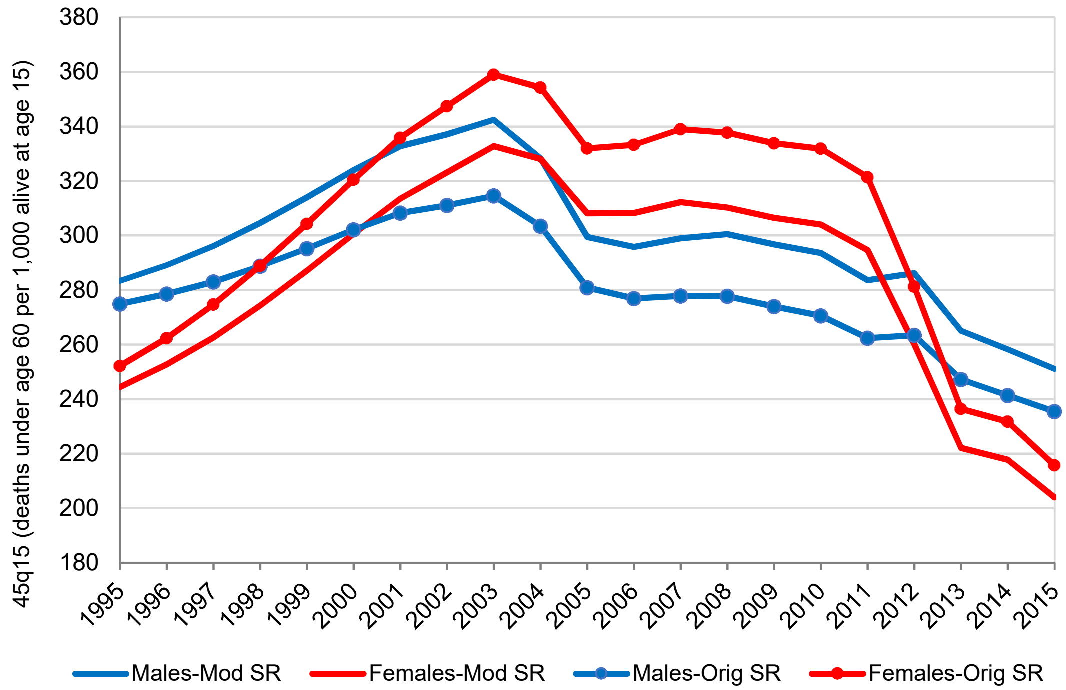
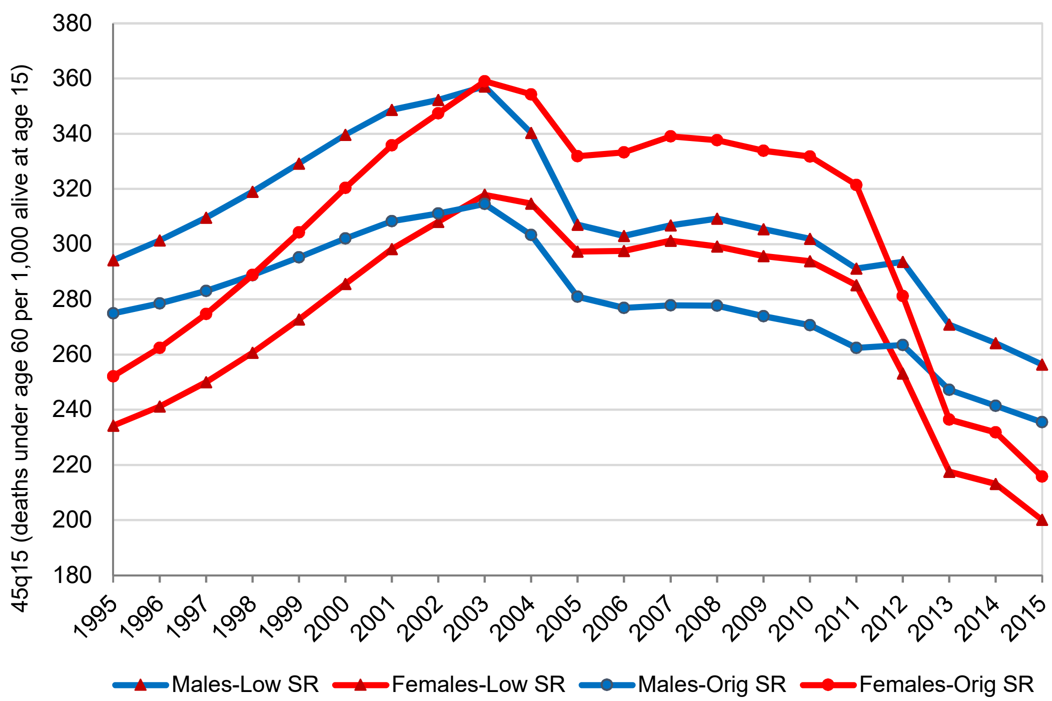


Figure 8. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and lower sex ratios of HIV incidence, Gabon, 1995-2015

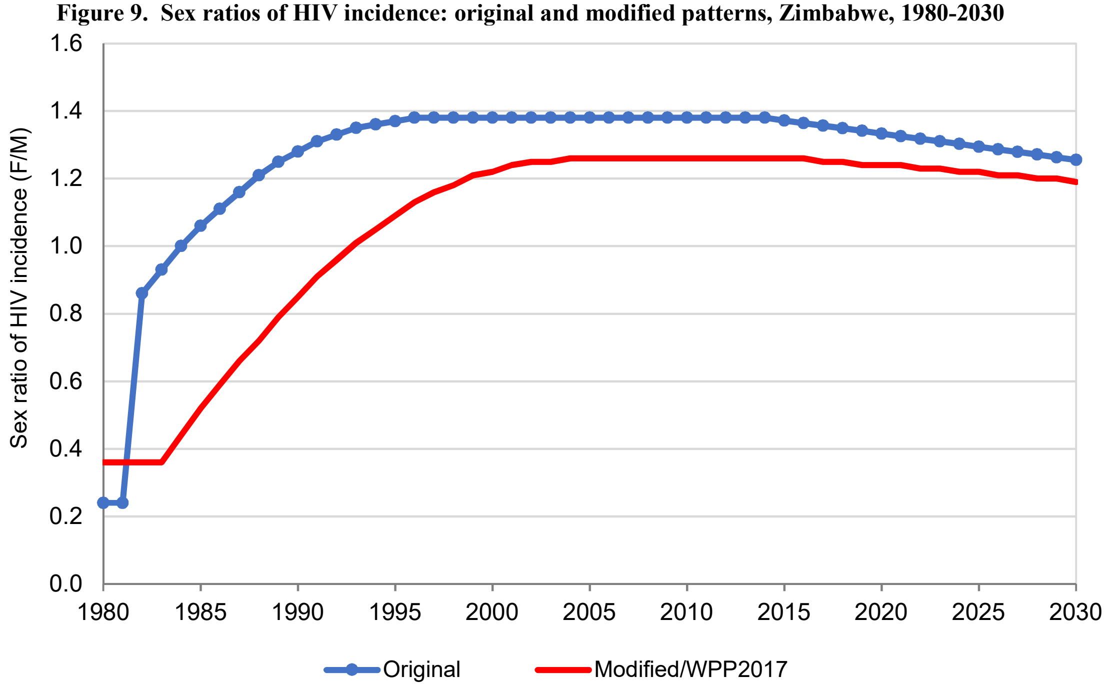


C. Zimbabwe

For the purpose of this sensitivity analysis, some results related to Zimbabwe are now presented with the objective of reiterating the role of the sex ratio of HIV incidence on the sex patterns of mortality (meaning it is not an isolated case) and illustrating how the levels and trends in antiretroviral therapy by sex play an important role on the estimated survival prospects.

As in the cases of both Gabon and Malawi, the sex ratios of HIV incidence for Zimbabwe were also modified in the *2017 Revision* (figure 9). Consequently, the derived adult mortality estimates for both men and women were altered (figure 10). Again, with the original scenario, female mortality is higher than that of males from about 2000 till 2007. However, it is interesting to note the sharp decline in the trajectories of both scenarios a few years after access to treatment is made available, starting in the early-mid 2000s, and how the mortality levels fluctuate in the year 2012[15].

Figure 9. Sex ratios of HIV incidence: original and modified patterns, Zimbabwe, 1980-2030



The observation of such patterns incited us to further explore the role of treatment on modelled mortality levels and trends in the context of the HIV/AIDS epidemic. It should be stated that "the most important recent change in HIV epidemiology has been the provision of antiretroviral therapy (ART) in low-income and middle-income countries…" (Eaton and others, 2015, p. e598). Indeed, access to treatment or antiretroviral therapy (ART) has modified substantially the survival prospects of men and women who have been diagnosed with HIV/AIDS.

[15] Within the *2017 Revision* of World Population Prospects, such fluctuations in mortality levels were not detected mainly because annual estimates (as reported here) were aggregated in five-year period estimates which smoothed the trends.

Figure 10. Adult mortality estimates (45q15) for males and females: AIDS scenarios with original and modified sex ratios of HIV incidence, Zimbabwe, 1995-2015

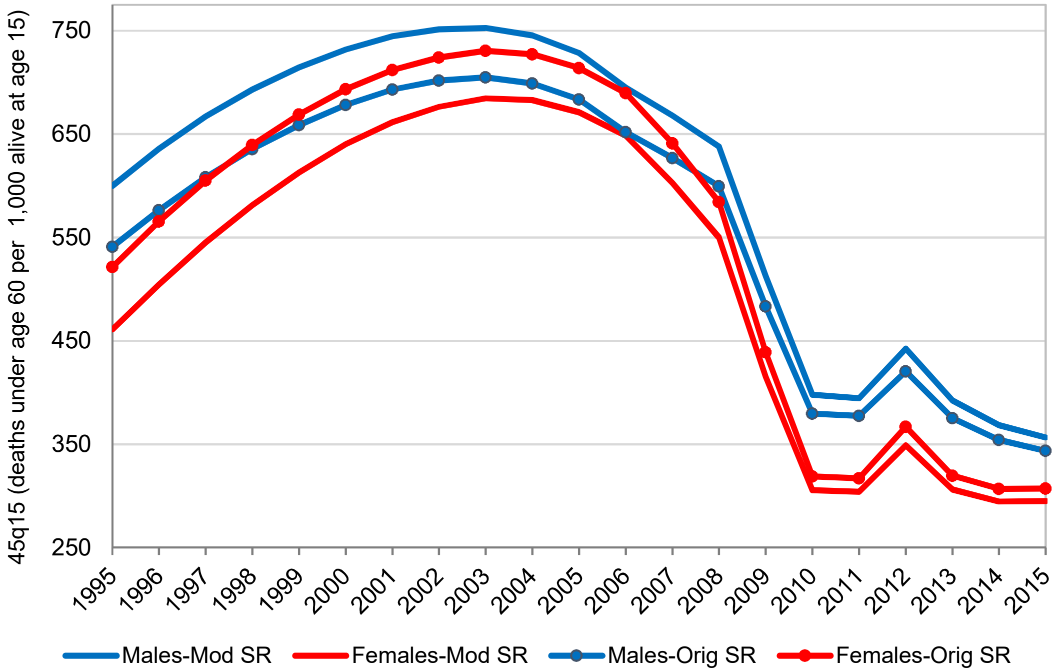
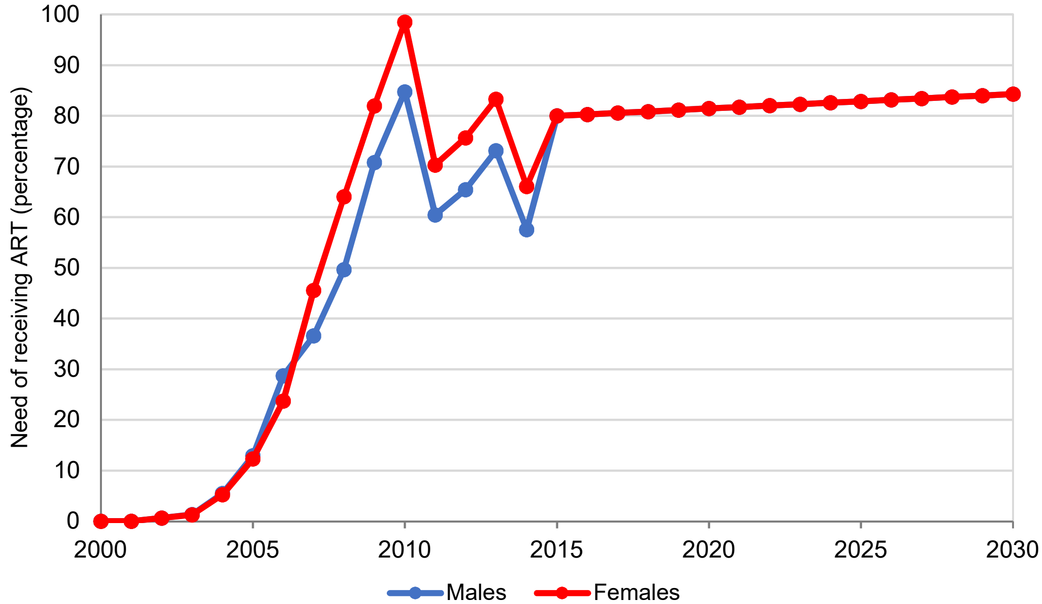


Figure 11 illustrates the estimates and projections of the percentage of HIV-positive adult men and women who are in need of receiving ART. These values were used in the *2017 Revision* within the AIM module of Spectrum to model adult treatment. As portrayed, on the whole, estimates for women are higher than for men and in both cases the levels fluctuate considerably between 2010 and 2015. These fluctuations are partly responsible for the oscillations in the mortality levels illustrated in the year 2012 in figure 10 (above) and in figure 12 (below).

Figure 12 presents levels of life expectancy at birth by sex and basically illustrates the significant impact of adult treatment on survival prospects, with a sharp increase in life expectancy at birth after 2005 (see series “with adult treatment”). Without adult treatment, life expectancy starting in about 2005 would have been substantially lower, with peak differences as compared to the all-cause mortality estimates surpassing 10 years of life expectancy in the period 2010-2015. In the scenario with treatment, as in the case of adult mortality, it can be observed that life expectancy estimates tend to fluctuate in the more recent years. Lastly, as observed in figure 13, the sex ratios of life expectancy at birth change dramatically from 2006 to 2009 in the treatment scenario, reflecting differences in treatment by gender. A few years later, it starts to decline until about 2016, when it starts to plateau off, in line with the harmonization of the treatment “prevalence” levels by sex.

Figure 11. Estimates and projections of the percentage of HIV-positive adult men and women who are in need of receiving ART, 2000-2030, Zimbabwe



NOTE: National estimates presented here for Zimbabwe were derived from sub-regional series, which required further calculations. Official estimates from UNAIDS may differ. Estimates of the need of receiving ART are based on those who are eligible. In Zimbabwe, the eligibility criteria for receiving ART has changed over the years, which may have contributed to the observed fluctuations.

Figure 12. Life expectancy at birth for males and females: AIDS scenarios with and without adult treatment, Zimbabwe, 1980-2030

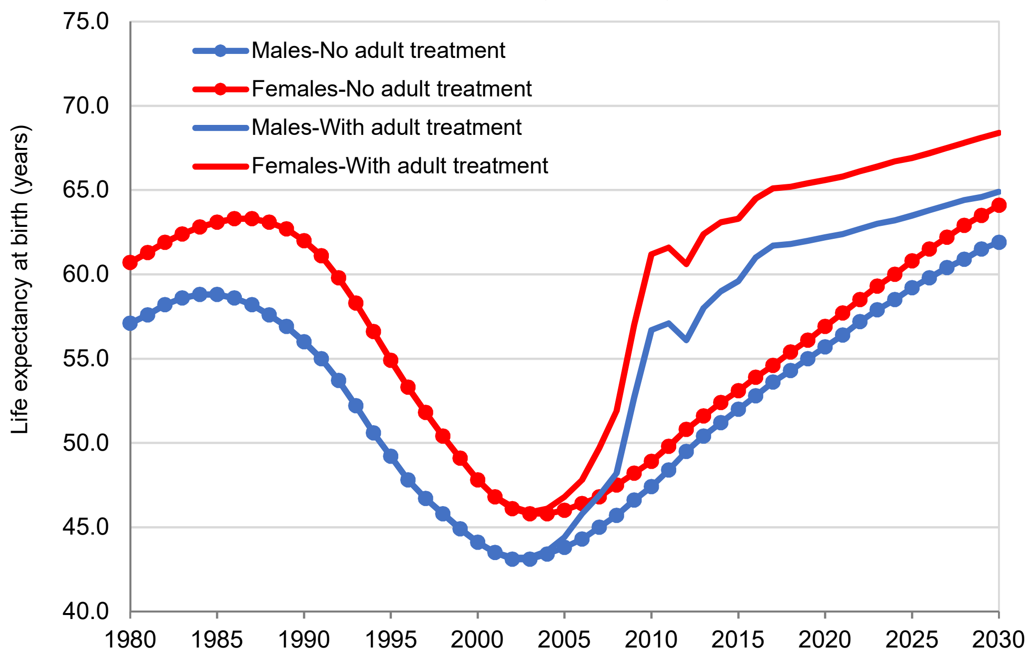
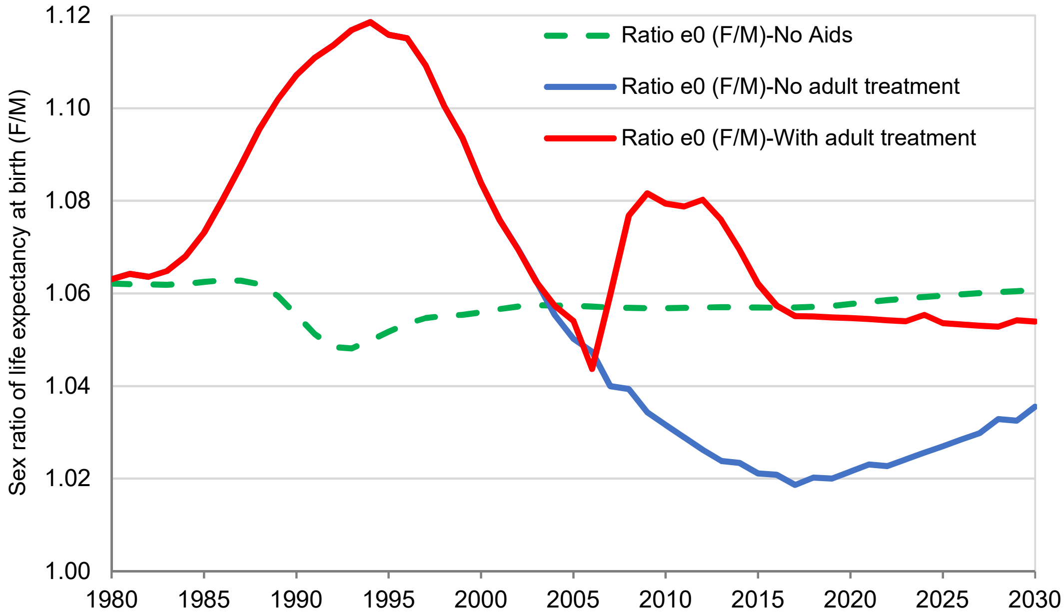


Figure 13. Sex ratios of life expectancy at birth (F/M): No-AIDS scenario and AIDS scenarios with and without adult treatment, Zimbabwe, 1980-2030



D. Measurement of treatment and it's role on mortality reduction

Within the AIM module of Spectrum, different options are made available to incorporate adult treatment in the modelling exercise. The module allows to introduce either the "number of adults receiving ART" or the "percent of adults in need of receiving ART". In the *2017 Revision*, the second option was used (and these values were used to derive the number of adults receiving ART). As stated above, for most time-series, estimates were derived from data provided by UNAIDS[16].

Over the years, there has been different efforts to measure the level of treatment received within populations affected by the HIV/AIDS epidemic (Mahy and others, 2010a and 2010b). However, the task at hand is quite complex and the quality of the information may vary considerably across countries and overtime. For illustration purposes, annex figures 2-A/B depict the levels and trends of the percentage of HIV-positive adult men and women who are in need of receiving ART for selected countries. Regardless of the accuracy of these estimates, what can be observed are important fluctuations over time. Considering the role that these fluctuations may have on the modelled mortality levels and trends (as shown in the case of Zimbabwe above), it was decided to compare the impact of fluctuating levels vs. smoothed levels of treatment on the modelled mortality estimates.

Figure 14 illustrates these two different approaches for which the cumulated "treatment levels" by sex in each scenario are comparable. Below, figure 15, illustrates the derived adult mortality estimates for both sexes combined using these different time-series of treatment. It can be observed that for some years (e.g. 2008) the mortality estimate may vary by over 65 deaths per 1,000 persons alive at age 15 (or over 10 per cent variation in some years), because of these variations.

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[16] Official estimates from UNAIDS may differ and they may have used a different option to incorporate adult treatment.

Figure 14. Estimates and projections of the percentage of HIV-positive adult men and women who are in need of receiving ART, with fluctuating and smoothed adult treatment levels, 2000-2020

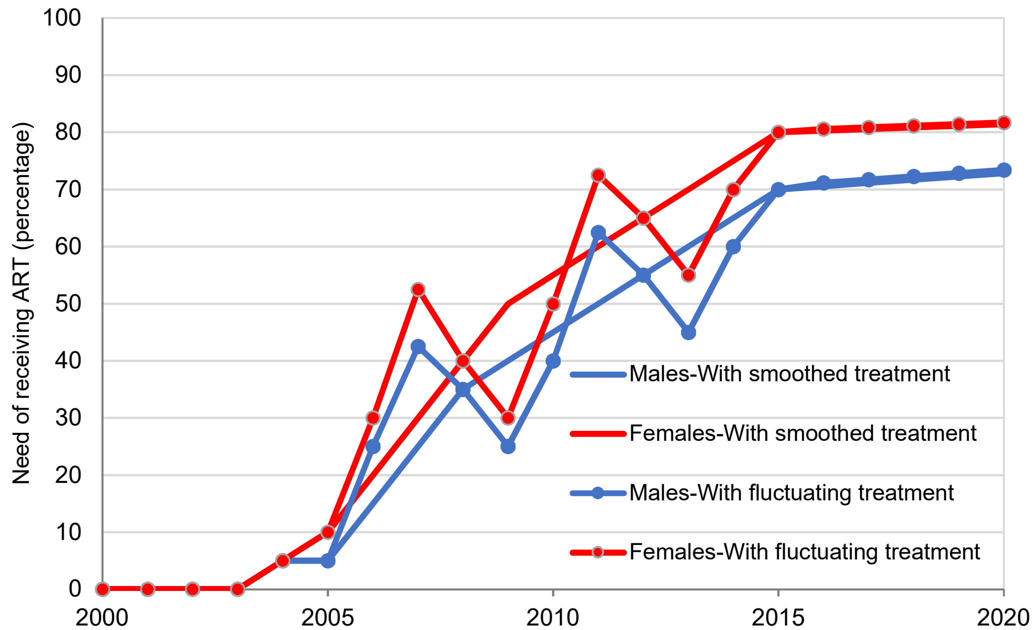
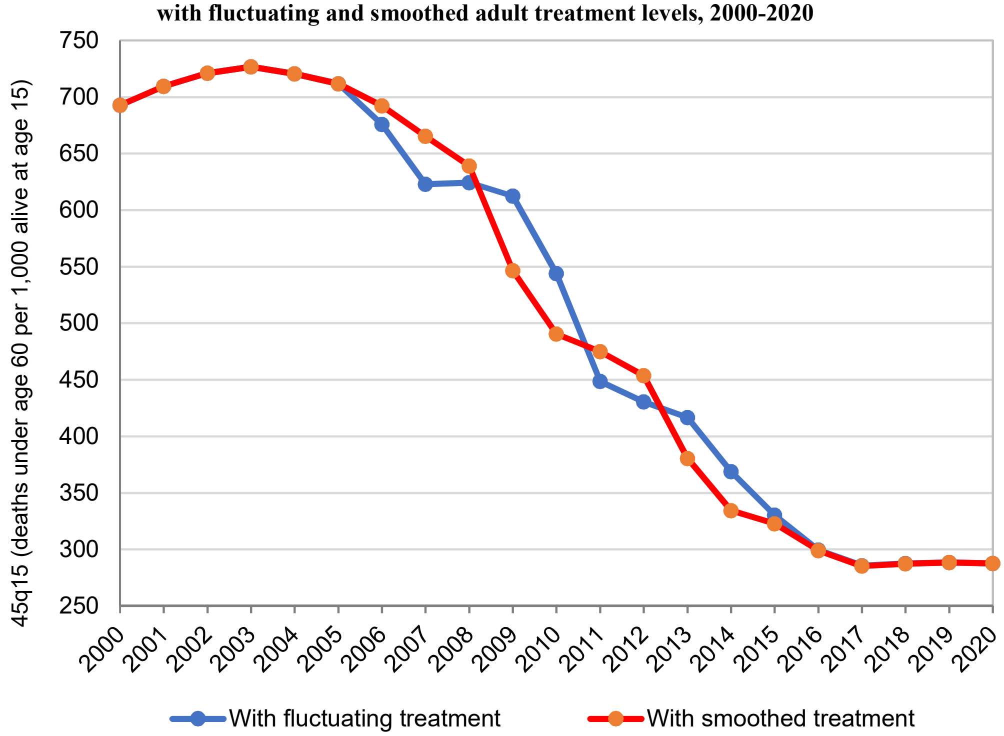


Figure 15. Adult mortality estimates (45q15) for both sexes combined: AIDS scenarios with fluctuating and smoothed adult treatment levels, 2000-2020



4. Discussion and recommendations

Civil registration systems that would allow to measure and monitor accurately the number of deaths by specific cause, including AIDS related deaths, are currently not available in the vast majority of countries highly affected by the HIV/AIDS epidemic. Even in countries where civil registration of deaths has yielded useful data (e.g. South Africa, Zimbabwe), deaths from HIV/AIDS are particularly likely to be reported as being from other diseases (Timaeus and others, 2004). Therefore, and for the time being, we are likely to continue to rely on models such as the one referred to in this paper to generate information related to AIDS mortality for many countries. "Model projections have become increasingly central to policy decision making and resource planning and allocation. For many uses, the value of these analyses for public health decision making depends on the accuracy of their projections" (Eaton and others, 2015, p. e598). "As models are increasingly used to support policy planning, advocate and allocate resources, and assess programmes, surveillance and trial data must also continue to be collected to validate and improve the information that underlie these processes" (ibid. p. e606). In that spirit, the results of this sensitivity analysis constitute a small step in trying to improve the modelling exercise of the HIV/AIDS epidemic and to contribute to a better assessment and measurement of different inputs and mortality outputs.

With close to 40 years after the onset of the HIV-AIDS epidemic, one could argue that using a model that relies on a no-AIDS scenario as the starting point is questionable. Indeed, the no-AIDS mortality levels and trends cannot be measured with a high degree of accuracy and could be responsible, in some cases, for inconsistencies in the modelled all-cause mortality estimates. When all-cause mortality estimates derived from such a "simulation" differed from observed mortality rates across multiple revisions or modelling exercises, it has been inferred by some researchers that the no-AIDS scenario could be one of the culprits (UNAIDS/WHO, 2003; Grassly and others, 2004; Masquelier and others, 2017). However, as observed in the case of Malawi above (figure 4) and with other countries highly affected by the HIV/AIDS epidemic (data not shown), the estimated no-AIDS mortality amongst adults can be relatively low as compared to the estimated all-cause mortality[17]. Considering that the so-called AIDS mortality may represent a large portion of the overall mortality in many countries at specific points in time, it was deemed important to further investigate what might be influencing the levels and trends by sex of the overall mortality once the AIDS impact had been incorporated, which is one of the objectives of this sensitivity analysis.

While looking at mortality estimates derived from surveys or other sources in several countries affected by the HIV/AIDS epidemic that are referred to in this paper, there is evidence that male mortality is usually higher than female mortality. By using the original sex ratios of HIV incidence, female mortality in several countries and age groups had been estimated to be similar or higher than that of male mortality. It was observed in different examples that the choice of the time-series in the sex ratio of HIV incidence had some implications on the derived mortality levels by sex and, overall, generated sex patterns mortality that were more in line with observed data. It was also highlighted that for most of the 18 countries included in figure A.1, the sex ratios of HIV incidence were not necessarily derived from country specific data. In that regard, it is recommended that more attention be given to better validate this input and evaluate its role on mortality patterns by sex. Attention should be given to both the level of the sex ratio and its trend overtime. Furthermore, if the derived input is based on a country specific survey (as in the case of Gabon), one should examine the implication of using such values and question the idea of deriving a full time-series starting in 1980 on limited data or data that refer to a much more recent period.

[17] It should be noted that across different revisions within the World Population Prospects, the mortality levels within the no-Aids scenario were in some cases intentionally maintained low in order to compensate for the high number of AIDS related deaths generated by the simulation exercise; this occurred mainly for selected countries with very high HIV prevalence levels.

Considering the difficulty in measuring treatment levels, the volatility of point estimates within the time-series and the important role that treatment plays on the estimated and projected survival prospects, it is recommended that more attention be given to the measurement of treatment. In the meantime, and within the framework of model estimates, it is suggested, as an interim solution, that the time-series be smoothed since they have the potential to distort mortality trends. Greater attention may also need to be given to the sex differentials in treatment levels and its impact on the projected survival prospects by sex.

Masquelier and others (2017, p. S77) had indicated that “discrepancies in levels, sex ratios and age patterns of adult mortality between empirical and UNAIDS estimates call for additional data quality assessments and improvements in estimation methods”. In that regard, aside from further investigation on the role of the treatment and the sex ratio of HIV incidence on mortality patterns, it could also be interesting to investigate the role of the age pattern of incidence by sex, and how such patterns may influence estimated and projected mortality levels and trends as well. Seemingly, these different inputs have the potential to distort the age and sex patterns of mortality.

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Annex Figures

Figure A. 1. Sex ratios of HIV incidence, original patterns, selected countries, 1980-2014

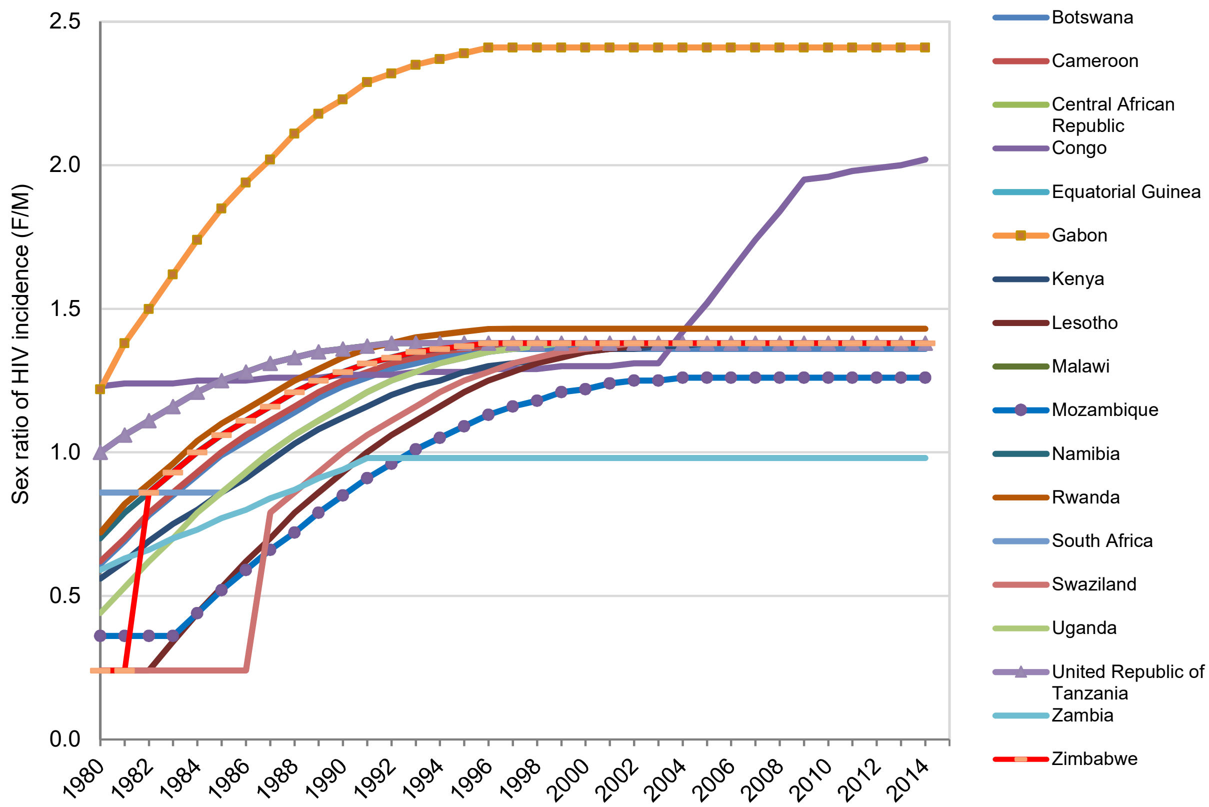
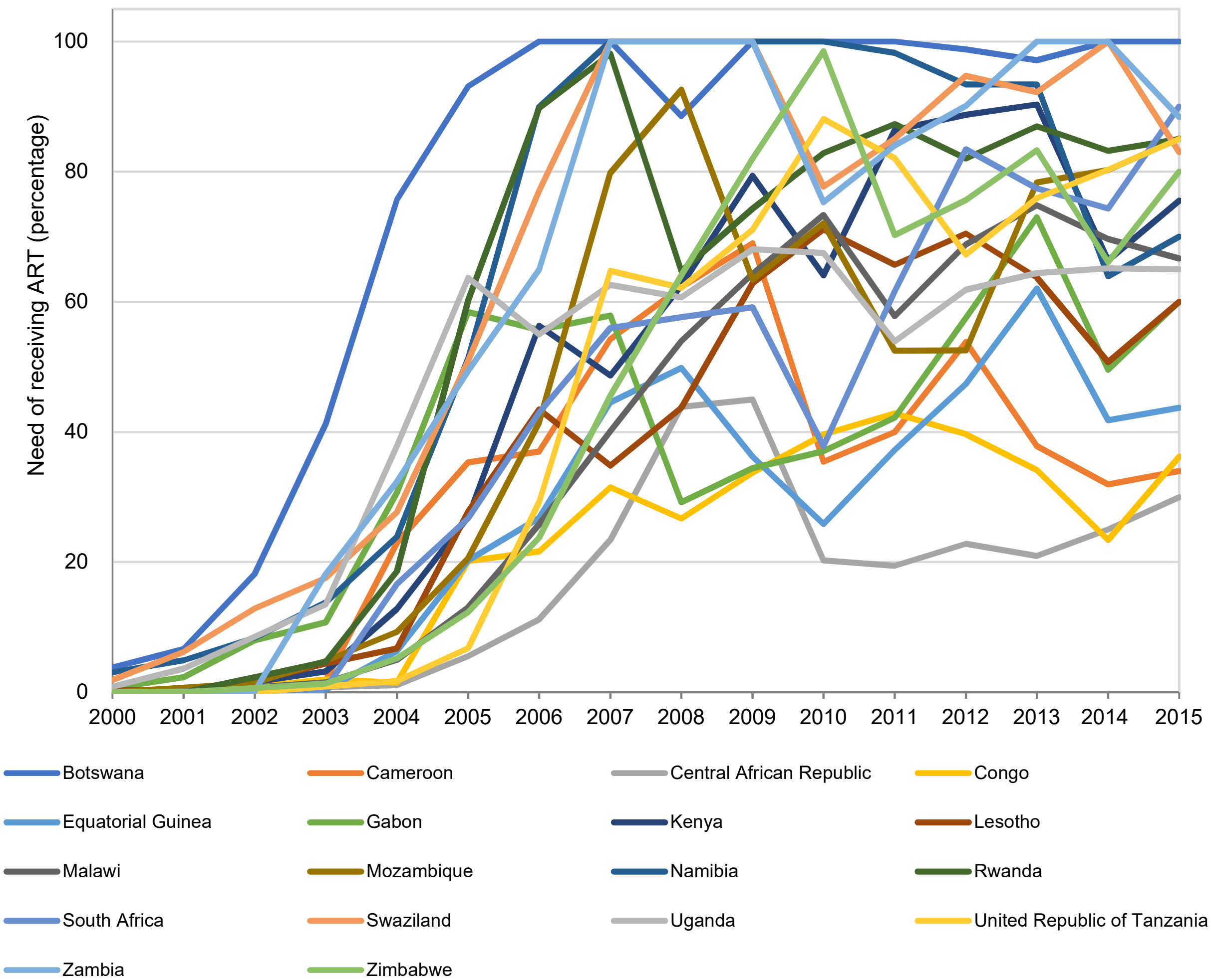


Figure A. 2. Estimates of the percentage of HIV-positive adult men (A) and women (B) who are in need of receiving ART, selected countries, 2000-2015[18]

A)



[18] Estimates presented in these figures are based on the original calculations while using data provided by UNAIDS. Within the *2017 Revision*, national estimates for a few countries were derived from sub-regional series, which required further calculations; in some series, point estimates with atypical values were also adjusted (not shown here). Official estimates from UNAIDS may differ and may be less volatile.

B)

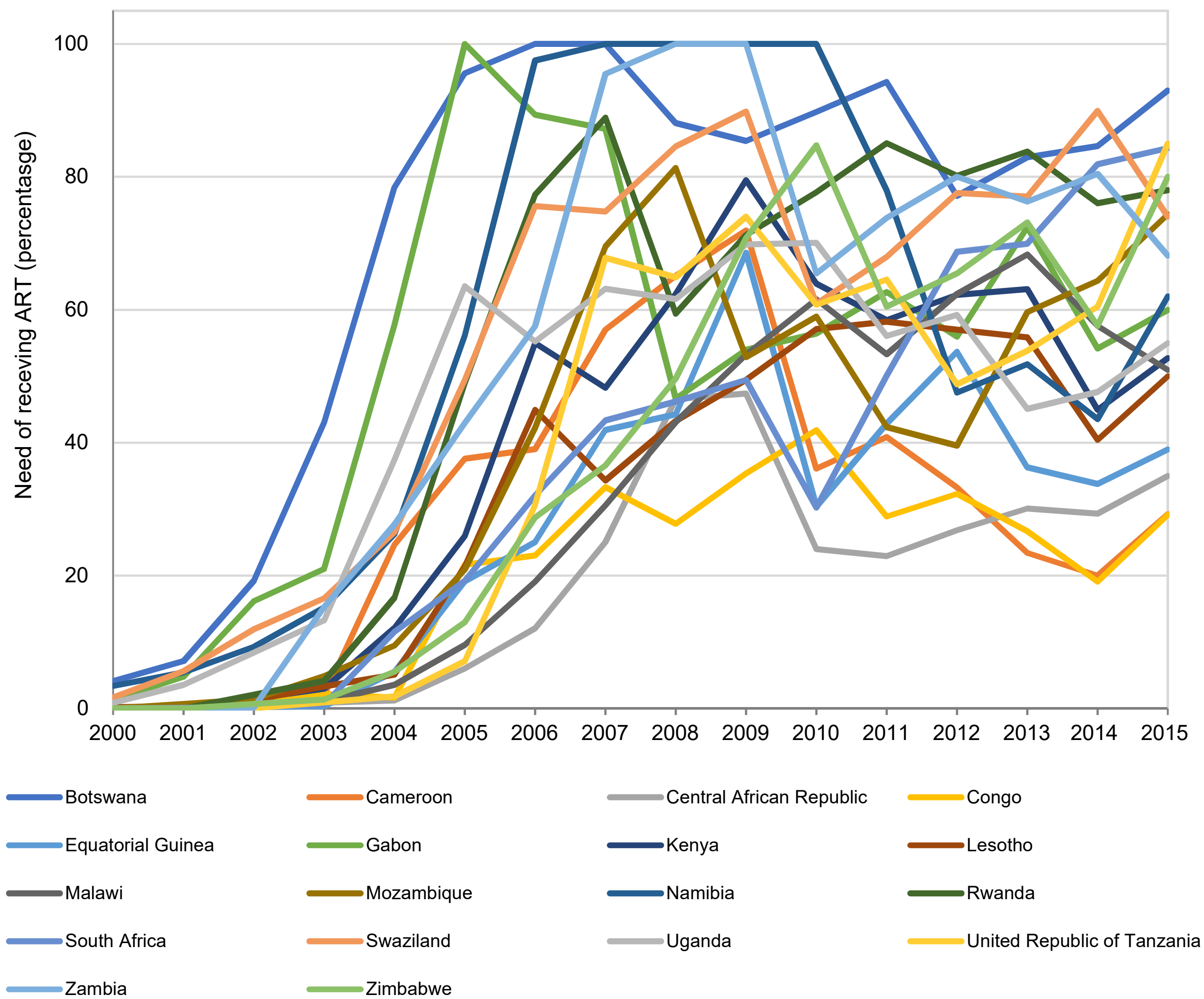
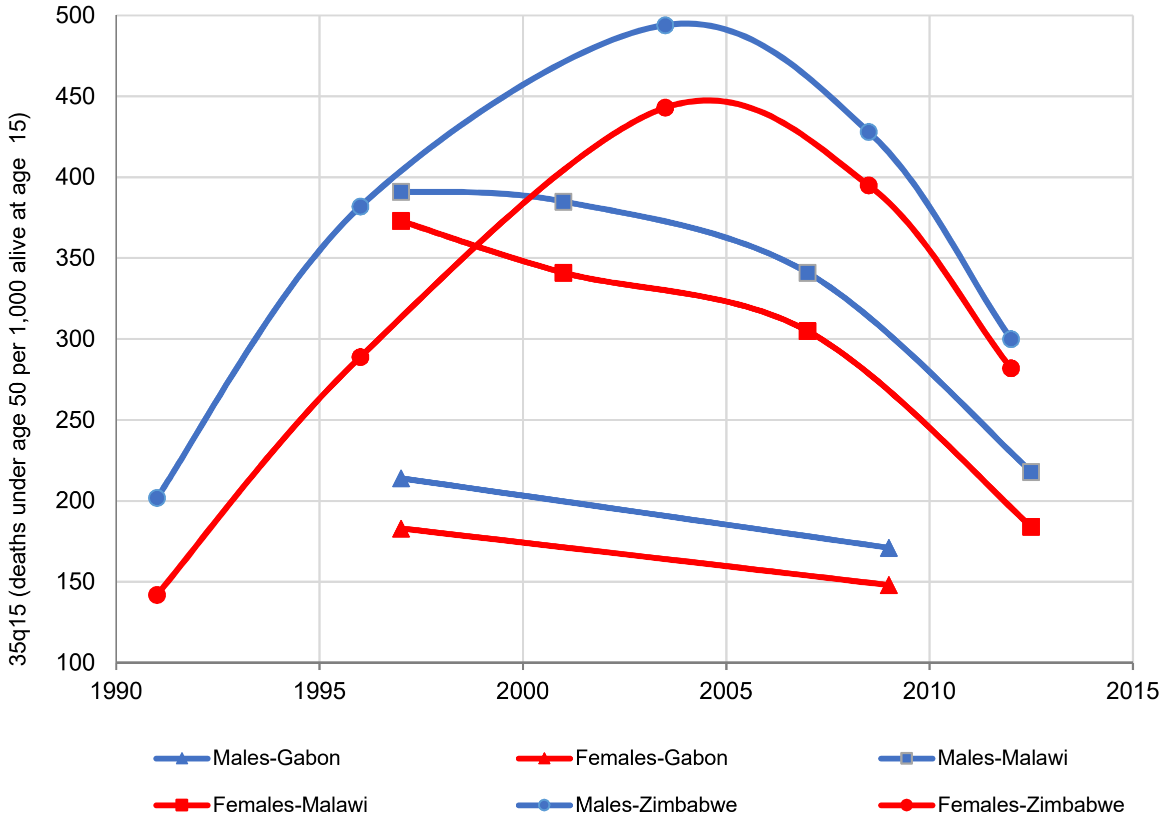

Need of receving ART (percentasge)
100
80
60
40
20
0
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Botswana
Cameroon
Central African Republic
Congo
Equatorial Guinea
Gabon
Kenya
Lesotho
Malawi
Mozambique
Namibia
Rwanda
South Africa
Swaziland
Uganda
United Republic of Tanzania
Zambia
Zimbabwe

Figure A. 3. Adult mortality estimates (35q15) for males and females based on Demographic Health Surveys - Gabon, Malawi and Zimbabwe- for selected periods



Source: Selected DHS reports (see sources in paper and references).