

Supplemental appendix to:

Modelling the Health Impact and Cost Threshold of Long-Acting ART for Adolescents and Young Adults in Kenya

- I. Technical specifications
- II. Cost parameters
- III. Epidemiological parameters
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I. Technical Specifications

Model Overview:

The mathematical model simulates heterosexual HIV transmission and is parameterized to Kenya. The model reproduces population-level dynamics and stratifies the population by age, gender, and sexual risk. The model begins with an entirely HIV-negative population at time $t = 0$ with a size and distribution reflecting Kenya in 1979. In the first iteration, 0.2% of the population becomes HIV-positive, and subsequent iterations evaluate the demography, enrollment, and aging of the population. The population dynamics are governed by a system of ordinary differential equations that are approximated by 0.05-year interval iterations in R. The natural history of HIV infection is modeled in stages defined by CD4 count and viral load as shown in Figure S1. When a person becomes HIV-infected, s/he enters the acute stage characterized by a short duration and high probability of HIV transmission. The person then progresses through stages of CD4 count and viral load. New births enter the population as a function of the fertility rate.

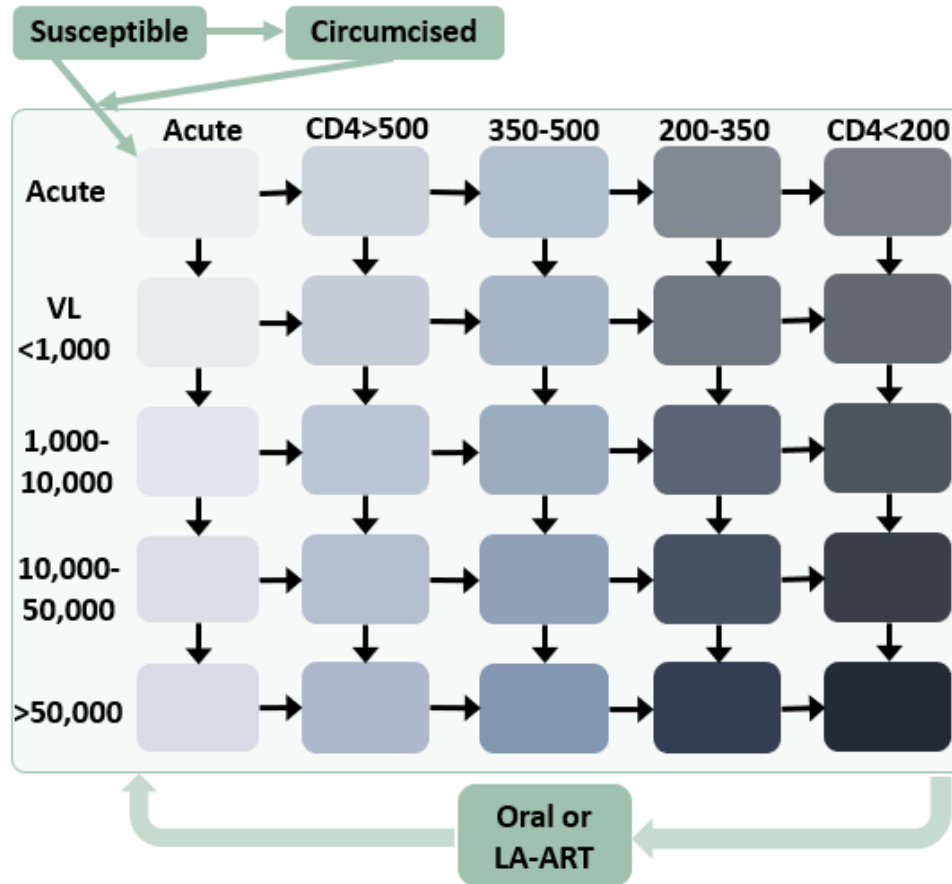


Figure S1. Model transition diagram. A diagram of the natural history of HIV infection. All movement is in one direction except for enrollment in and dropout from interventions from ART.

Model states and equations:

The model simulates a population from ages 0 to 59 in five-year age groups, capturing vertical transmission and aging. Model states ($dX_{a,r}^{g,d,v}$) are based on age, gender, CD4 state, viral load, circumcision status, and sexual risk group. The model approximates a system of equations with the following indices:

Gender:

- $g = 0$ for females
- $g = 1$ for males

Disease state defined by CD4 cell count, treatment status, and circumcision status

- $d = 1$ for acute infection
- $d = 2$ for CD4 > 500 cells/ μ L
- $d = 3$ for CD4 350-500 cells/ μ L

- d = 4 for CD4 200-350 cells/ μ L
- d = 5 for CD4 < 200 cells/ μ L
- d = 6 for HIV-negative, circumcised
- d = 7 for HIV-negative, not circumcised
- d = 8 for HIV positive, on ART

Viral load status:

- v = 1 for acute infection
- v = 2 for VL < 1,000 copies/mL
- v = 3 for VL 1,000-10,000 copies/mL
- v = 4 for VL 10,000-50,000 copies/mL
- v = 5 for VL > 50,000 copies/L
- v = 6 for HIV-negative
- v = 7 for HIV-positive and on ART

Risk group:

- r = 1 for low risk
- r = 2 for medium risk
- r = 3 for high risk

Age group:

- a = 1 for ages 0-4
- a = 2 for ages 5-9
- a = 3 for ages 10-14
- a = 4 for ages 15-19
- a = 5 for ages 20-24
- a = 6 for ages 25-29
- a = 7 for ages 30-34
- a = 8 for ages 35-39
- a = 9 for ages 40-44
- a = 10 for ages 45-49
- a = 11 for ages 50-54
- a = 12 for ages 55-59

The equations for the eight disease states are:

$$\frac{dY_{a,r}^{g,1,1}(t)}{dt} = b_{r,1}^{g,1}(t) + \psi \lambda_{a,r}^1(t) X_{a,r}^{1,6,6}(t) + \lambda_{a,r}^g(t) X_{a,r}^{g,7,6}(t) + \sigma_a^g X_{a,r}^{g,8,7}(t) - (\mu_a^g(t) + \alpha_a^{g,1} + v_1 + \omega_v + \pi_a^g(t)) X_{a,r}^{g,1,v}(t)$$

$$\frac{dY_{a,r}^{g,2,v}(t)}{dt} = v_1 X_{a,r}^{g,1,v}(t) + \omega_{v-1} X_{a,r}^{g,2,v-1}(t) + \sigma_a^g X_{a,r}^{g,8,7}(t) - (\mu_a^g(t) + \alpha_a^{g,2} + v_2 + \omega_v + \pi_a^g(t)) X_{a,r}^{g,2,v}(t)$$

$$\frac{dY_{a,r}^{g,3,v}(t)}{dt} = v_1 X_{a,r}^{g,2,v}(t) + \omega_{v-1} X_{a,r}^{g,3,v-1}(t) + \sigma_a^g X_{a,r}^{g,8,7}(t) - (\mu_a^g(t) + \alpha_a^{g,3} + v_3 + \omega_v + \pi_a^g(t)) X_{a,r}^{g,3,v}(t)$$

$$\frac{dY_{a,r}^{g,4,v}(t)}{dt} = v_1 X_{a,r}^{g,3,v}(t) + \omega_{v-1} X_{a,r}^{g,4,v-1}(t) + \sigma_a^g X_{a,r}^{g,8,7}(t) - (\mu_a^g(t) + \alpha_a^{g,4} + v_4 + \omega_v + \pi_a^g(t)) X_{a,r}^{g,4,v}(t)$$

$$\frac{dY_{a,r}^{g,5,v}(t)}{dt} = v_1 X_{a,r}^{g,4,v}(t) + \omega_{v-1} X_{a,r}^{g,5,v-1}(t) + \sigma_a^g X_{a,r}^{g,8,7}(t) - (\mu_a^g(t) + \alpha_a^{g,5} + \omega_v + \pi_a^g(t)) X_{a,r}^{g,5,v}(t)$$

$$\frac{dX_{a,r}^{1,6,6}(t)}{dt} = b_{r,6}^{g,6}(t) - (\mu_a^g(t) + \lambda_{a,r}^1(t) \psi) X_{a,r}^{1,6,6}(t)$$

$$\frac{dX_{a,r}^{g,7,6}(t)}{dt} = b_{r,7}^{g,7}(t) - (\mu_a^g(t) + \lambda_{a,r}^g(t) X_{a,r}^{g,7,6}(t))$$

$$\frac{dY_{a,r}^{g,8,7}(t)}{dt} = \sum_{v=1}^5 \sum_{d=1}^5 [\pi_{a,r}^g(t) X_{a,r}^{g,d,v}(t) - (\mu_a^g(t) + \sigma_{a,r}^g) X_{a,r}^{g,8,7}(t)]$$

The equation variables are:

$b_{r,c}^{g,d}(t)$	The number of births that are HIV-positive, not on ART (d=1), HIV-negative (d=6, 7), or HIV-positive and on ART (d=8)
$\lambda_{a,r}^g(t)$	The force of infection for HIV-negative persons
ψ	The reduction in HIV transmission due to circumcision
μ_a^g	The background mortality
$\alpha_a^{g,d}$	The HIV-associated mortality
v_d	The rate of progressing from CD4 state d to $d + 1$
ω_v	The rate of progressing from VL state v to $v + 1$
σ_a^g	ART dropout (not virally suppressed) rate
π_a^g	ART coverage rate

Births:

The number of births, $b_{r,c}^{g,d}(t)$, determines how many newborns enter the population of gender g , disease state d , sexual risk group r , and circumcision status c ($c = 0$ for uncircumcised, $c = 1$ for circumcised males). We assume that infected births enter the acute stage, and that women age 15–49 give birth. Fertility rates are stratified by age. Each birth is multiplied by 0.5 given an assumed gender ratio at birth of 1:1. Births from uninfected mothers, $bS(t)$, and from HIV-positive mothers, $bI(t)$, are:

$$bS(t) = \sum_{a=3}^9 \sum_{r=1}^3 \gamma_a^7 X_{a,r}^{0,7,6}(t)$$

$$bI(t) = \sum_{a=3}^9 \sum_{r=1}^3 \sum_{d=1}^5 \sum_{v=1}^5 \gamma_a^d X_{a,r}^{0,d,v}(t) + \sum_{a=3}^9 \sum_{r=1}^3 \gamma_a^8 X_{a,r}^{0,8,7}(t)$$

HIV-negative births for uncircumcised males, $b_{r,0}^{1,7}(t)$, are:

$$b_{r,0}^{1,7}(t) = 0.5 * \phi_{0,r}^{1,0} * (bS(t) + (1 - \eta(t))bI(t)) * (1 - \pi_{0,r}^{1,6}(t))$$

HIV-negative births for circumcised males, $b_{r,1}^{1,6}(t)$, are:

$$b_{r,1}^{1,6}(t) = 0.5 * \phi_{0,r}^{1,0} * (bS(t) + (1 - \eta(t))bI(t)) * \pi_{0,r}^{1,6}(t)$$

HIV-negative births for females, $b_{r,0}^{0,7}(t)$, are:

$$b_{r,0}^{0,7}(t) = 0.5 * \phi_{0,r}^{0,0} * (bS(t) + (1 - \eta(t))bI(t))$$

HIV-positive births for males and females, $b_{r,0}^{g,t}(t)$, are:

$$b_{r,0}^{g,1}(t) = 0.5 * \phi_{0,r}^{g,t} * \eta(t)bl(t)$$

The equation variables are:

$\phi_{a,r}^{g,t}$	The proportion of individuals in age a , gender g , and treatment status t ($t = 0$, no treatment; $t = 1$, ART) that is born into sexual risk group r
$\eta(t)$	The proportion of births from HIV-positive females that result in vertical transmission
$\pi_{0,r}^{1,6}(t)$	The proportion of HIV-negative males that is circumcised at birth
γ_a^d	The annual fertility rate for females by age and disease state

Mortality:

People leave the population due to death or aging past age 59. Mortality is represented by mortality caused by HIV, $\alpha_a^{g,d}$, and all other background mortality, μ_a^g . Mortality caused by HIV varies by stage of disease and age, and individuals on ART are assumed to have no disease-induced mortality.^{1,2} The background mortality rate is estimated by subtracting out the mortality due to HIV from the overall mortality rate.

Disease transmission:

Disease transmission is governed by the force of infection, $\lambda_{a,r}^g(t)$, which determines the number of people who are infected at each time-step.

$$\lambda_{a,r}^g(t) = \sum_{a'=1}^{12} \sum_{r'=1}^3 \left[c_{g,a,r}^{*a',r'}(t) \rho_{g,a,r}^{a',r'}(t) * \frac{\sum_{v=1}^5 X_{a',r'}^{g',d',v'}(t) \beta_{g,r,v'} + X_{a',r'}^{g',d',7'}(t) \beta_{g,r,7'}}{\sum_{v=1}^5 X_{a',r'}^{g',d',v'}(t) + X_{a',r'}^{g',d',7'}(t)} \right]$$

$c_{g,a,r}^{*a',r'}(t)$ The number of partners from age a' and sexual risk group r' that an individual has per year, adjusted

$\rho_{g,a,r}^{a',r'}(t)$ The mixing matrix which describes the distribution of partners from each age and sexual risk group

$\beta_{g,r,v'}$ The probability of HIV transmission per partnership between an HIV-positive person of stage v' and HIV-negative person of risk group r

The overall force of infection for a specific age-group is the sum of the risk of acquiring HIV from all possible partners.

Mixing Matrix:

Using methods similar to other models, the mixing matrix, $\rho_{g,a,r}^{a',r'}(t)$, describes patterns of sexual contact by calculating the proportion of one's sexual partners that come from a specific age and sexual-risk group.

$$\rho_{g,a,r}^{a',r'}(t) = \left[\epsilon_a \frac{\sum_{r'=1}^3 (c_{a',r'}^{g'} \sum_{d'=1}^8 \sum_{v'=1}^7 X_{a',r'}^{g',d',v'}(t))}{\sum_{a'=1}^{12} \sum_{r'=1}^3 (c_{a',r'}^{g'} \sum_{d'=1}^8 \sum_{v'=1}^7 X_{a',r'}^{g',d',v'}(t))} + (1 - \epsilon_a) \delta_a^{a'} \right] * \left[\epsilon_r \frac{c_{a',r'}^{g'} \sum_{d'=1}^8 \sum_{v'=1}^7 X_{a',r'}^{g',d',v'}(t)}{\sum_{r'=1}^3 (c_{a',r'}^{g'} \sum_{d'=1}^8 \sum_{v'=1}^7 X_{a',r'}^{g',d',v'}(t))} + (1 - \epsilon_r) \delta_r^{r'} \right]$$

Where $\delta_r^{r'} = 1.0$ if $r = r'$
 $= 0.0$ if $r \neq r'$

Before 2005: $\delta_a^{a'} = 0.3$ if $a = a'$
 $= 0.7$ if $a = a' + 1$ (for males)

$$\begin{aligned} & \text{if } a = a' - 1 \text{ (for females)} \\ & = 0.0 \text{ otherwise} \end{aligned}$$

After 2005:

$$\begin{aligned} \delta_a^{a'} &= 0.7 \text{ if } a = a' \\ &= 0.3 \text{ if } a = a' + 1 \text{ (for males)} \\ & \quad \text{if } a = a' - 1 \text{ (for females)} \\ &= 0.0 \text{ otherwise} \end{aligned}$$

Mixing patterns vary between random and assortative, as determined by the parameter ϵ . Random mixing ($\epsilon = 1$) is mixing proportional to the relative sizes of all compartments and this method is consistent for both random mixing by risk and by age. However, assortative mixing ($\epsilon = 0$) is among groups with similar characteristics and differs for mixing by risk and age. Assortative mixing by risk ($\epsilon_r = 0$) is defined by the identity matrix $\delta_r^{r'}$, whereas assortative mixing by age ($\epsilon_a = 0$) is defined by an off-diagonal matrix $\delta_a^{a'}$. The off-diagonal pattern results in females of age a being more likely to form partnerships with males of age $a = a' - 1$, which is consistent with reports of such age discrepancies in sub-Saharan Africa.^{3,4} This off-diagonal method results in two age groups having fewer than 100% of their partnerships; therefore, males in the youngest age group and females in the oldest age group are set to $\delta_a^{a'} = 1$ if $a = a'$. We assume that this tendency for age-gaps diminishes in 2005. Furthermore, ϵ_a and ϵ_r shift from random to assortative over the course of the simulation, given the decline in risky sexual behavior.⁵

Per-Partnership Probability of Transmission:

The per-partnership probability of transmission, $\beta^{g,r,v'}$, depends on the sexual risk group of the HIV-negative partner and the disease state of the HIV-positive partner. The probabilities of transmission per partnership are:

$$\begin{aligned} \beta^{0,r,v'} &= 1 - (1 - \tau^{v'})^{A_r^0(t)} && \text{for female HIV-negative partners} \\ \beta^{1,r,v'} &= 1 - (1 - \tau^{v'})^{A_r^1(t)} && \text{for male HIV-negative partners} \end{aligned}$$

$\tau^{v'}$ is the per-act probability of transmission for an HIV-positive partner of HIV stage d' , and the exponent, $A_r^g(t)$, is the number of coital acts based on the HIV-negative partner's sexual risk group and gender.

Rate of Partner Change:

Data on sexual behavior and specifically, sexual contact rates, $c_{a,r}^g$, are often subject to biases leading to contact rate data that, when assuming solely heterosexual contact, are inconsistent between males and females.⁶ We account for this variability by using an adjusted contact rate, $c_{g,a,r}^{*a',r'}(t)$, which equilibrates the reported number of sexual partners by males and females.⁷ The adjusted contact rate can be male- or female-driven, as determined by the parameter θ , where $\theta = 1$ for male-driven, $\theta = 0$ for female-driven, and $\theta = 0.5$ when compromised equally. We assume $\theta = 0.5$ given the lack of data to assume otherwise.

For females, the adjusted contact rate is:

$$c_{0,a,r}^{*a',r'}(t) = c_{a,r}^0(t) B_{a,r}^{a',r'}(t)^{-(1-\theta)}$$

For males, the adjusted contact rate is:

$$c_{1,a,r}^{*a',r'}(t) = c_{a,r}^1(t) B_{a,r}^{a',r'}(t)^\theta$$

The discrepancy between the two populations, $B_{a,r}^{a',r'}$, is defined as:

$$B_{a,r}^{a',r'}(t) = \frac{c_{a,r}^0 \rho_{0,a,r}^{a',r'}(t) * \sum_{d=1}^8 \sum_{v=1}^7 X_{a,r}^{0,d,v}(t)}{c_{a,r}^1 \rho_{1,a,r}^{a',r'}(t) * \sum_{d=1}^8 \sum_{v=1}^7 X_{a,r}^{1,d,v}(t)}$$

Aging:

One-fifth of each compartment enters into the next age group with same gender and disease state. Their sexual risk is redistributed to match a set sexual-risk profile ($\Phi_{a,r}^{g,d}$) that varies by age, gender, and treatment status. All compartments, except for the youngest and oldest age-groups, experience influx from the prior age and efflux into the next age. The 0 to 4 age-group only receives influx through births while the 55 to 59 age-group exits the population rather than entering the next age.

II. Cost Parameters

Cost of oral ART in SSA was estimated at \$72.⁸ Costs of health care for those on treatment and those not in care were inflated to 2017 (adjusting for exchange rates).

	Kenya, 2017 (USD)
Costs of ART provision	
Oral antiretroviral drug cost (per person-year)	\$72
Non-antiretroviral cost (per person-year)	\$161
Costs of pre-ART health-care use	\$155
Reference	CDC/Kenya MoH ⁹

III. Epidemiological Parameters

Population

Table S1. Initial population size. Kenya total population in 1979 by age and sex.

Age	Initial Population Size		Reference
	Male	Female	
0 – 4	1,422,021	1,421,385	UN population data ¹⁰
5 – 9	1,247,091	1,244,749	
10 – 14	1,050,932	1,023,839	
15 – 19	854,123	887,722	
20 – 24	641,401	686,003	
25 – 29	514,451	541,261	
30 – 39	405,385	412,691	
35 – 39	290,227	325,367	
40 – 44	261,480	273,702	
45 – 49	218,914	221,965	
50 – 54	182,908	191,022	
55 – 59	140,777	134,534	
TOTAL	7,229,710	7,364,240	

Table S2. Total population size. Kenya total population over time for model calibration

Year	Total population size	Reference
1979	14,593,950	UN population data ¹⁰
1989	20,398,625	
1999	27,154,357	
2009	36,662,970	

Circumcision

Reduction in force of infection due to circumcision: Several studies show that circumcised males have a 60% ($\Psi_0 = 0.6$) lower risk of acquiring HIV, but are not at a reduced risk of transmitting HIV.^{11–13} The proportion circumcised by 2030 was based on 2014 proportions, accounting for aging cohorts (e.g., the 35–39 proportion from 2030 is equal to the 20–24 proportion from 2014).

Table S3. Coverage of adult voluntary medical male circumcision:

Age	Percent Circumcised					Reference
	2003	2008	2012	2014	2030	
0 – 4	0.039	0.041	0.045	0.047	0.047	2014 DHS Kenya ¹⁴
5 – 9	0.148	0.156	0.172	0.180	0.180	
10 – 14	0.353	0.373	0.411	0.430	0.430	
15 – 19	0.715	0.755	0.832	0.871	0.871	
20 – 24	0.890	0.894	0.941	0.965	0.965	
25 – 29	0.883	0.850	0.914	0.946	0.965	
30 – 34	0.893	0.892	0.920	0.934	0.965	
35 – 39	0.893	0.892	0.920	0.934	0.965	
40 – 44	0.837	0.916	0.918	0.919	0.946	

45 – 49	0.837	0.916	0.918	0.919	0.934
50 – 54	0.837	0.916	0.918	0.919	0.934
55 – 59	0.837	0.916	0.918	0.919	0.919

CD4 progression

Table S4. The duration of time in each CD4 stage by sex. Ying *et al.*¹⁵

CD4	VL									
	Time for Males (years)					Time for Females (years)				
	Acute	≤1,000	1,000-10,000	10,000-50,000	>50,000	Acute	≤1,000	1,000-10,000	10,000-50,000	>50,000
Acute	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
>500	1.71	2.00	2.23	1.60	1.33	1.94	3.38	1.97	1.64	1.30
500-350	1.05	2.12	1.33	1.24	0.68	1.35	3.06	2.31	1.19	0.53
350-200	4.71	5.05	24.67	9.93	2.03	6.71	22.67	15.73	5.79	3.22

Viral load progression

Table S5. The duration of time in each viral load stage by sex. Ying *et al.*¹⁵

CD4	VL							
	Time for Males (years)				Time for Females (years)			
	Acute	≤1,000	1,000-10,000	10,000-50,000	Acute	≤1,000	1,000-10,000	10,000-50,000
Acute	0.25	3.44	1.45	3.04	0.25	3.06	2.27	5.45
>500	0.25	3.21	2.21	4.90	0.25	3.34	2.97	7.49
500-350	0.25	3.53	0.95	2.19	0.25	2.85	1.88	4.60
350-200	0.25	4.15	0.39	2.09	0.25	2.52	1.27	3.67
<200	0.25	1.50	1.45	1.08	0.25	1.50	2.00	5.17

ART coverage rate of people living with HIV

Table S6. Proportion of HIV-positive persons receiving ART. ART coverage for adults and children is assumed to reach 90-90-90 target of 81% by 2030. Adult females under age 40 are assumed to have 34% higher ART coverage based on UNAIDS estimates.¹⁶

Year	ART coverage				Reference
	Adult Males	Adult Females	Adults 40+	Children (0-14)	
2003	-	-	-	-	World Bank Development Indicators ¹⁷
2004	0.02	0.02	0.02	0.01	
2005	0.03	0.05	0.04	0.03	
2006	0.08	0.10	0.09	0.07	
2007	0.11	0.15	0.13	0.10	
2008	0.15	0.21	0.19	0.14	
2009	0.20	0.27	0.25	0.18	
2010	0.27	0.37	0.33	0.24	
2011	0.32	0.43	0.39	0.35	
2012	0.36	0.48	0.43	0.42	
2013	0.38	0.51	0.46	0.47	
2014	0.43	0.58	0.52	0.53	
2015	0.50	0.68	0.61	0.62	

2016	0.57	0.76	0.69	0.72
2017	0.62	0.83	0.75	0.82

ART non-adherence proportion

Table S7. Pre-intervention ART non-adherence proportion. Proportions are based on a study of viral suppression of individuals on ART from routine viral load testing data in Kenya.

Age	Non-adherence	Reference
0 – 4	0.40	Mwau <i>et al.</i> ¹⁸
5 – 9	0.35	
10 – 14	0.37	
15 – 19	0.37	
20 – 24	0.19	
25 – 29	0.19	
30 – 34	0.13	
35 – 39	0.13	
40 – 44	0.13	
45 – 49	0.13	
50 – 54	0.13	
55 – 59	0.13	

Fertility

Table S8. Fertility rate by age and HIV status. No changes in fertility rates were assumed after 2012.

Age	Fertility Rate (per year)								Reference
	1979	1986	1991	1996	1999	2001	2007	2012	
0 – 4	0	0	0	0	0	0	0	0	2014 DHS Kenya ¹⁴
5 – 9	0	0	0	0	0	0	0	0	
10 – 14	0	0	0	0	0	0	0	0	
15 – 19	0.168	0.152	0.110	0.111	0.142	0.114	0.103	0.096	
20 – 24	0.342	0.314	0.257	0.248	0.254	0.243	0.238	0.206	
25 – 29	0.357	0.303	0.241	0.218	0.236	0.231	0.216	0.183	
30 – 34	0.293	0.255	0.197	0.188	0.185	0.196	0.175	0.148	
35 – 39	0.239	0.183	0.154	0.109	0.127	0.123	0.118	0.100	
40 – 44	0.145	0.099	0.070	0.051	0.056	0.055	0.050	0.038	
45 – 49	0.059	0.035	0.050	0.016	0.007	0.015	0.012	0.009	
50 – 54	0	0	0	0	0	0	0	0	
55 – 59	0	0	0	0	0	0	0	0	

Table S9. Fertility rate multipliers for HIV-positive women. HIV-positive women are assumed to have lower fertility rates than uninfected women, except for the 15-19 age group. Those on ART or in the acute stage are assumed to have equal fertility to HIV-negative women. Fertility for HIV-negative women is adjusted so that the overall fertility rate is equal to Table S8.

Age	Fertility Multiplier	Reference
15 – 19	1.454	Marston <i>et al.</i> ¹⁹
20 – 24	0.720	

25 – 29	0.619
30 – 34	0.497
35 – 39	0.526
40 – 44	0.331
45 – 49	0.648

Background mortality

Table S10. Background mortality. The background mortality rate is estimated by adjusting the overall Kenyan mortality rate estimated by WHO²⁰ for the mortality due to HIV in Kenya estimated by IHME.²¹ Mortality rates were estimated for 1990 and each year from 2000-2015. After 2015, age 0-4 mortality rate is assumed to decrease by 2% per year. Table S10 shows 2015 annual rates.

Age	2015 Background Mortality	
	Male	Female
0 – 4	0.0106	0.0088
5 – 9	0.0024	0.0017
10 – 14	0.0013	0.0010
15 – 19	0.0018	0.0011
20 – 24	0.0030	0.0015
25 – 29	0.0026	0.0014
30 – 34	0.0026	0.0015
35 – 39	0.0034	0.0022
40 – 44	0.0043	0.0031
45 – 49	0.0057	0.0040
50 – 54	0.0084	0.0061
55 – 59	0.0121	0.0093

HIV-associated mortality

Table S11. HIV-associated mortality. Values are annual estimates from observational studies of untreated HIV-positive persons.

Age	HIV Mortality								Reference
	Male				Female				
	Acute	CD4 >350	200-350	CD4 <200	Acute	CD4 >350	200-350	CD4 <200	
0 – 4	0.05	0.12	0.20	0.66	0.04	0.09	0.15	0.50	Chaudhury <i>et al.</i> ²²
5 – 9	0.02	0.06	0.10	0.32	0.05	0.12	0.19	0.65	Chaudhury <i>et al.</i> ²²
10 – 14	0.03	0.08	0.13	0.43	0.03	0.07	0.11	0.36	Chaudhury <i>et al.</i> ²²
15 – 19	0.04	0.11	0.18	0.60	0.01	0.03	0.05	0.18	Chaudhury <i>et al.</i> ²²
20 – 29	0.02	0.05	0.08	0.27	0.02	0.05	0.08	0.27	Badri <i>et al.</i> ²³
30 – 34	0.02	0.05	0.09	0.29	0.02	0.05	0.09	0.29	Balslev <i>et al.</i> ²⁴
35 – 39	0.02	0.05	0.09	0.29	0.02	0.05	0.09	0.29	Balslev <i>et al.</i> ²⁴
40 – 44	0.03	0.07	0.10	0.35	0.03	0.07	0.10	0.35	Balslev <i>et al.</i> ²⁴
45 – 49	0.03	0.07	0.10	0.35	0.03	0.07	0.10	0.35	Balslev <i>et al.</i> ²⁴
50 – 54	0.03	0.09	0.14	0.47	0.03	0.09	0.14	0.47	Balslev <i>et al.</i> ²⁴
55 – 59	0.03	0.09	0.14	0.47	0.03	0.09	0.14	0.47	Balslev <i>et al.</i> ²⁴

Force of infection

Mixing matrix

Table S12. Sexual mixing by age and sexual risk group. The mixing parameter varies from random ($\epsilon = 1$) to assortative ($\epsilon = 0$), calibrated to fit age-specific HIV incidence and prevalence data.

Year	Force of Infection Mixing		Reference
	ϵ_a (age)	ϵ_r (sexual risk)	
Before 1994	0.7	0.7	Calibrated to
After 1998	0.1	0.1	fit data

Number of coital acts

Table S13. The number of coital acts per partnership by gender and sexual risk group. Values are calibrated to fit age-specific HIV incidence and prevalence data.

Gender	Coital Acts per Partnership			Reference
	Low-Risk	Moderate-Risk	High-Risk	
Male	95	30	3.2	Calibrated to
Female	80	24	2.2	fit data

Probability of transmission and acquisition

Table S14. Probability of HIV transmission by viral load.

Baseline Transmission Probability	Increase in transmission probability by HIV stage					Reference
	Acute	VL	VL	VL	VL	
		$\leq 1,000$	1,000-10,000	10,000-50,000	$>50,000$	
0.00049 ^a	9 ^b	1 ^c	5.8 ^c	6.9 ^c	11.9 ^c	0.04 ^d

^aPowers *et al.*, Boily *et al.*^{25,26}
^bHollingsworth *et al.*²⁷
^cQuinn *et al.*²⁸
^dAttia *et al.*, Cohen *et al.*, Donnell *et al.*²⁹⁻³¹

Table S15. Proportion of births from HIV-positive females not on ART that result in mother-to-child transmission. No transmissions are assumed from HIV-positive females on ART.

Year	MTCT rate	Reference
1993	0.255	Connor <i>et al.</i> ³²
2009	0.24	UNAIDS ³³
2014	0.17	UNAIDS ³³

Table S16. Pregnancy HIV acquisition risk factor. Pregnant women are assumed to have a 2.76 times greater risk of acquiring HIV.³⁴ This factor is combined with fertility rates to create acquisition multipliers applied to all women in a year and age group.

Pregnancy acquisition	Reference
2.76	Thomson <i>et al.</i> ³⁴

Table S17. Age-specific STI prevalence. Coinfections representing HSV2 and other STIs are assumed to increase HIV acquisition by a factor of 3.4 for women and 2.8 for men³⁵ and transmission by a factor of

two.³⁶ STIs are distributed by age and sex according to the observed HSV2 prevalence in sub-Saharan Africa.

Age	Prevalence (%)		Reference
	Men	Women	
15-19	0.055	0.126	KAIS 2007 ³⁷
20-24	0.102	0.277	
25-29	0.207	0.409	
30-34	0.291	0.514	
35-39	0.371	0.559	
40-44	0.473	0.594	
45-49	0.450	0.556	
50-54	0.424	0.543	
55+	0.396	0.573	

Risk behavior

Table S18. Risk behavior parameter by year. Risk behavior includes the number of partners and risk group distribution. The change in risk behavior as a result of the HIV epidemic is measured as a value between 0 and 1, with 0 being the least risky (lowest number of partners and lower proportion of people in the higher risk groups). Values up to the year 2000 are calibrated to the HIV incidence and prevalence in Kenya by year; values after 2000 are derived by fitting an exponential curve to historical prevalence from 2001-2017.

Year	Behavior	Year	Behavior
1990	0.95	2010	0.26
1991	0.80	2011	0.28
1992	0.70	2012	0.28
1993	0.60	2013	0.31
1994	0.50	2014	0.37
1995	0.35	2015	0.41
1996	0.25	2016	0.44
1997	0.15	2017	0.53
1998	0.10	2018	0.54
1999	0.05	2019	0.55
2000	0.01	2020	0.57
2001	0.01	2021	0.58
2002	0.02	2022	0.59
2003	0.04	2023	0.60
2004	0.06	2024	0.62
2005	0.09	2025	0.63
2006	0.12	2026	0.64
2007	0.14	2027	0.65
2008	0.17	2028	0.67
2009	0.18	2029	0.68

2030

0.70

Number of sexual partners

Table S19. Annual number of sexual partnerships by age, gender, and sexual risk. Values are based on a previous study and calibrated to fit age-specific HIV incidence and prevalence data. The number of partnerships is interpolated between S19a and S19b based on the risk behavior parameter in that year. For example, the number of partnerships for low-risk 20-24 year-old males in 2000, when the risk behavior parameter is 0.01, is $0.99*0.2 + 0.01*0.8 = 0.21$.

S19a: Sexual partnerships when risk behavior parameter = 0

Age	Male Partnerships per Year			Female Partnerships per Year			Reference
	Low Risk	Moderate Risk	High Risk	Low Risk	Moderate Risk	High Risk	
0 – 4	0.00006	0.00006	0.00006	0.00006	0.00012	0.00012	Adapted from Barnabas ³⁸
5 – 9	0.0006	0.006	0.06	0.0007	0.007	0.12	
10 – 14	0.0	0.1	0.6	0.01	0.06	0.4	
15 – 19	0.2	1.2	32.0	0.23	0.06	27.9	
20 – 24	0.2	1.5	32.0	0.28	1.2	25.3	
25 – 29	0.3	1.9	20.0	0.18	0.81	15.4	
30 – 34	0.2	1.1	18.0	0.09	0.57	10.4	
35 – 39	0.2	0.8	18.0	0.09	0.49	9.5	
40 – 44	0.2	0.6	10.5	0.09	0.41	8.7	
45 – 49	0.2	0.6	10.5	0.09	0.41	8.1	
50 – 54	0.2	0.6	10.5	0.09	0.41	6.1	
55 – 59	0.1	0.4	8.5	0.07	0.41	1.6	

S19b: Sexual partnerships when risk behavior parameter = 1

Age	Male Partnerships per Year			Female Partnerships per Year			Reference
	Low Risk	Moderate Risk	High Risk	Low Risk	Moderate Risk	High Risk	
0 – 4	0.00006	0.00006	0.00006	0.00006	0.00012	0.00012	Adapted from Barnabas ³⁸
5 – 9	0.0006	0.006	0.06	0.0007	0.007	0.12	
10 – 14	0.02	0.2	2	0.09	0.18	1.8	
15 – 19	0.8	3.6	82	0.72	2.16	72	
20 – 24	0.8	6	82	0.68	6	68	
25 – 29	1.2	9.4	68	0.56	4.06	44.8	
30 – 34	0.6	5.3	52.7	0.28	2.87	41.8	
35 – 39	0.5	4.1	52.7	0.28	2.45	38.1	
40 – 44	0.5	2.9	46.8	0.21	2.03	34.8	
45 – 49	0.5	2.9	46.8	0.21	2.03	32.2	
50 – 54	0.5	2.9	46.8	0.21	1.61	24.5	
55 – 59	0.4	1.8	35.1	0.07	0.63	6.3	

Risk distribution

Table S20. Sexual risk distribution by age and sex. Values are calibrated to fit age-specific HIV incidence and prevalence data. The sexual risk distribution is interpolated between S20a and S20b based on the risk behavior parameter in that year. For example, the percentage of low-risk 20-24 year-old males in 2000, when the risk behavior parameter is 0.01, is $0.99 \cdot 0.71 + 0.01 \cdot 0.60 = 0.709$.

S20a: Sexual risk distribution when risk behavior parameter = 0							
Age	Male Risk Distribution			Female Risk Distribution			Reference
	Low-Risk	Moderate-Risk	High-Risk	Low-Risk	Moderate-Risk	High-Risk	
0 – 4	0.999	0.0005	0.0005	0.998	0.001	0.001	Calibrated to fit data
5 – 9	0.999	0.0005	0.0005	0.998	0.001	0.001	
10 – 14	0.98	0.015	0.005	0.975	0.015	0.01	
15 – 19	0.72	0.25	0.03	0.68	0.26	0.06	
20 – 24	0.71	0.25	0.04	0.64	0.33	0.03	
25 – 29	0.75	0.22	0.03	0.75	0.22	0.03	
30 – 34	0.75	0.22	0.03	0.75	0.22	0.03	
35 – 39	0.79	0.18	0.03	0.82	0.15	0.03	
40 – 44	0.85	0.12	0.03	0.86	0.11	0.03	
45 – 49	0.86	0.11	0.03	0.87	0.1	0.03	
50 – 54	0.92	0.05	0.03	0.91	0.07	0.02	
55 – 59	0.96	0.015	0.025	0.975	0.015	0.01	

S20b: Sexual risk distribution when risk behavior parameter = 1							
Age	Male Risk Distribution			Female Risk Distribution			Reference
	Low-Risk	Moderate-Risk	High-Risk	Low-Risk	Moderate-Risk	High-Risk	
0 – 4	0.999	0.0005	0.0005	0.998	0.001	0.001	Calibrated to fit data
5 – 9	0.999	0.0005	0.0005	0.998	0.001	0.001	
10 – 14	0.98	0.015	0.005	0.975	0.015	0.01	
15 – 19	0.7	0.26	0.04	0.68	0.26	0.06	
20 – 24	0.6	0.28	0.12	0.52	0.36	0.12	
25 – 29	0.55	0.38	0.07	0.55	0.38	0.07	
30 – 34	0.65	0.28	0.07	0.64	0.3	0.06	
35 – 39	0.67	0.27	0.06	0.7	0.24	0.06	
40 – 44	0.74	0.2	0.06	0.77	0.17	0.06	
45 – 49	0.77	0.17	0.06	0.79	0.16	0.05	
50 – 54	0.87	0.08	0.05	0.84	0.13	0.03	
55 – 59	0.96	0.035	0.005	0.94	0.045	0.015	

HIV prevalence for model calibration

Table S21. HIV prevalence for model calibration (age 15-49)

Year	Prevalence	Reference
1995	0.105	UNDP, Kenya
2003	0.067	AIDS Indicator
2007	0.076	Survey, DHS Kenya
2008	0.063	³⁹⁻⁴¹
2012	0.056	

Table S22. Age-specific HIV prevalence

Age	2012 HIV prevalence	Reference
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	Male	Female	
0 – 4	0.9%	2.3%	
5 – 9	0.6%	0.9%	
10 – 14	0.6%	0.5%	
15 – 19	0.9%	1.1%	
20 – 24	1.3%	4.6%	
25 – 29	4.3%	7.9%	Kenya AIDS Indicator Survey ⁴⁰
30 – 34	6.6%	6.6%	
35 – 39	5.0%	12.3%	
40 – 44	8.1%	10.6%	
45 – 49	8.9%	10.7%	
50 – 54	6.7%	10.2%	
55 – 59	3.7%	5.1%	

Utility rates for DALYs

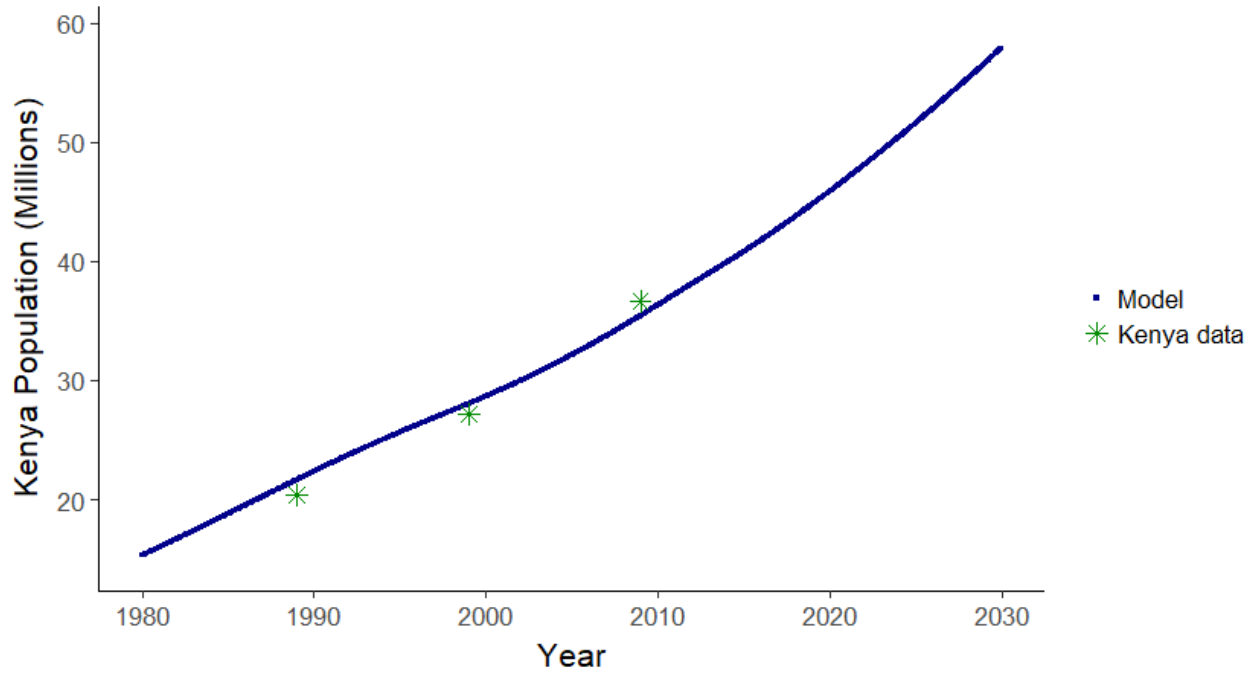
Table S23. Utility weights for estimating disability-adjusted life-years averted

Health State	DALY Weight	Reference
HIV-negative	0	
HIV-positive CD4>350	0.078	Salomon <i>et al.</i> ⁴²
HIV-positive CD4 200-350	0.274	
HIV-positive CD4<200	0.582	
HIV-positive on ART	0.078	
Dead	1	

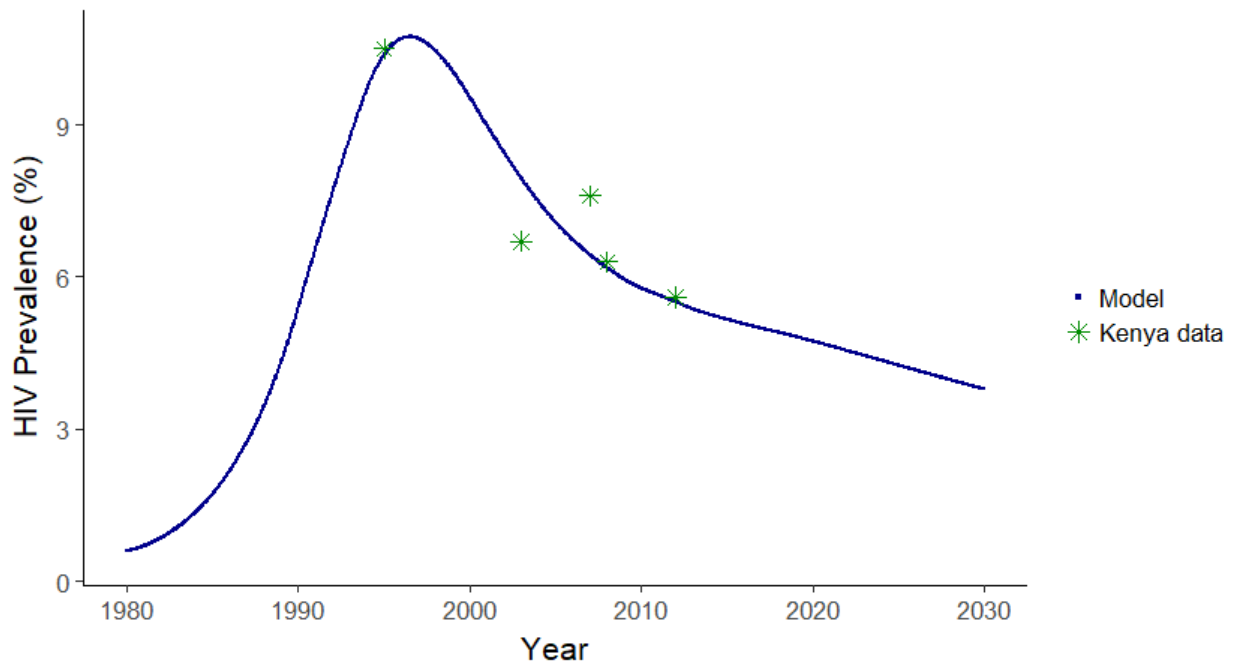
IV. Calibration results

The following figures display model outputs and primary data from Kenya listed in the tables in the previous section of this supplemental appendix.

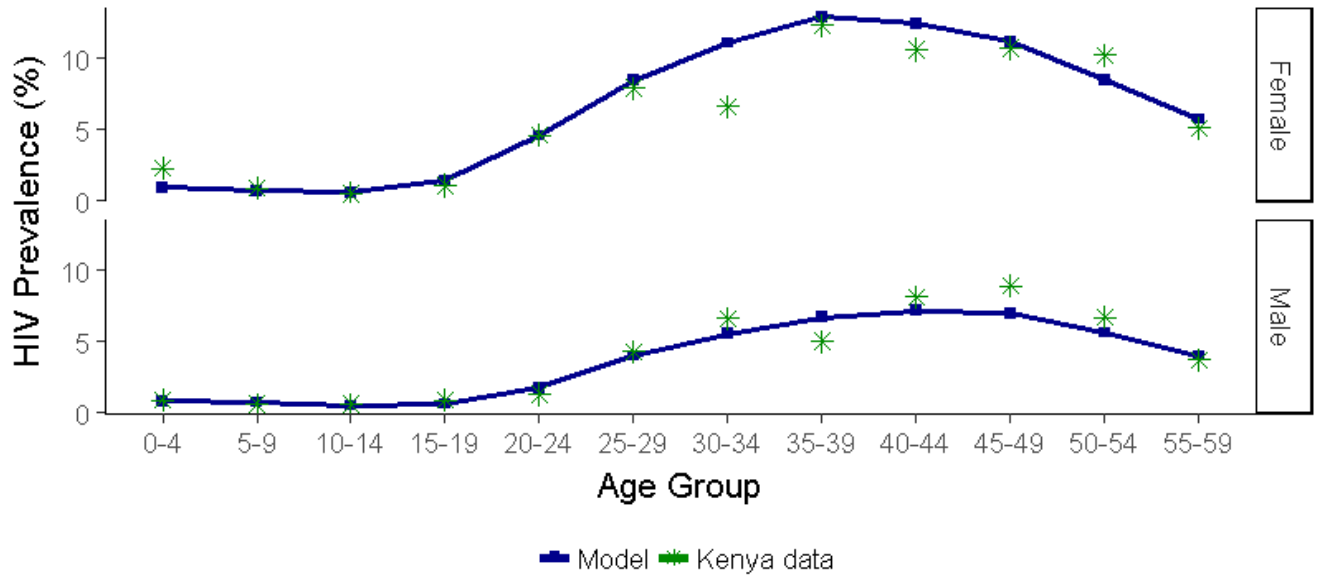
Population size



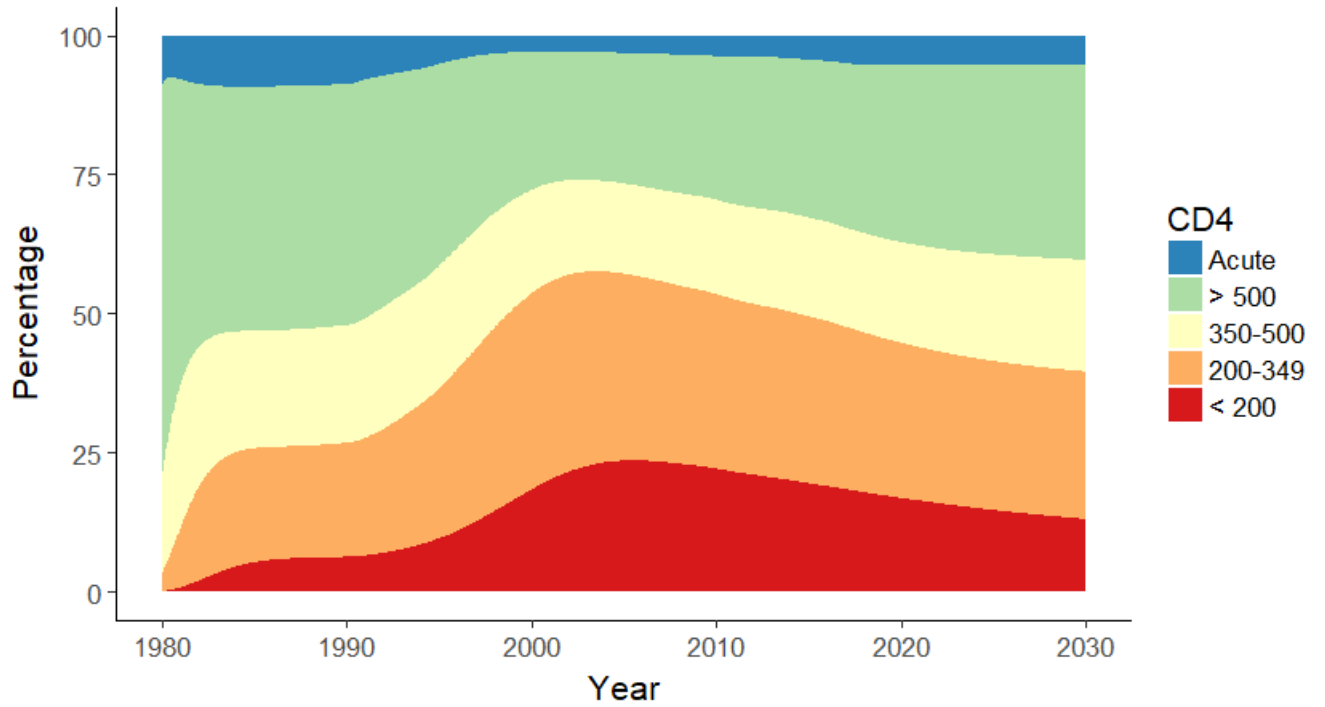
HIV prevalence (15-49) over time



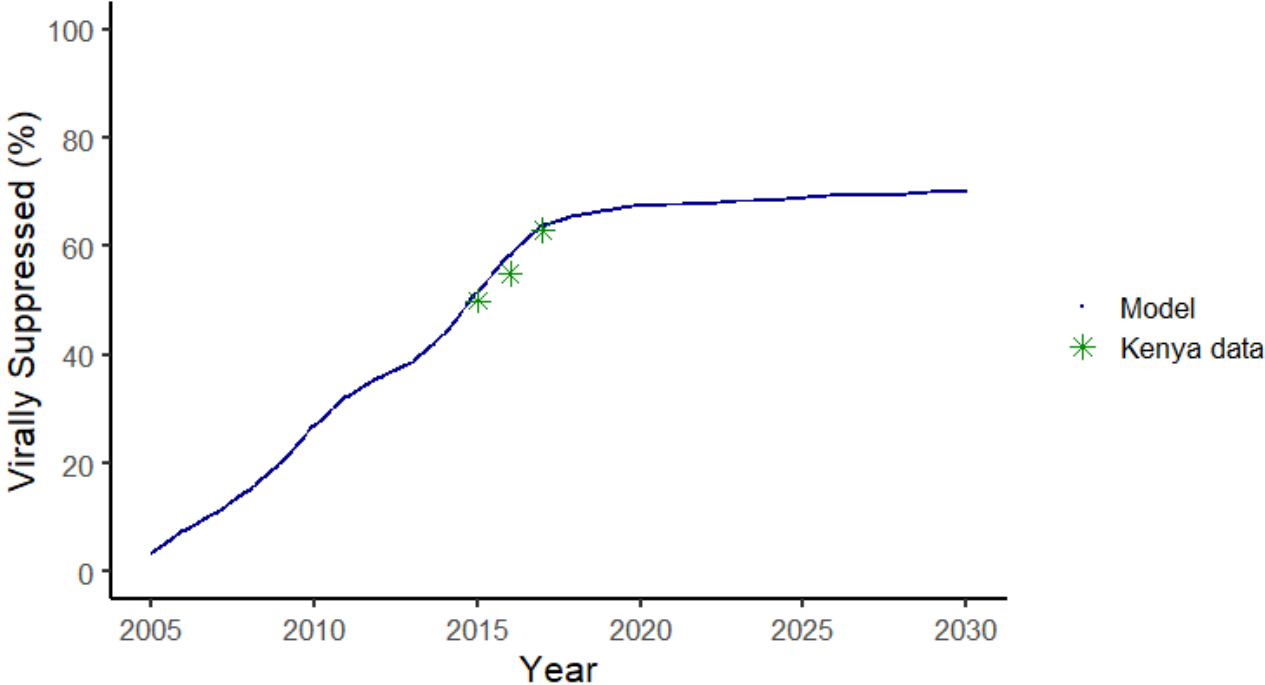
Age-specific HIV prevalence (2012)



CD4 Distribution among HIV-positive over time



ART Coverage (proportion of all HIV-positive on ART and virally suppressed)



V. References

1. Adler WH, Baskar P V, Chrest FJ, Dorsey-Cooper B, Winchurch RA, Nagel JE. HIV infection and aging: Mechanisms to explain the accelerated rate of progression in the older patient. *Mech Ageing Dev.* 1997;96(1-3):137-155. doi:10.1016/S0047-6374(97)01888-5
2. Mills EJ, Bakanda C, Birungi J, et al. Mortality by baseline CD4 cell count among HIV patients initiating antiretroviral therapy: evidence from a large cohort in Uganda. *AIDS.* 2011;25(6):851-855. doi:10.1097/QAD.0b013e32834564e9
3. Anderson RM, May RM, Ng TW, Rowley JT. Age-dependent choice of sexual partners and the transmission dynamics of HIV in sub-Saharan Africa. *Philos Trans - R Soc London, B.* 1992;336(1277):135-155. doi:10.1098/rstb.1992.0052
4. Ott MQ, Bärnighausen T, Tanser F, Lurie MN, Newell M-L. Age-gaps in sexual partnerships: seeing beyond 'sugar daddies.' *AIDS.* 2011;25(6):861-863. doi:10.1097/QAD.0b013e32834344c9
5. Cheluget B, Baltazar G, Orege P, Ibrahim M, Marum LH, Stover J. Evidence for population level declines in adult HIV prevalence in Kenya. *Sex Transm Infect.* 2006;82(SUPPL. 1):i21-6. doi:10.1136/sti.2005.015990
6. Burington B, Hughes JP, Whittington WLH, et al. Estimating duration in partnership studies: issues, methods and examples. *Sex Transm Infect.* 2010;86(2):84-89. doi:10.1136/sti.2009.037960
7. Garnett GP, Gregson S. Monitoring the course of the HIV-1 epidemic: The influence of patterns of fertility on HIV-1 prevalence estimates. *Math Popul Stud.* 2000;8(3):251-277. doi:10.1080/08898480009525485
8. Clinton Health Access Initiative. *HIV Market Report.*; 2018. https://clintonhealthaccess.org/content/uploads/2018/09/2018-HIV-Market-Report_FINAL.pdf. Accessed December 11, 2018.
9. U.S. Centers for Diseases Control and Kenya Ministry of Health. *The Cost of Comprehensive HIV Treatment in Kenya. Report of a Cost Study of HIV Treatment Programs in Kenya.* Atlanta, GA (USA) and Nairobi, Kenya; 2013.
10. UNdata | Population by age, sex and urban/rural residence. <http://data.un.org/Data.aspx?d=POP&f=tableCode%3A22>. Accessed December 4, 2017.
11. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial. Deeks S, ed. *PLoS Med.* 2005;2(11):e298. doi:10.1371/journal.pmed.0020298
12. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet (London, England).* 2007;369(9562):657-666. doi:10.1016/S0140-6736(07)60313-4
13. Weiss H a, Quigley M a, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. *AIDS.* 2000;14(July):2361-2370. doi:10.1016/S1473-3099(09)70235-X
14. Kenya 2014 Demographic and Health Survey. <https://dhsprogram.com/pubs/pdf/fr308/fr308.pdf>. Accessed December 6, 2017.
15. Ying R, Sharma M, Celum C, et al. Home testing and counselling to reduce HIV incidence in a generalised epidemic setting: a mathematical modelling analysis. *Lancet HIV.* 2016;3(6):e275-e282. doi:10.1016/S2352-3018(16)30009-1
16. UNAIDS. <http://aidsinfo.unaids.org>. Accessed December 10, 2018.
17. World Bank Development Indicators. <https://data.worldbank.org/country/kenya>. Accessed December 16, 2017.

18. Mwaui M, Syeunda CA, Adhiambo M, et al. Scale-up of Kenya's national HIV viral load program: Findings and lessons learned. *PLoS One*. 2018;13(1):e0190659. doi:10.1371/journal.pone.0190659
19. Marston M, Nakiyingi-Miiri J, Kusemererwa S, et al. The effects of HIV on fertility by infection duration: Evidence from African population cohorts before antiretroviral treatment availability. *Aids*. 2017;31:S69-S76. doi:10.1097/QAD.0000000000001305
20. Life Tables for WHO Member States: Kenya. <http://www.who.int/gho/countries/ken/en/>. Accessed December 16, 2017.
21. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2016 (GBD 2016) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2017. <http://ghdx.healthdata.org/gbd-results-tool>. Accessed December 16, 2017.
22. Chaudhury S, Hertzmark E, Muya A, et al. Equity of child and adolescent treatment, continuity of care and mortality, according to age and gender among enrollees in a large HIV programme in Tanzania. 2018. doi:10.1002/jia2.25070/full
23. Badri M, Lawn SD, Wood R. Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study. *Lancet*. 2006;368(9543):1254-1259. doi:10.1016/S0140-6736(06)69117-4
24. Balslev U, Monforte AD, Stergiou G, et al. Influence of Age on Rates of New AIDS-defining Diseases and Survival in 6546 AIDS Patients. *Scand J Infect Dis*. 1997;29(4):337-343. doi:10.3109/00365549709011827
25. Powers KA, Poole C, Pettifor AE, Cohen MS. Rethinking the heterosexual infectivity of HIV-1: a systematic review and meta-analysis. 2008:553. doi:10.1016/S1473
26. Boily MC, Baggaley RF, Wang L, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. *Lancet Infect Dis*. 2009;9(2):118-129. doi:10.1016/S1473-3099(09)70021-0
27. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 Transmission, by Stage of Infection. 2008. doi:10.1086/590501
28. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral Load and Heterosexual Transmission of Human Immunodeficiency Virus Type 1. *N Engl J Med*. 2000;342(13):921-929. doi:10.1056/NEJM200003303421303
29. Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: Systematic review and meta-analysis. *AIDS*. 2009;23(11):1397-1404. doi:10.1097/QAD.0b013e32832b7dca
30. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 Infection with Early Antiretroviral Therapy. *N Engl J Med*. 2011;365(6):493-505. doi:10.1056/NEJMoa1105243
31. Donnell D, Baeten JM, Kiarie MBChB J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet*. 2010;375:2092-2098. doi:10.1016/S0140-6736(10)60705-2
32. Connor EM, Sperling RS, Gelber R, et al. Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment. *N Engl J Med*. 1994;331(18):1173-1180. doi:10.1056/NEJM199411033311801
33. 2015 Progress Report on the Global Plan. 2009. http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf. Accessed February 24, 2018.
34. Thomson KA, Hughes J, Baeten JM, et al. Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners. *J Infect Dis*. March 2018. doi:10.1093/infdis/jiy113

35. Glynn JR, Biraro S, Weiss HA. Herpes simplex virus type 2: A key role in HIV incidence. *Aids*. 2009;23(12):1595-1598. doi:10.1097/QAD.0b013e32832e15e8
36. Hughes JP, Baeten JM, Lingappa JR, et al. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Infect Dis*. 2012;205(3):358-365. doi:10.1093/infdis/jir747
37. Kenya AIDS indicator Survey 2007. <https://stacks.cdc.gov/view/cdc/12122>. Accessed June 12, 2017.
38. Barnabas R. Mathematical Modelling of the Natural History of Human Papillomavirus Infection and Cervical Carcinoma: The Impact of Intervention Strategies on Disease Incidence. *Univ Oxford*. 2005.
39. Kenya AIDS Strategic Framework. [http://www.undp.org/content/dam/kenya/docs/Democratic Governance/KENYA AIDS STRATEGIC FRAMEWORK.pdf](http://www.undp.org/content/dam/kenya/docs/Democratic%20Governance/KENYA%20AIDS%20STRATEGIC%20FRAMEWORK.pdf). Accessed June 12, 2017.
40. Kenya AIDS indicator Survey 2012. <http://nacc.or.ke/wp-content/uploads/2015/10/KAIS-2012.pdf>. Accessed June 12, 2017.
41. 2008 Kenya Demographic and Health Survey. <http://statistics.knbs.or.ke/nada/index.php/catalog/23>. Accessed December 6, 2017.
42. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *Artic Lancet Glob Heal*. 2015;3:712-735. www.thelancet.com/lancetgh. Accessed July 10, 2018.