## Population Dynamics Strongly Influence HIV Estimates: A Descriptive Study

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### Background

Antiretroviral therapy (ART) and prevention of mother-to-child -transmission (PMTCT) interventions have been integral in the efforts to achieve HIV epidemic control and, at least in some areas, roll-out has been extensive. However, population growth will potentially result in an increasing burden of HIV even once transmission has been reduced to low levels, requiring sustained investment in HIV clinical services and prevention. Many high burden countries are experiencing stabilizing, post-peak levels of many key indicators used for measuring an HIV epidemic in a population, most notably incidence. However, while prevalence is declining and leveling off, factors such as a slow fertility decline and low background mortality and HIV mortality can impact the size of the HIV population, affecting the need for PMTCT and ART.

Estimates of HIV burden are required for policymaking and evaluation of policies and interventions, and even in contexts with relatively robust case and death reporting some modeling is required for estimating prevalence and new infections. Given the long duration of infection and its heterosexual transmission to infants, incorporating population dynamics is necessary for producing estimates. Different approaches to modeling have been used in the literature (see Eaton et al, 2013 for a comparison of many models), but UNAIDS and most countries make use of the Avenir Health software, Spectrum, and Estimates and Projections Package (EPP), which estimate the force of infection, incidence and prevalence using available data. Population projections, which include projecting the HIV population through time and illness categories, are done by Spectrum with a cohort component projection. Details about the methods used can be found in the Spectrum manual (Avenir Health, 2017). The methods have been discussed extensively in the literature and are not summarized here (Walker et al, 2001; Ghys et al, 2004; Stover et al, 2014; Stover et al, 2017). The cohort component projection methods have been stable for many iterations of the software, while some parameters for the HIV population are updated based on relevant study findings. UNAIDS produces yearly summaries of the global HIV burden based on national level estimates obtained using the Spectrum software. These estimates, produced in collaboration with country governments, are often used as national estimates and with other global partners, such as PEPFAR.

The purpose of this analysis is to investigate how population dynamics shape HIV projections, with particular focus on HIV indicators used from projections for program planning and evaluation. This study will look at the projections obtained when HIV incidence and prevalence estimates are held constant through time and then projections are made based on different population inputs, specifically by altering the fertility inputs. This approach allows an exploration of how the different population inputs change the projections when HIV is held constant. The analysis is descriptive and functionally a sensitivity analysis exploring how the same epidemic curves result in different key HIV indicators given different population contexts.

## Methods and Data

Spectrum 5.63 (Avenir Health, 2017) was used for all HIV estimates and population projections. This version was used by countries for the UNAIDS estimates published in 2018 (UNAIDS, 2018). The AIM module of Spectrum applies estimated incidence trends for adults age 15-49 to a cohort component population projection to project the population of people living with HIV (PLHIV) through time based on historical HIV prevalence, and program and surveillance data. In this analysis populations were projected to 2035 so that in examples where UNAIDS Fast Track targets of 90-90-90 (diagnose 90% of those infected, provide ART to 90% of those diagnosed, and achieve viral suppression for 90% of those on treatment) and then 95-95-95 are attained in 2020 and 2030 respectively, there would be adequate time to see the impact of low (epidemic controlled) HIV incidence on the population. Incidence curves used are based on the incidence curve from UNAIDS Lesotho projections in 2018. Lesotho was chosen because of its high HIV burden and because, as indicated by PEPFAR, Lesotho is close to attaining epidemic control (PEPFAR, 2018), thus representing a possible best case scenario for the incidence pattern in a high prevalence country. For projections with no ART, the incidence was used without alteration. For projection scenarios where epidemic control was attained according to Fast Track targets, incidence was obtained by using the Spectrum EPP tool to estimate incidence through 2035 with high levels of ART and PMCT coverage, corresponding to the Fast Track targets.

Analysis was conducted on a stationary population[1] with an initial population of 9,235,416 in 1970 and total fertility rate of 3 in all years and life expectancy of 55 years for men and 58 years for women in all years.  As this was a stationary population analysis, international migration was set to zero for all projections.

Using the stationary population as a baseline, projections were made with a growing population (TFR ) and with a declining population (TFR ) in each of the ART scenarios (no interventions and Fast Track interventions). To look at more realistic fertility scenarios, projections were also made for four fertility trends reflecting very high, high, medium and low fertility and adapted from the total fertility rates estimated for PEPFAR countries. As past fertility is not something that can be altered, I also looked at the timing of fertility decline. Starting with the medium fertility scenario, which reached a replacement TFR in 2035, I looked at scenarios where replacement was reached in 2020, 2010, 2000 and 1990 to see how, in this medium fertility paradigm, different timing of decline changed the HIV population projections and associated indicators.

## Results

Key indicators of the HIV population projected for different populations are compared below. Table 1 summarizes indicators from the stable, growing and declining populations in 2020 and 2030. Table 2 summarizes indicators from the different fertility scenarios in 2020 and 2030. Figures show results for the full projection through time.

**Stable Population with and without ART.** In a stable population with high burden of HIV, attaining the Fast Track goals would result in a slight increase in the total population, as mortality related to HIV is mitigated by ART. The effect on the HIV population is much more marked, as HIV survival is improved with ART. Achieving the Fast Track goals decreases new infections and the need for prevention of mother to child transmission, or the number of pregnancies to HIV positive women.

**Population Growth and Decline without ART.** As expected, in the absence of ART, the dynamics of the population dictate the HIV population: larger in a growing population and smaller in a shrinking

[1] A stable population has unchanging growth rate and age structure. A stationary population is the special case wherein that growth rate is zero (see Rowland, 2003).

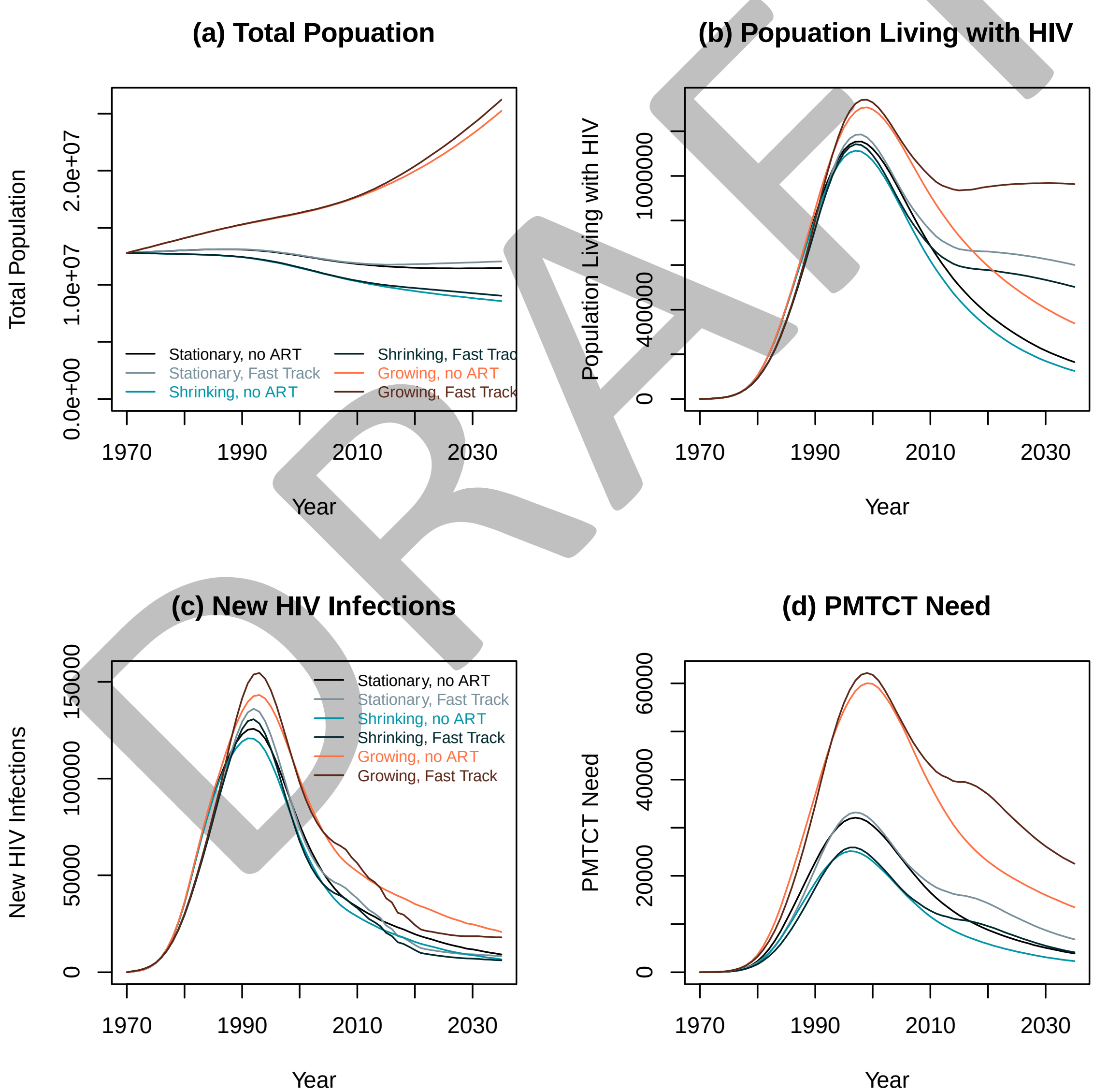
population. Considering the population of people living with HIV, Figure 1 shows that while the presence of the epidemic control interventions change the shape of the curve, it is the underlying population dynamics that are determining the level, as would be expected as the population living with HIV, for example, is a function of the estimated prevalence and the total population.

**Population Growth and Decline with ART.** In the scenario where Fast Track targets of 95-95-95 are achieved by 2030, the impact of population dynamics are pronounced. Notably, the stable and shrinking population have similar numbers of people living with HIV, though the shrinking population has slightly less. However, population growth coupled with high survival of PLHIV results in a steadily increasing PLHIV population even while ART coverage is high and incidence is low. As the population increases, even with incidence reduced by epidemic control efforts, the absolute number of new cases represented by that incidence rate can be quite large.

**Table 1**: Population Living with HIV, New Infections and Prevention of Mother-to-Child HIV Transmission (PMTCT) Need in Stable, Growing and Shrinking Populations in 2020 and 2030

| | **Total PLHIV Population** | | **New Infections** | | **PMTCT need** | |
|---|---|---|---|---|---|---|
| | **2020** | **2030** | **2020** | **2030** | **2020** | **2030** |
| *NO ART* | | | | | | |
| **Stable Model** | 380,306 | 216,572 | 19,605 | 11,765 | 8,177 | 5,059 |
| **Growing Population** | 595,026 | 405,850 | 35,214 | 24,749 | 23,012 | 16,015 |
| **Shrinking Population** | 321,206 | 169,704 | 15,666 | 8,806 | 5,859 | 3,114 |
| *Fast Track Targets Attained* | | | | | | |
| **Stable Model** | 660,494 | 627,289 | 14,076 | 9,217 | 14,311 | 8,706 |
| **Growing Population** | 951,633 | 967,400 | 24,398 | 18,578 | 36,952 | 26,163 |
| **Shrinking Population** | 577,215 | 533,595 | 11,388 | 6,996 | 9,572 | 5,490 |

**Figure 1:** Indicators over the projection period, from 1970 to 2035, are shown for the stationary model (black) and growing (orange) and shrinking (teal) populations in the no antiretroviral intervention and the Fast Track scenarios. (a) Total Population, (b) Population Living with HIV, (c) New HIV Infections and (d) PMTCT Need.



In all scenarios but the Fast Track growing population, the PLHIV population is declining by 2030 along with new infections and the need for prevention of PMTCT. However, having started with the same population in 1970 and having identical incidence trajectories, having a growing population can increase the absolute overall burden of HIV. Furthermore, the growing population can reduce the size of improvement linked to prevention and treatment interventions; the stationary model sees a 39% reduction in PMTCT need between 2020 and 2030, while the growing population declines 29% for the same levels of ART and PMTCT coverage and the same incidence level. While this study is not designed to provide statistical measures of how these populations are impacting the indicators, this difference that is driven solely by the underlying population dynamics suggests that fertility levels need to be considered when planning and evaluating program implementation based on these indicators.

**Fertility Levels and HIV Indicators.** In most countries, fertility levels are determining the growth (or decline) of population and many countries with high HIV burden have seen HIV undermine mortality gains and have persistent high fertility or minimal fertility decline. Four fertility scenarios were projected with the two ART intervention scenarios; these four scenarios were based on total fertility rate trends for Niger, Burkina Faso, Swaziland and Vietnam (UN WPP, 2017), representing very high, high, medium and low fertility regimes from within the PEPFAR countries. Table 2 shows that all but the low fertility scenario resulted in a much larger PLHIV population by 2035, as expected. The total numbers of PLHIV, new infections and PMTCT need behaved similarly, reflecting the fertility level whether in an ART or no ART environment.

In Figure 2, it can be seen that the uncertainty bounds given by the model overlap but that, for example, the lowest fertility and high fertility projections' uncertainty intervals do not overlap suggesting that while we cannot determine how large the difference due to the fertility trends are, these different scenarios are unlikely to be producing similar estimates of the population living with HIV in scenarios with epidemic control interventions. This is also true for new infections, as seen in Figure 3, and is much more pronounced for PMTCT need (or the number of pregnancies to women living with HIV) as seen in Figure 4.

**Table 2**: PLHIV Population, New Infections and PMTCT Need in Stable Population and Four Fertility Scenarios.

| | Total PLHIV Population | | New Infections | | PMTCT need | |
|---|---|---|---|---|---|---|
| | 2020 | 2030 | 2020 | 2030 | 2020 | 2030 |
| *NO ART* | | | | | | |
| **Stationary Model** | 380,306 | 216,572 | 19,605 | 11,765 | 8,177 | 5,059 |
| **Very High Fertility** | 1,567,438 | 1,389,693 | 122,809 | 110,032 | 127,250 | 109,009 |
| **High Fertility** | 1,431,532 | 1,209,872 | 105,705 | 89,101 | 94,821 | 75,016 |
| **Medium Fertility** | 1,046,080 | 747,876 | 64,296 | 44,845 | 35,377 | 21,436 |
| **Low Fertility** | 701,247 | 421,427 | 37,548 | 22,596 | 15,380 | 8,791 |
| *Fast Track Targets Attained* | | | | | | |
| **Stationary Model** | 660,494 | 627,289 | 14,076 | 9,217 | 14,311 | 8,706 |
| **Very High Fertility** | 2,205,780 | 2,544,943 | 79,090 | 76,589 | 197,274 | 165,398 |
| **High Fertility** | 2,057,803 | 2,325,524 | 69,917 | 64,050 | 147,539 | 115,391 |
| **Medium Fertility** | 1,615,876 | 1,709,447 | 45,324 | 34,668 | 56,413 | 34,304 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Low Fertility** | 1,172,524 | 1,166,326 | 27,120 | 17,781 | 25,255 | 14,703 |

**Figure 2**: Projected Population Living with HIV, 1970-2035, by fertility scenario with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.

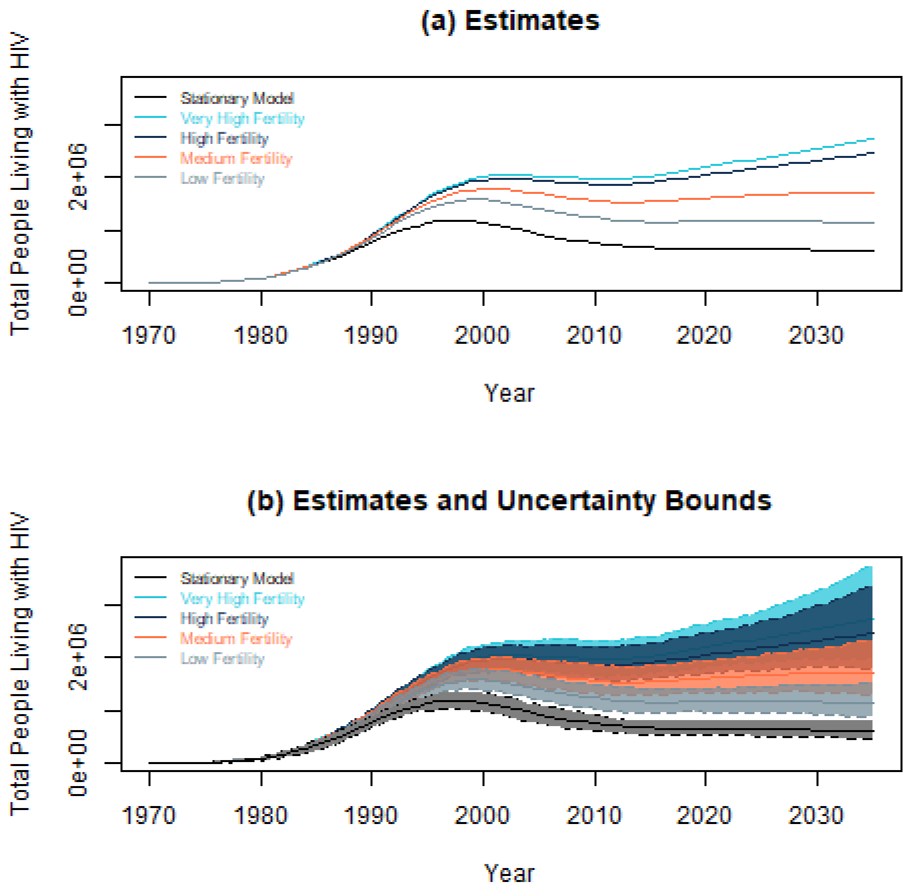


**Figure 3**: Projected New HIV Infections, 1970-2035, by fertility scenario with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.

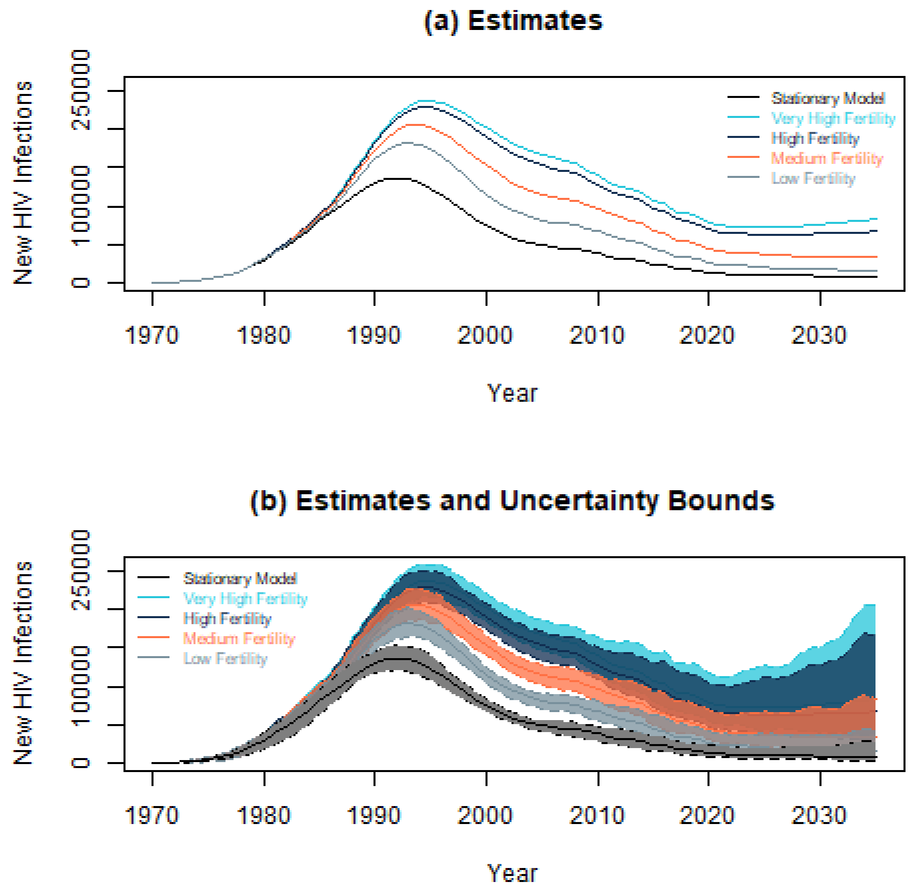
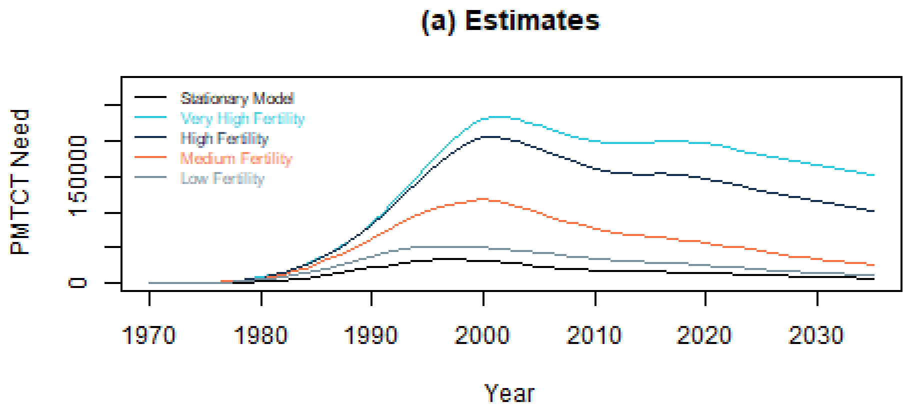
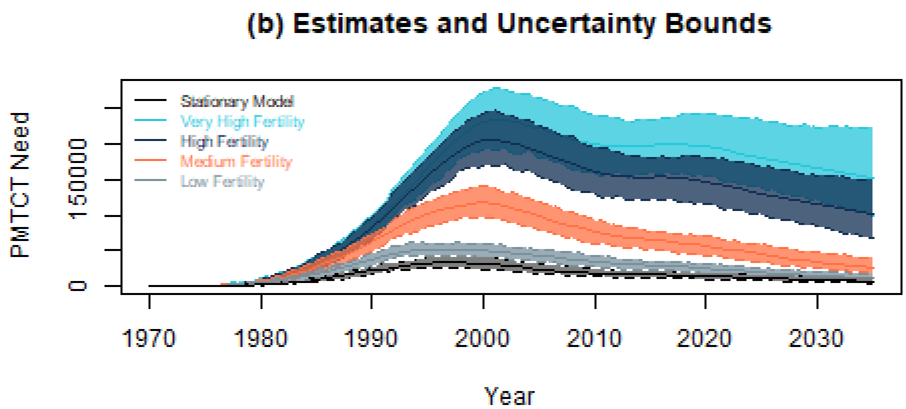


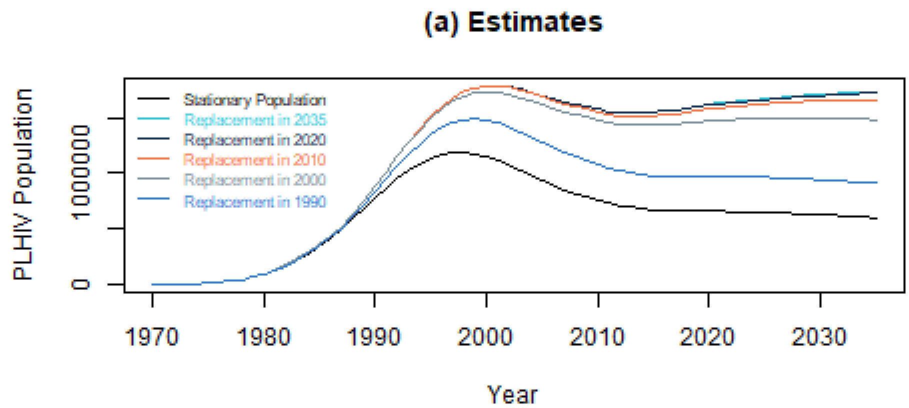
**Figure 4**: Projected PMTCT Need, 1970-2035, by fertility scenario with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.




**Timing of Fertility Decline and HIV indicators.** Low fertility scenarios have had substantial effects on HIV indicators, and the timing of that fertility decline can also greatly reduce the burden of HIV on a population. Five fertility scenarios are modeled in the Fast Track attainment scenario: replacement fertility achieved in 2035, in 2020, in 2010, in 2000 and in 1990. Population levels in these projections level off when fertility decline takes hold. However, this is not true for the PLHIV population. Reducing the fertility after the peak of the HIV epidemic has muted effects on HIV burden, while reduction of fertility at the same time as the peak of the HIV epidemic results in fewer numbers of PLHIV as the epidemic plateaus (see Figure 5). When the timing of fertility decline preceded the peak of the HIV epidemic, the burden of disease is further reduced, looking more like the PLHIV population in the stable population. New infections follow a similar pattern (Figure 6) where fertility decline occurring after the peak of the HIV epidemic has a minimal impact on the numbers of new infections. Fertility decline concurrent with the HIV epidemic's peak results in lower numbers of new infections throughout the epidemic, but when fertility declined before the peak of the HIV epidemic projections showed fewer new infections throughout the projection. PMTCT need (Figure 7), however, is the HIV indicator that sees the most pronounced effect from fertility decline. As soon as there is a decline in fertility there is a precipitous drop in the need for PMTCT, which corresponds to new infant infections. However, considering the uncertainty bands the model provides for the estimates of this indicator, it is challenging to make any comparisons.

**Figure 5**: Projected Population Living with HIV, 1970-2035, by fertility scenario based on timing of replacement (2035, 2020, 2010, 2000, 1990) with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.



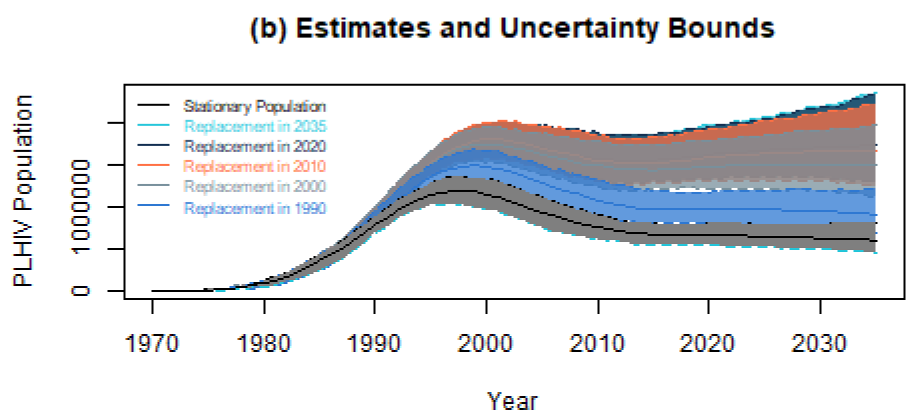
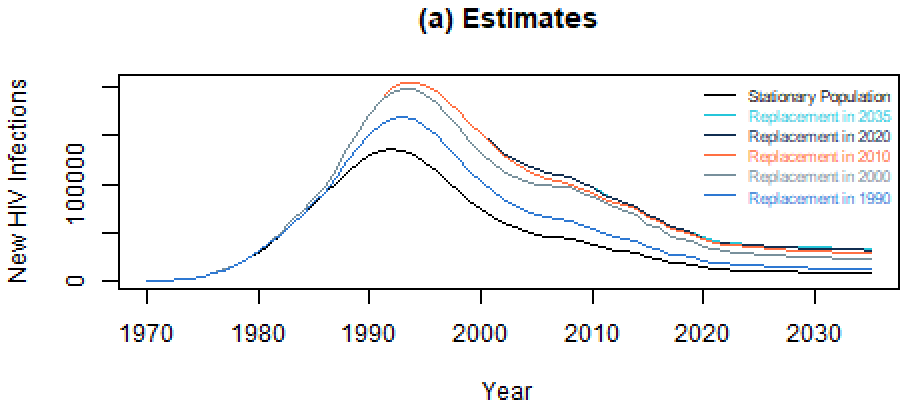



**Figure 6**: Projected New Infections, 1970-2035, by fertility scenario based on timing of replacement (2035, 2020, 2010, 2000, 1990) with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.



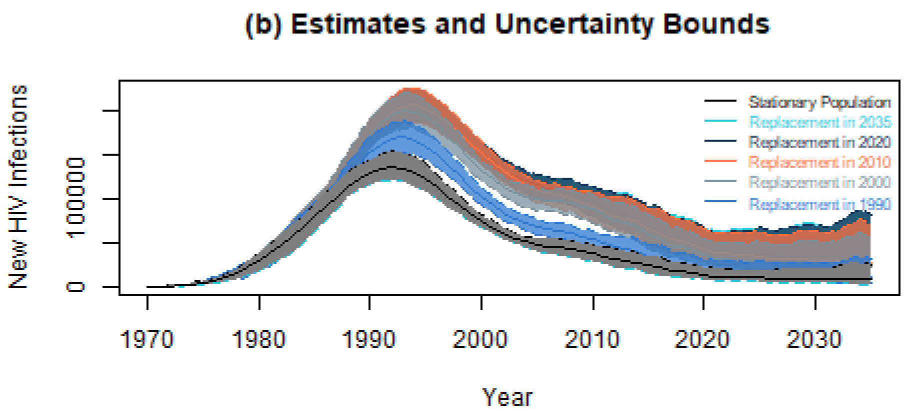
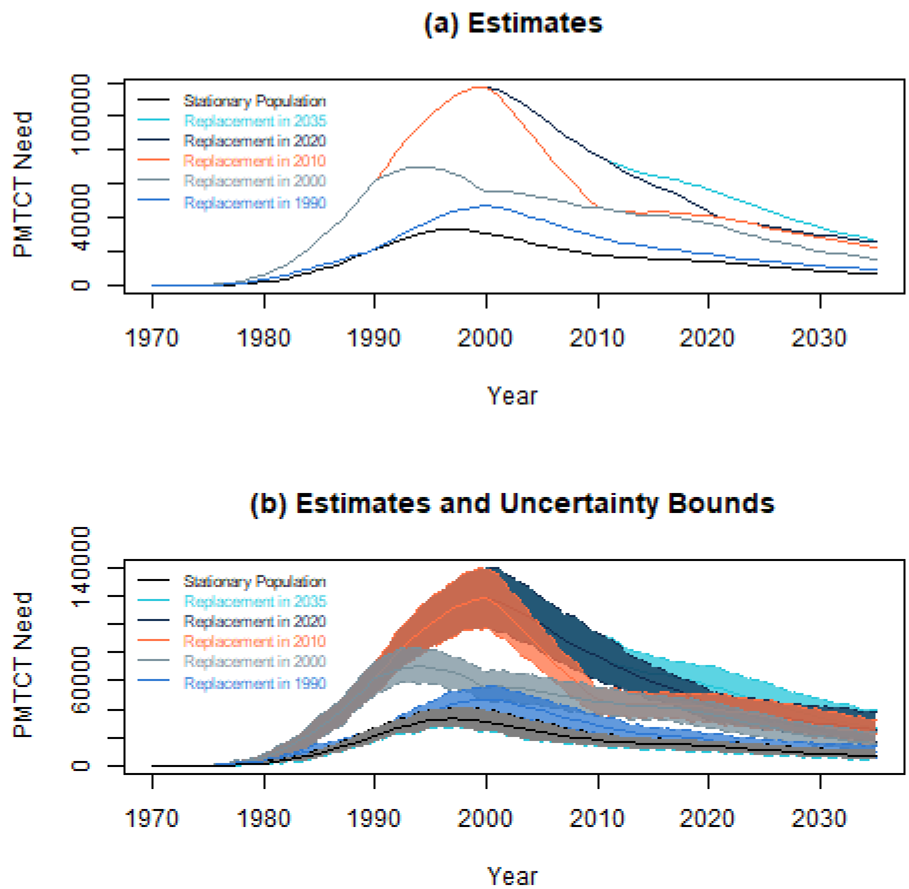



**Figure 7**: Projected PMTCT Need, 1970-2035, by fertility scenario based on timing of replacement (2035, 2020, 2010, 2000, 1990) with attained Fast Track targets, (a) Estimates and (b) Estimates with Uncertainty Bounds.




**Discussion**

The results seen in the stationary population isolate the estimated HIV force of infection (and associated incidence and prevalence) curve's influence on the HIV indicators. With a constant age structure and growth rate of zero, population dynamics are unchanging and thus not contributing to the changing of these HIV indicators through time. Comparing this to the simple examples of the growing or shrinking population demonstrate how large the effects of changes in the population dynamics, specifically altering the growth rate, will be on these HIV indicators. As we alter the population dynamics, shifting fertility so as to largely maintain the age structure while we see a constant growth rate (in either the growing or shrinking population), I have sought to underline the role that population growth has on the estimates. Moving into the fertility trajectories based on observed data from countries with high HIV burden, the age structure is no longer largely stable (nor is the growth rate), and we see that these elements are also having an effect on the HIV indicators, particularly compared to our stationary population wherein there were no population dynamics, only the stationary population upon which to project the HIV estimates. Fertility has a profound influence on these indicators, and particular if we consider simple comparisons of percent reduction through time, may greatly influence how the HIV epidemic is perceived to have changed.

In a generalized epidemic, the HIV epidemic is linked to population dynamics because transmission is predominantly through heterosexual sex and thus inextricably linked to fertility. It is no surprise that PLHIV populations, even when holding incidence trends and prevention and clinical interventions stable, will vary across fertility level. The contribution of this analysis is to provide quantifiable examples of the effects of population dynamics on the HIV estimates while holding the other drivers of the epidemic constant across projections. These estimates are used for program planning as well as assessment of how effective interventions are in addressing HIV epidemics. The analysis demonstrates that not only the level but also the timing of fertility decline can impact these indicators, highlighting the importance of capturing population dynamics accurately in these models. If the population projections fail to correspond well to the changing population of a country or area, these HIV estimates will be impacted. While many countries that use these estimates have substantial national level data on fertility and mortality to inform the population projections, as these projections are done at smaller and smaller geographic areas to attempt to obtain more granular HIV estimates, it is important to consider that limited information may be available to inform the population dynamics on which the projection is based and would alter, even with the same program data and incidence curve applied, the HIV indicators obtained from those projections.

The HIV indicators produced by these estimates have large uncertainty bounds, particularly as projected out past the data informing the HIV curves. When plotting the indicators with the uncertainty bounds, it is clear that the uncertainty bounds overlap for many of the fertility scenarios looked at in this analysis. However, it should be noted that while these uncertainty bounds are published, often point estimates are used and, even if the uncertainty bounds are quite wide, the differences in the point estimates across the different scenarios were in some cases in the thousands and tens of thousands. Even if still within the uncertainty bounds of both scenarios, these differences would have a profound effect on program planning or evaluation because of their scale. These uncertainty bounds are substantial to begin with for the HIV indicators of interest, and also are not used per se. The reliance on the point estimates as, for example, denominators for assessing program performance or persistent need for services, means that even changes that are small relative to total population can still be important from a planning or evaluation perspective. Not significant, in all likelihood, but then in the *use* of official statistics, one cannot guarantee that this issue of statistical significance is necessarily taken into consideration, particularly as the user becomes more and more distant from the person who did the calculation.

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