Supplementary appendix

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### Appendix

**Table A1.** HIV prevalence data by age and sex from three population-based surveys (SDHS 2007, SHIMS 2011, and PHIA 2016). Note that the youngest age-group in 2011 was 18-19 year-olds.

| Year | Sex   | Age     | Count | Prevalence (%) | 95% lb | 95% ub | Source    |
|------|-------|---------|-------|----------------|--------|--------|-----------|
| 2007 | Male  | 15 - 20 | 1272  | 1.9            | 1.2    | 2.7    | SDHS 2007 |
| 2007 | Male  | 20 - 25 | 779   | 12.4           | 10.2   | 14.8   | SDHS 2007 |
| 2007 | Male  | 25 - 30 | 553   | 27.8           | 24.1   | 31.6   | SDHS 2007 |
| 2007 | Male  | 30 - 35 | 380   | 43.7           | 38.8   | 48.7   | SDHS 2007 |
| 2007 | Male  | 35 - 40 | 321   | 44.9           | 39.5   | 50.4   | SDHS 2007 |
| 2007 | Male  | 40 - 45 | 230   | 40.7           | 34.4   | 47.1   | SDHS 2007 |
| 2007 | Male  | 45 - 50 | 229   | 27.9           | 22.3   | 33.9   | SDHS 2007 |
| 2007 | Male  | 50 - 55 | 106   | 28.3           | 20.2   | 37.2   | SDHS 2007 |
| 2007 | Male  | 55 - 60 | 70    | 17.4           | 9.5    | 27.0   | SDHS 2007 |
| 2007 | Male  | 60 - 65 | 227   | 13.3           | 9.2    | 18.0   | SDHS 2007 |
| 2007 | Female| 15 - 20 | 1151  | 10.1           | 8.4    | 11.9   | SDHS 2007 |
| 2007 | Female| 20 - 25 | 922   | 38.4           | 35.3   | 41.6   | SDHS 2007 |
| 2007 | Female| 25 - 30 | 648   | 49.2           | 45.4   | 53.0   | SDHS 2007 |
| 2007 | Female| 30 - 35 | 536   | 45.2           | 41.0   | 49.4   | SDHS 2007 |
| 2007 | Female| 35 - 40 | 441   | 37.7           | 33.2   | 42.3   | SDHS 2007 |
| 2007 | Female| 40 - 45 | 382   | 27.9           | 23.5   | 32.5   | SDHS 2007 |
| 2007 | Female| 45 - 50 | 342   | 21.4           | 17.2   | 25.9   | SDHS 2007 |
| 2007 | Female| 50 - 55 | 144   | 24.3           | 17.7   | 31.6   | SDHS 2007 |
| 2007 | Female| 55 - 60 | 102   | 9.6            | 4.7    | 16.0   | SDHS 2007 |
| 2007 | Female| 60 - 65 | 342   | 7              | 4.5    | 9.9    | SDHS 2007 |
| 2011 | Male  | 18 - 20 | 997   | 1              | 0.5    | 1.7    | SHIMS 2011|
| 2011 | Male  | 20 - 25 | 2093  | 7              | 5.9    | 8.1    | SHIMS 2011|
| 2011 | Male  | 25 - 30 | 1679  | 21             | 19.1   | 23.0   | SHIMS 2011|
| 2011 | Male  | 30 - 35 | 1267  | 37             | 34.4   | 39.7   | SHIMS 2011|
| 2011 | Male  | 35 - 40 | 993   | 47             | 43.9   | 50.1   | SHIMS 2011|
| 2011 | Male  | 40 - 45 | 726   | 46             | 42.4   | 49.6   | SHIMS 2011|
| 2011 | Male  | 45 - 50 | 571   | 43             | 39.0   | 47.1   | SHIMS 2011|
| 2011 | Female| 18 - 20 | 989   | 14             | 11.9   | 16.2   | SHIMS 2011|
| 2011 | Female| 20 - 25 | 2488  | 31             | 29.2   | 32.8   | SHIMS 2011|
| 2011 | Female| 25 - 30 | 1925  | 47             | 44.8   | 49.2   | SHIMS 2011|
| 2011 | Female| 30 - 35 | 1361  | 54             | 51.3   | 56.6   | SHIMS 2011|
| 2011 | Female| 35 - 40 | 1208  | 49             | 46.2   | 51.8   | SHIMS 2011|
| 2011 | Female| 40 - 45 | 976   | 40             | 36.9   | 43.1   | SHIMS 2011|
| 2011 | Female| 45 - 50 | 893   | 32             | 29.0   | 35.1   | SHIMS 2011|
| 2011 | Male  | 15 - 20 | 540.72| 3.9            | 2.4    | 5.7    | SHIMS 2011|
| 2016 | Male  | 20 - 25 | 901.2 | 4.2            | 3.0    | 5.6    | SHIMS2 2016|
| 2016 | Male  | 25 - 30 | 901.2 | 13.3           | 11.2   | 15.6   | SHIMS2 2016|

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| Year | Gender | Age Range | SHIMS2 2016 |
|------|--------|-----------|-------------|
| 2016 | Male   | 30 - 35   | 675.9       |
| 2016 | Male   | 35 - 40   | 540.72      |
| 2016 | Male   | 40 - 45   | 405.54      |
| 2016 | Male   | 45 - 50   | 180.24      |
| 2016 | Male   | 50 - 55   | 135.18      |
| 2016 | Male   | 55 - 60   | 135.18      |
| 2016 | Male   | 60 - 65   | 90.12       |
| 2016 | Female | 15 - 20   | 642.8       |
| 2016 | Female | 20 - 25   | 1414.2      |
| 2016 | Female | 25 - 30   | 964.2       |
| 2016 | Female | 30 - 35   | 771.36      |
| 2016 | Female | 35 - 40   | 771.36      |
| 2016 | Female | 40 - 45   | 578.52      |
| 2016 | Female | 45 - 50   | 578.52      |
| 2016 | Female | 50 - 55   | 257.12      |
| 2016 | Female | 55 - 60   | 257.12      |
| 2016 | Female | 60 - 65   | 192.84      |
Table A2. Select model parameters used to fit the EMOD transmission model to survey data on HIV prevalence, ART coverage, and population demographics from the Kingdom of eSwatini. Median and interquartile ranges (IQRs) reported for all dynamic parameters used in the calibration process (N=24) from 250 best-fitting parameter sets. A full description of all parameters and references available is at: http://idmod.org/docs/hiv/parameter-configuration.html

| Parameter                                           | Description                                                                                                                                                                                                 | Dynamic | Static value / fitted median (IQR) | Source |
|-----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------------------------|--------|
| Acute_Duration_In_Months                           | The time since infection, in months, over which the Acute_Stage_Infectivity_Multiplier is applied to coital acts occurring in that time-period.                                                          | no      | 3                                  | 1      |
| Acute_Stage_Infectivity_Multiplier                 | Multiplier acting on Base_Infectivity to determine the per-act transmission probability of an individual during acute stage.                                                                                | no      | 26                                 | 1      |
| AIDS_Duration_In_Months                            | The length of time, in months, prior to an AIDS-related death over which the AIDS_Stage_Infectivity_Multiplier is applied                                                                                 | no      | 9                                  | 1      |
| AIDS_Stage_Infectivity_Multiplier                  | Multiplier acting on Base_Infectivity to determine the per-act transmission probability of an individual during AIDS stage.                                                                                 | no      | 4.5                                | 1      |
| ART_CD4_at_Initiation_Saturating_Reduction_in_Mortality | The duration from ART enrollment to on-ART HIV-caused death increases with CD4 at ART initiation up to a threshold determined by this parameter value.                                                   | no      | 350                                |        |
| ART_dropout                                         | Exponentially distributed mean number of days from ART initiation until ART dropout.                                                                                                                        | no      | 7300                               |        |
| ART_Link_Max                                        | The right asymptote for the sigmoid trend of probability of ART linkage (given eligibility) over time.                                                                                                      | yes     | 0.952 (0.948 - 0.955)              |        |
| ART_Link_Mid                                        | The time of the inflection point in the sigmoid trend of probability of ART linkage (given eligibility) over time.                                                                                         | yes     | 2010.7 (2010.4 - 2010.9)           |        |
| ART_link_Min                                        | The left asymptote for the sigmoid trend of probability of ART linkage (given eligibility) over time.                                                                                                       | no      | 0                                  |        |
| ART_link_Rate                                       | The slope of the inflection point in the sigmoid trend of probability of ART linkage over time. A Rate of 1 sets the slope to a 25% change in probability per year.                                              | no      | 1                                  |        |
| Parameter                                      | Description                                                                 | Value       |
|-----------------------------------------------|-----------------------------------------------------------------------------|-------------|
| ART_Viral_Suppression_Multiplier              | Multiplier acting on Base_Infectivity to determine the per-act transmission probability of an individual on ART. Less-than-perfect (<100%) reduction in risk is attributed to sub-optimal adherence, drug resistance, and delay in viral load suppression from ART initiation. | no 0.08     |
| Base_Infectivity                              | The probability of transmission when none of the transmission multipliers apply to a coital act (or when all multipliers are set to 1). | yes 0.00233 (0.00231 - 0.00234) |
| CD4_At_Death_LogLogistic_Heterogeneity        | The inverse shape parameter of a Weibull distribution that represents the at-death CD4 cell count. | no 0.7      |
| CD4_At_Death_LogLogistic_Scale                | The scale parameter of a Weibull distribution that represents the at-death CD4 cell count. | no 2.96     |
| CD4_Post_Infection_Weibull_Heterogeneity      | The inverse shape parameter of a Weibull distribution that represents the post-acute-infection CD4 cell count. | no 0.2756   |
| CD4_Post_Infection_Weibull_Scale              | The scale parameter of a Weibull distribution that represents the post-acute-infection CD4 cell count. | no 560.43   |
| Circumcision_REduced_Acquire                  | The reduction of susceptibility to HIV by voluntary male medical circumcision (VMMC) | no 0.6      |
| Coital_Act_Rate                               | Number of coital acts per day for all relationships except commercial ones | no 0.33     |
| Coital_Act_Rate_Commercial                    | Number of coital acts per day for commercial relationships | no 0.002739726 |
| Coital_Dilution_Factor_2_Partners             | The multiplicative reduction in the coital act rate for all relationship types when an individual has exactly two current partners. Represents coital dilution. | no 0.75     |
| Coital_Dilution_Factor_3_Partners             | The multiplicative reduction in the coital act rate for all relationship types when an individual has exactly three current partners. Represents coital dilution. | no 0.6      |
| Coital_Dilution_Factor_4_Plus_Partners        | The multiplicative reduction in the coital act rate for all relationship types when an individual has exactly three current partners. Represents coital dilution. | no 0.45     |
| Parameter                                      | Description                                                                                                                                                                                                 | Default | Value |
|------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-------|
| Commercial_Condom_Max                          | The maximum asymptote for commercial relationships                                                                                                                                                               | no      | 0.85  |
| Commercial_Condom_Mid                          | The year of the inflection point for commercial relationships                                                                                                                                                 | no      | 1999.5|
| Commercial_Condom_Min                          | The minimum asymptote of the probability of condom use per coital act for informal relationships for commercial relationships                                                                                 | no      | 0.5   |
| Commercial_Condom_Rate                         | The rate proportional to the slope at the inflection point for commercial relationships                                                                                                                      | no      | 1     |
| Commercial_Form_Rate                           | Exponentially distributed mean number new relationships formed per day for commercial relationships                                                                                                         | no      | 0.15  |
| Condom_Transmission_Blocking_Probability       | The per-act multiplier of the transmission probability when a condom is used                                                                                                                                  | no      | 0.8   |
| Days_Between_Symptomatic_And_Death_Weibull_Heterogeneity | The time between the onset of AIDS symptoms and death is sampled from a Weibull distribution; this parameter governs the heterogeneity (inverse shape) of the Weibull.                   | no      | 0.5   |
| Days_Between_Symptomatic_And_Death_Weibull_Scale | The time between the onset of AIDS symptoms and death is sampled from a Weibull distribution; this parameter governs the scale of the Weibull.                                                               | no      | 618.34|
| Delay_Period_Mean                              | Delay from HIV infection until ART initiation for future ART scale-up scenarios, post 2016 (in days).                                                                                                         | no      | 180   |
| HIV_Adult_Survival_Scale_Parameter_Intercept    | Determines the intercept of the scale parameter for the Weibull distribution used to determine HIV survival time. Survival time with untreated HIV infection depends on the age of the individual at the time of infection, and is drawn from a Weibull distribution with shape parameter (see HIV_Adult_Survival_Shape_Parameter) and scale parameter. The scale parameter is allowed to vary linearly with age as follows $\lambda = HIV_{Adult\text{--}Survival\text{--}Scale\text{--}Parameter\text{–}Intercept} + HIV_{Adult\text{--}Survival\text{--}Scale\text{--}Parameter\text{–}Slope \times Age$ (in years). | no      | 21.182|
| Parameter Name                                           | Description                                                                                                                                                                                                 | Value |
|----------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| HIV_Adult_Survival_Scale_Parameter_Slope                 | This parameter determines the slope of the scale parameter for the Weibull distribution used to determine HIV survival time.                                                                                     | -0.2717 |
| HIV_Adult_Survival_Shape_Parameter                        | This parameter determines the shape of the Weibull distribution used to determine age-dependent survival time for individuals infected with HIV.                                                                  | 2     |
| HIV_Age_Max_for_Adult_Age_Dependent_Survival             | Survival time with untreated HIV infection depends on the age of the individual at the time of infection, and is drawn from a Weibull distribution with shape parameter and scale parameters (See HIV_Adult_Survival_Scale_Parameter_Intercept, HIV_Adult_Survival_Scale_Parameter_Slope, and HIV_Adult_Survival_Shape_Parameter). Although the scale parameter for survival time declines with age, it cannot become negative. To avoid negative survival times at older ages, this parameter, HIV_Age_Max_for_Adult_Age_Dependent_Survival, determines the age beyond which HIV survival is no longer affected by further aging. | 50    |
| HIV_Age_Max_for_Child_Survival_Function                   | The maximum age at which an individual's survival will be fit to the child survival function. If the value of this parameter falls between zero and the age of sexual debut, model results are not sensitive to this parameter as there is no mechanism for children to become infected between infancy and sexual debut. | 15    |
| HIV_Child_Survival_Rapid_Progressor_Fraction             | The proportion of HIV-infected children who are rapid HIV progressors.                                                                                                                                       | 0.57  |
| HIV_Child_Survival_Rapid_Progressor_Rate                 | The exponential decay rate, in years, describing the distribution of HIV survival for children who are rapid progressors.                                                                                               | 1.52  |
| HIV_Child_Survival_Slow_Progressor_Scale                  | The Weibull scale parameter describing the distribution of HIV survival for children who are slower progressors.                                                                                                  | 16    |
| Variable                                         | Description                                                                 | Constraint | Value | Range          |
|-------------------------------------------------|-----------------------------------------------------------------------------|------------|-------|----------------|
| HIV_Child_Survival_Slow_Progressor_Shape         | The Weibull shape parameter describing the distribution of HIV survival for children who are slower progressors. | no         | 2.7   |                |
| Informal_Condom_Max                             | The maximum asymptote for informal relationships                            | yes        | 0.337 | (0.321 - 0.355)|
| Informal_Condom_Mid                             | The year of the inflection point for informal relationships               | yes        | 1992.6| (1992.2 - 1992.9)|
| Informal_Condom_Min                             | The minimum asymptote of the probability of condom use per coital act for informal relationships | no         | 0     |                |
| Informal_Condom_Rate                            | The rate proportional to the slope at the inflection point for informal relationships |            | 3.003 | (2.941 - 3.076)|
| Informal_Form_Rate                              | Exponentially distributed mean number new relationships formed per day for informal relationships | yes        | 0.00146| (0.00134 - 0.00155)|
| Male_To_Female_Relative_Infectivity_Multiplier_Old | An array of scale factors governing the susceptibility of females relative to males, by age ≥ 25 | yes        | 2.844 | (2.727 - 2.958)|
| Male_To_Female_Relative_Infectivity_Multiplier_Young | An array of scale factors governing the susceptibility of females relative to males, by age < 25 | yes        | 4.894 | (4.747 - 5.041)|
| Marital_Condom_Max                              | The maximum asymptote for marital relationships                            | yes        | 0.218 | (0.207 - 0.231)|
| Marital_Condom_Mid                              | The year of the inflection point for marital relationships               | yes        | 2001.8| (2001.5 - 2002.1)|
| Marital_Condom_Min                              | The minimum asymptote of the probability of condom use per coital act for informal relationships for marital relationships | no         | 0     |                |
| Marital_Condom_Rate                             | The rate proportional to the slope at the inflection point for marital relationships | yes        | 2.407 | (2.252 - 2.524)|
| Marital_Form_Rate                               | Exponentially distributed mean number new relationships formed per day for marital relationships | yes        | 0.00046| (0.00044 - 0.0005)|
| Maternal_Infection_Transmission_Probability     | The probability of transmission of infection from mother to infant at birth. |            | 0.3    |                |
| Maternal_Transmission_ART_Multiplier            | The maternal transmission multiplier for on-ART mothers.                   | no         | 0.03334|                |
| Variable                          | Description                                                                 | Allowed Values                                                                 | Value          |
|----------------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------|
| preART_Link_Max                  | The right asymptote for the sigmoid trend of probability of preART linkage (given eligibility) over time. | yes                                                                          | 0.807 (0.783 - 0.829) |
| preART_Link_Mid                  | The time of the inflection point in the sigmoid trend of probability of preART linkage (given eligibility) over time. | yes                                                                          | 1995.7 (1995.1 - 1996.4) |
| preART_link_Min                  | The left asymptote for the sigmoid trend of probability of preART linkage (given eligibility) over time. | yes                                                                          | 0.00325 (0 - 0.03031) |
| preART_link_Rate                 | The slope of the inflection point in the sigmoid trend of probability of preART linkage over time. A Rate of 1 sets the slope to a 25% change in probability per year. | no                                                                           | 1              |
| Proportion_Low_Risk              | Proportion of the initial population that is low risk                        | yes                                                                          | 0.73 (0.721 - 0.742) |
| Seed_Year                        | Year in which the epidemic is seeded into high risk groups                    | yes                                                                          | 1982.7 (1982.4 - 1983.2) |
| Sexual_Debut_Age_Female_Weibull_Heterogeneity | The inverse shape of the Weibull distribution for female debut age. | yes                                                                          | 0.309 (0.293 - 0.322) |
| Sexual_Debut_Age_Female_Weibull_Scale | The scale term of the Weibull distribution for female debut age. | yes                                                                          | 16.302 (16.166 - 16.396) |
| Sexual_Debut_Age_Male_Weibull_Heterogeneity | The inverse shape of the Weibull distribution for male debut age. | yes                                                                          | 0.042 (0.04 - 0.05) |
| Sexual_Debut_Age_Male_Weibull_Scale | The scale term of the Weibull distribution for male debut age. | yes                                                                          | 17.499 (17.357 - 17.699) |
| Sexual_Debut_Age_Min             | The minimum age at which individuals become eligible to form sexual relationships. | no                                                                           | 13             |
| Transitory_Condom_Max            | The maximum asymptote for transitory relationships                            | yes                                                                          | 0.103 (0.089 - 0.117) |
| Transitory_Condom_Mid            | The year of the inflection point for transitory relationships                 | yes                                                                          | 1996.7 (1996.1 - 1997) |
| Transitory_Condom_Min            | The minimum asymptote of the probability of condom use per coital act for informal relationships for transitory relationships | no                                                                           | 0              |
| Transitory_Condom_Rate           | The rate proportional to the slope at the inflection point for transitory relationships. | yes                                                                          | 2.998 (2.878 - 3.106) |
| Transitory_Form_Rate                  | Exponentially distributed mean number new relationships formed per day for transitory relationships | no      | 0.001047839 |
|--------------------------------------|---------------------------------------------------------------------------------------------------|---------|------------|
| Transitory_Weibull_Heterogeneity     | Inverse of the Weibull shape (1/kappa) parameter of relationship duration in years for transitory relationships | no      | 0.833333333 |
| Transitory_Weibull_Scale             | Weibull scale parameter of relationship duration in years for transitory relationships.           | no      | 0.956774771 |
Figure A1. Best-fitting HIV prevalence trajectories (N=250) by sex, five-year age group, and year, with survey prevalence point estimates and 95% confidence intervals from three surveys [SDHS (2007), SHIMS (2011), and PHIA (2016)] overlaid.
Modelled effect estimates

We used four metrics to quantify the population-level effectiveness of each scenario: 1) annual incidence, 2) annual mortality, 3) attributable reduction in cumulative incidence, and 4) percent reduction in cumulative mortality. Annual incidence was calculated as the number of new infections over a one-year period divided by the number of uninfected individuals at the mid-year, reported per 100 person-years (py). Annual mortality was calculated as the number of HIV/AIDS deaths in a year divided by the number of individuals alive at the mid-year, reported per 100 py. The attributable reduction in cumulative incidence (AR) between an intervention scenario \( i \) and a counterfactual scenario \( j \) was calculated as the difference in cumulative incidence between scenarios \( j \) and \( i \) divided by the cumulative incidence in scenario \( j \),

\[
AR_{ij} = 1 - \frac{\sum_{\text{year}=n}^{m} ninf_{i, \text{year}}}{\sum_{\text{year}=n}^{m} py_{i, \text{year}}}
\]

\[
= \frac{\sum_{\text{year}=n}^{m} ninf_{j, \text{year}}}{\sum_{\text{year}=n}^{m} py_{j, \text{year}}}
\]

where cumulative incidence is the sum over a time horizon (start year = \( n \), end year = \( m \)) of the number of yearly new infections (ninf\(_{\text{year}}\)) occurring divided by the sum over the same time horizon (n-m) of the number of yearly person-years (py\(_{\text{year}}\)) among uninfected individuals. Percent reduction in mortality was estimated similarly, with the denominator being all person-years lived regardless of HIV status. LOESS (Locally weighted smoothing) was used to smooth and plot the time series of each metric from 250 model parametrizations. Credible intervals (CrI) for all effect estimates are calculated as 95% quantiles of the 250 best-fitting parameter sets.
Figure A2. Number of individuals on ART by age and sex under three ART scale-up scenarios. The intersection of curves indicates the year in which a more aggressive ART scale-up scenario results in fewer PLHIV on treatment.
Figure A3. Proportion of transmissions from index cases in the acute (< 3 months) and early (< 1 year) stages of infection, by sex and year, under the status-quo scenario (scenario 1). Loess curves (dark lines) of 250 best-fitting simulations overlaid.
Figure A4. Proportion of transmissions over time by ART state of transmitter (never initiated ART, currently on ART, or dropped out from ART) for two modelling scenarios. ART coverage among adults 15-49 (% of HIV infected currently on ART) shown in dashed black line.
Figure A5. Age-distribution of HIV-1 acquisitions (a) and transmissions (b) by sex and year (2005 – 2050) under the status-quo scenario (scenario 1). The scale-up of ART over time shifted both the age of acquisition and age of transmission older. The phenomenon of the aging HIV-1 epidemic has been observed in age-shifts in HIV prevalence across sub-Saharan Africa (SSA) \(^{49,50}\), (including in the Kingdom of Eswatini\(^{51}\)) over the past two decades. Age-specific shifts in HIV incidence over time are the result of dynamic epidemic processes that lead to differential changes in the transmission rate by age and sex. These processes, which may be acting simultaneously, include aging HIV prevalence (the source of transmissions), age-specific targeting of HIV prevention to younger cohorts, and delayed age at infection with a declining force of infection. While most of the empirical data on epidemic aging is on shifting prevalence, our results confirm previous model-based evidence of shifting age-distribution of HIV incidence \(^{52}\).
Sensitivity analyses:

We conducted sensitivity analyses around the contribution of four key parameters, both univariately and bivariately, to our incidence estimates for scenario 1:

- a. Acute_Duration_In_Months
- b. Acute_Stage_Infectivity_Multiplier
- c. Delay_Period_Mean (time from infection to ART initiation in the UTT era)
- d. ART_Viral_Suppression_Multiplier

1) Acute stage parameters

The primary sources of uncertainty in our model arise from the extent to which unsuppressed individuals contribute to onward transmission in the era of test and treat. Estimating this quantity has been challenging, as it is governed by parameters with high levels of uncertainty and disagreement in the literature, including the duration of acute and early HIV infection (literature modelled parameter ranges from 2 - 5 months\(^7,8\)) and the elevated infectiousness during those periods (literature modelled parameter ranges from a multiplier of 10 - 30\(^7,9\)). Sensitivity analyses around the contribution of four key parameters to our incidence estimates for scenario 1 in our model are shown below. Though the overall shape of the incidence curves over time remained relatively the same, results of this analysis highlight the sensitivity of our incidence (age 15-49) estimates to uncertainty of both acute stage infectivity multiplier and acute stage duration. We tested five values for acute stage infectivity multiplier (ranging from 10 - 30 by 5-unit increments), and five values of acute stage duration in months (ranging from 1 - 5 months by 1-month increments).
Figure A6. Sensitivity of HIV incidence over time (baseline scenario) varying two key parameters: a) acute stage duration in months, b) acute stage infectivity multiplier (relative to the chronic stage), and c) the bivariate sensitivity over combinations of both parameter estimates, evaluated at four time-points (2016, 2020, 2030, and 2050). The parameter values used in the final calibrated model noted with a (+). In each univariate sensitivity analysis, all other parameters are held according to the original calibration.
Table A3. Numerical results of the effect of varying acute stage infectivity multiplier and acute duration on incidence. Varying acute duration between 1-5 months contributed more to overall uncertainty in incidence than varying acute phase multiplier from 10-30. The combination of both parameters resulted in year-specific incidence varying by ~0.5 per 100 py (for example, in year 2050 the combination of uncertainty from both parameters resulted in incidence ranging between 0.4 and 0.9 per 100py).

| Year | Acute stage infectivity multiplier (acute duration set to 3 month) | Acute duration in months (acute stage multiplier set to 26) | Both parameters |
|------|---------------------------------------------------------------|------------------------------------------------------------|-----------------|
| 2016 | 1.2 – 1.5                                                     | 1.2 – 1.6                                                  | 1.0 – 1.6       |
| 2020 | 1.1 – 1.4                                                     | 1.1 – 1.5                                                  | 1.0 – 1.5       |
| 2030 | 0.9 – 1.1                                                     | 0.8 – 1.2                                                  | 0.7 – 1.2       |
| 2050 | 0.5 – 0.8                                                     | 0.5 – 0.9                                                  | 0.4 – 0.9       |

2) ART efficacy and time to ART initiation

For the parameters ART_Viral_Suppression_Multiplier (ART efficacy) and Delay_Period_Mean (time from infection to ART initiation), the overall shape of the incidence curves over time also remained relatively similar to the calibrated model, and incidence was highly sensitive to ART efficacy. We tested eleven values for ART_Viral_Suppression_Multiplier (ranging from 0.8 - 1 by 0.02-unit increments), and seven values of Delay_Period_Mean (ranging from 0 - 360 days by 60-day increments). The full uncertainty analysis for each univariate and bivariate uncertainty analysis is shown below.
Figure A7. Sensitivity of HIV incidence over time in the baseline scenario (model scenario 1) varying two key parameters: a) ART efficacy, b) time from infection to ART initiation, and c) the bivariate sensitivity over each combination of the two parameter values, evaluated at four time-points (2016, 2020, 2030, and 2050). Dashed black lines in univariate and (+) in bivariate sensitivity analyses indicate actual model parameters used in final calibrated model. In each univariate sensitivity analysis, all other parameters are held according to the original calibration.
**Table A4.** Numerical results of the effect of varying ART_Viral_Suppression_Multiplier and the Delay_Period_Mean on incidence. Varying ART efficacy contributed substantially more to overall uncertainty than varying time from infection until ART initiation. The combination of both parameters resulted in year-specific incidence per 100 py varying from 0.8 to 0.9 per 100 py (for example, in year 2016 the combination of uncertainty from both parameters resulted in incidence ranging between 1.0 and 1.9 per 100py). Most of the variability in the results were driven by varying ART efficacy with negligible differences in incidence varying the time from infection until ART initiation.

| Year | ART Viral Suppression Multiplier (Delay Period Mean set to 180 days) | Delay Period Mean (ART Viral Suppression Multiplier set to 0.92) | Both parameters |
|------|---------------------------------------------------------------|---------------------------------------------------------------|-----------------|
| 2016 | 1.0 – 1.8                                                    | 1.4 – 1.5                                                    | 1.0 – 1.9       |
| 2020 | 1.0 – 1.8                                                    | 1.3 – 1.4                                                    | 0.9 – 1.8       |
| 2030 | 0.7 – 1.5                                                    | 1.0 – 1.1                                                    | 0.6 – 1.5       |
| 2050 | 0.4 – 1.1                                                    | 0.7 – 0.8                                                    | 0.4 – 1.2       |
3) **ART efficacy and time to ART initiation**

Given that our model did not predict epidemic control even under the most optimistic ART coverage, we sought to understand what intensity of test and treat could lead to theoretical epidemic control (below an incidence of 1/1000 in our model). Under the optimistic 100% ART scenario (scenario 5 in our model), three factors limit epidemic control: 1) the time from infection to diagnosis and treatment, 2) the efficacy of ART, and 3) the rate of ART dropout. We reran our model under 100% ART coverage but decreasing the time from infection to ART uptake (from 180 days to 0 days), while also varying the efficacy of ART in reducing transmission (from 92% to 100% efficacy). Epidemic control was reached only where ART efficacy was at or above 98% and time from HIV infection until ART initiation is immediate. Time from infection until ART initiation at 100% ART coverage accounted for less of the variability in HIV incidence and only had a strong effect when set to zero, or immediate uptake of ART once infected. Even initiation within an average of 2 months from infection resulted in enough onward transmission to sustain the incidence above epidemic control. This model assumes that individuals drop out of ART exponentially with a mean duration of 20 years.
Figure A8. Sensitivity of HIV incidence in the 100% ART scenario (model scenario 5) to varying two key parameters: a) ART efficacy (between 80% - 100%), b) average time in days from infection until ART initiation (between 0 and 360), and c) the bivariate sensitivity over all combinations of the two parameter estimates, evaluated at four time-points (2016, 2020, 2030, and 2050). Dashed black lines (in univariate plots) and + symbol (in bivariate plot) indicate the incidence according to actual model parameter values used in final calibrated model. In each sensitivity analysis, all other parameters are held according to the original calibration. Dashed red lines (in univariate plots) and solid red outline (in bivariate plot) indicates epidemic control threshold reached (incidence = 1/1000).
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