Supplementary appendix to:

Cost-effectiveness of home HIV testing and education for male partners of pregnant women in Kenya: A mathematical modeling analysis of the HOPE intervention

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 Nyanza in 1979. The population dynamics are governed by a system of ordinary differential equations (ODEs) that are solved in MATLAB 2014a[1]. The model iterates in three-month intervals. 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. Pregnancy was incorporated into the model by the addition of health states for pregnancy stratified by CD4 count and viral load. Women transition into pregnancy states at a fertility rate determined by their age and CD4 count status (if HIV-positive). New births enter the population as a function of the fertility rate. Women have a 40% higher HIV susceptibility compared to men based on the UNAIDS Spectrum model will uses a ratio of female-to-male incidence of 1.4.[2]

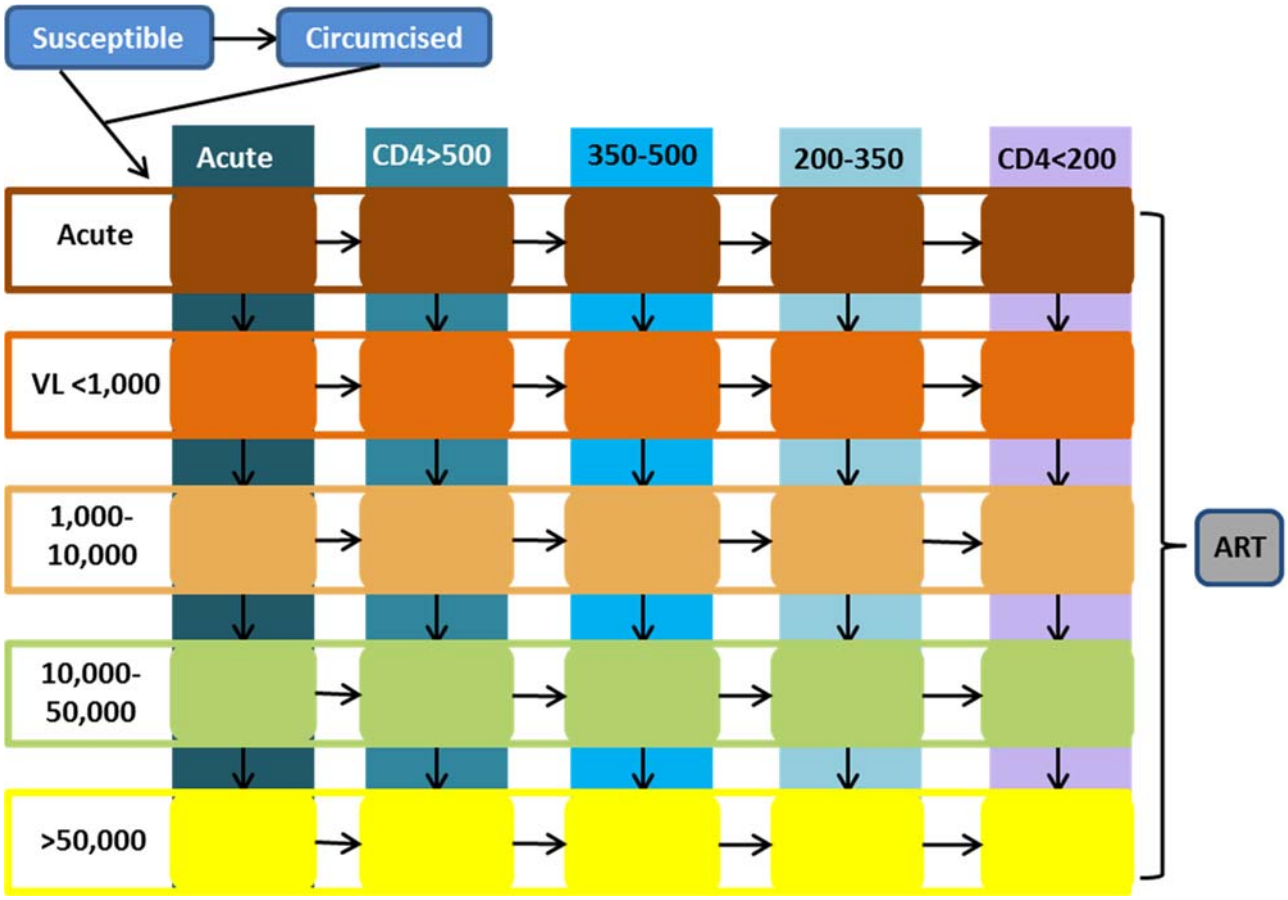

Figure S1. Model transition diagram. A diagram of the natural history of HIV infection. All movement is in one direction except for enrollment in and dropout from interventions from ART.

II. Interventions

ART Treatment Enrollment:

ART treatment is assumed to reduce the likelihood of HIV transmission by 96% and persons on ART are expected to have the same life expectancy as HIV-negative persons of similar age and sex, and thus, are assumed not to be subject to HIV-associated mortality [3-7]. The annual drop-out rate is 6%, which is equally likely for all individuals regardless of their HIV state prior to treatment. Individuals who drop out of ART return to the infected stages at the same proportion with which they enrolled. This

model includes a background level of circumcision of 66% as observed in Nyanza. We assume a 60% lower risk of acquiring HIV based on prior studies. [8-10]

III. Cost Parameters

Cost estimates:

Costs were collected onsite in June 2014 in Kisumu, Kenya from the HOPE study, a randomized control trial of home testing of male partners of pregnant women. Time and motion observation of the HOPE intervention was conducted to determine staff time and resource utilization per home visit and also to facilitate removal of research time and costs for the operational cost estimate. We observed that the HOPE educational component and couples HIV testing and counseling take approximately 1 hour per couple (slightly longer for couples with discordant HIV-status who require additional counseling). After accounting for travel time to participant's home, follow-ups, paperwork, and other staff responsibilities, we estimated that a community care worker could test 3 couples per day. We assumed a program of 20 community care workers and 4 supervisory nurses. Staff were assumed to work 7 hours per day, 215 days per year after accounting for national holidays, sick days, and paid vacations. Total program costs were divided by the number of persons tested by HIV status under each scenario to determine the cost per person tested. Supply costs per person tested included gloves, HIV screening test kit, lancet, cotton balls, and alcohol swabs. Additional supplies for HIV+ persons tested included confirmatory test, and tie breaker test (assumed to be used in 5% of all HIV+ cases).

Costs of a facility-based HIV test was obtained from a costing exercise conducted in Kenya and inflated to 2014 USD (Obure).[11] ART costs were estimated by using a multi-country analysis of treatment costs in five countries in sub-Saharan Africa.[12] Since costs for Kenya were not evaluated, we generated a linear regression to describe the relationship between each country's GDP per capita and ART costs

(R2=98%) (shown below). We then put the GDP per capita into the equation described below to estimate yearly ART costs: 150.47 + 0.0586*1,167.50 = $218.96 per year.

```
      Source |       SS       df       MS              Number of obs =       5
-------------+------------------------------           F(  1,     3) =  233.51
       Model |  132256.083     1  132256.083           Prob > F      =  0.0006
    Residual |    1699.117     3  566.372334           R-squared     =  0.9873
-------------+------------------------------           Adj R-squared =  0.9831
       Total |    133955.2     4     33488.8           Root MSE      =  23.799

------------------------------------------------------------------------------
        cost |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         GDP |    .058662   .0038388    15.28   0.001     .0464451    .0708789
       _cons |   150.4761    13.4603    11.18   0.002     107.6394    193.3128
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We estimated the HIV-related hospitalization costs using primary cost data from South Africa (Meyer-Rath)[13] and adjusting it by multiplying by the ratio of ART costs in Kenya/South Africa from the model above.

IV. Epidemiological Parameters

Table S1. Initial population size. Nyanza total population 1979 size scaled with Kenya national data for age and sex distribution.

Age Cohort	Initial Population Size		Reference
	Male	Female	
0 – 4	293,191	287,674	Kenya Bureau of Statistics, UN population data [14,15]
5 – 9	221,895	218,405	
10 – 14	184,334	182,359	
15 – 19	149,528	151,279	
20 – 24	114,647	120,244	
25 – 29	89,629	95,951	
30 – 39	68,154	72,704	
35 – 39	54,083	57,338	
40 – 44	45,403	47,338	
45 – 49	37,906	38,974	
50 – 54	30,905	31,547	
55 – 59	25,188	25,279	
TOTAL	1,329,093	1,314,863	

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

Year	Total population size	
1979	2,643,956	Kenya Bureau of Statistics[14]
1989	3,507,162	
2009	4,392,196	

Table S3. Sexual risk distribution by age and sex. Values are calibrated to fit age-specific HIV incidence and prevalence data.

Age Cohort	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	
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	0.80	0.17	0.03	0.80	0.17	0.03	
20 – 24	0.78	0.20	0.02	0.62	0.31	0.05	
25 – 29	0.65	0.29	0.06	0.60	0.35	0.05	Calibrated to fit data
30 – 34	0.66	0.28	0.05	0.65	0.30	0.05	
35 – 39	0.68	0.27	0.05	0.65	0.30	0.05	
40 – 44	0.75	0.20	0.05	0.78	0.17	0.05	
45 – 49	0.78	0.17	0.05	0.80	0.16	0.04	
50 – 54	0.88	0.08	0.04	0.85	0.13	0.02	
55 – 59	0.96	0.035	0.005	0.95	0.045	0.005	

Table S4. 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.

Age Cohort	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 *et al.* [13]
5 – 9	0.0006	0.006	0.06	0.0007	0.007	0.12	
10 – 14	0.006	0.06	0.6	0.006	0.06	0.9	
15 – 19	0.1	1.8	41.0	0.1	0.6	32.2	
20 – 24	0.3	2.3	41.0	0.4	3.5	61.4	
25 – 29	0.6	4.7	52.7	0.4	2.9	58.5	
30 – 34	0.6	5.3	52.7	0.4	4.1	59.7	
35 – 39	0.5	4.1	52.7	0.4	3.5	54.4	
40 – 44	0.5	2.3	46.8	0.3	2.9	49.7	
45 – 49	0.5	2.3	43.9	0.3	2.9	43.9	
50 – 54	0.5	2.9	46.8	0.3	2.3	30.4	
55 – 59	0.4	1.8	35.1	0.1	0.3	5.9	

Table S5. Background mortality. Values for age 5-59 years are Kenya's age-specific mortality in 1990, prior to the generalized HIV epidemic. Values for under 5 mortality are 2012 mortality estimates adjusted for the contribution of HIV/AIDS to mortality using UNAIDS World Mortality Report[16].

Age Cohort	Background Mortality		Reference
	Male	Female	
0 – 4	0.01502	0.01304	UNICEF [17]
5 – 9	0.00405	0.00345	WHO [18]
10 – 14	0.00216	0.00195	
15 – 19	0.00295	0.00245	
20 – 24	0.00457	0.00338	
25 – 29	0.00511	0.00395	
30 – 34	0.00551	0.00428	
35 – 39	0.00610	0.00475	
40 – 44	0.00709	0.00573	
45 – 49	0.00842	0.00680	
50 – 54	0.01176	0.00874	
55 – 59	0.01575	0.01157	

Table S6. Fertility rate by age and HIV status. Females on ART are assumed to have equal fertility to HIV-negative females. Source: DHS 2008 Kenya rural estimates. [19]

Age Cohort	Fertility Rate (per year)					Reference
	Uninfected RR=1	**Acute** RR=1	**>350** RR=0.59	**200-350** RR=0.42	**<200** RR=0.42	
0 – 4	0	0	0	0	0	Anderson *et al.*, Ross *et al.* [20,21]
5 – 9	0	0	0	0	0	
10 – 14	0	0	0	0	0	
15 – 19	0.108	0.064	0.046	0.108	0.064	
20 – 24	0.289	0.171	0.122	0.289	0.171	
25 – 29	0.262	0.155	0.110	0.262	0.155	
30 – 34	0.209	0.123	0.088	0.209	0.123	
35 – 39	0.141	0.083	0.059	0.141	0.083	
40 – 44	0.061	0.036	0.025	0.061	0.036	
45 – 49	0.013	0.008	0.006	0.013	0.008	
50 – 54	0	0	0	0	0	
55 – 59	0	0	0	0	0	

Table S7. HIV-associated mortality. Values are estimates are from observational studies of untreated HIV-positive persons.

Age Cohort	HIV Mortality				Reference
	Acute	**CD4>350**	**CD4 200 to 350**	**CD4<200**	
0 – 4	0.47	0.47	0.47	0.47	Newell *et al.* [22]
5 – 49	0.01	0.05	0.08	0.27	Badri *et al.* [23]
50 – 59	0.02	0.10	0.16	0.54	Adler *et al.* [24]

Table S8. Probability of HIV transmission by viral load.

Baseline Transmission Probability	Increase in transmission probability by HIV stage						Reference
	Acute	**VL≤1,000**	**VL 1,000-10,000**	**VL 10,000-50,000**	**VL>50,000**	**ART**	
0.00053	26	1	5.8	6.9	11.9	0.04	Quinn *et al.*, Boily *et al.* [25,26]

Table S9. The duration of time in each CD4 and viral load stage by sex (Ying et al. [27])

CD4 Transition	Acute	CD4>500	500-350	350-200
Time for Males (years)	0.25	1.71	1.05	4.71
Time for Females (years)	0.25	1.94	1.35	6.71
Viral Load Transition	**Acute**	**VL≤1,000**	**1,000-10,000**	**10,000-50,000**
Time for Males (years)	0.25	3.44	1.45	3.04
Time for Females (years)	0.25	3.06	2.27	5.45

Table S10. Proportion of births from HIV-positive females that result in mother-to-child transmission

Year	MTCT rate	Reference
Overall	0.151	Sirgeno *et al.* [28]
Without PMTCT	0.25	Connor et al[29]
With PMTCT	0.05	Thomas et al[30]

Table S11. Coverage treatment for prevention of mother to child transmission (PMTCT)*

Kenya estimate		
Year	**PMTCT coverage**	**Reference**
2012	0.901	Kenya AIDS Indicator Survey[31]

*Among women who were tested at the clinic or aware of HIV infection

Table S12. Proportion of pregnant women attending antenatal care during last pregnancy

Nyanza estimates		
Year	**ANC coverage**	**Reference**
2012	0.968	Kenya AIDS Indicator Survey[31]

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	99	33	3.3	Calibrated
Female	77	22	3.3	to fit data

Table S14. 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 1998	0.7	0.7	Calibrated to fit data
2003	0.5	0.5	
After 2010	0.1	0.1	

Table S15. HIV prevalence for model calibration

Kenya national data		Reference
Year	**Prevalence**	
1995	0.105	Kenya AIDS Indicator Surveys[31,32]
2003	0.067	
2007	0.071	
2008	0.063	
2010	0.062	
2012	0.056	
Nyanza data		
Year	**Prevalence**	
2003	0.151	Kenya AIDS Indicator Surveys[31,32]
2007	0.149	
2008	0.139	
2012	0.151	

Table S16. Age-specific HIV prevalence: Nyanza estimates*

Age	2012 HIV prevalence		Reference
	Male	**Female**	
15 – 19	0.028	0.026	Kenya AIDS Indicator Survey [31]
20 – 24	0.041	0.107	
25 – 29	0.136	0.184	
30 – 34	0.209	0.154	
35 – 39	0.158	0.287	
40 – 44	0.256	0.247	
45 – 49	0.281	0.250	
50 – 54	0.212	0.238	
55 – 59	0.117	0.119	

*Estimates were calculated by using Kenya national prevalence data scaled up to reflect the overall HIV prevalence of Nyanza.

Table S17. Utility weights for estimating disability-adjusted life-years averted

Health State	DALY Weight Salomon *et al.* [33]
HIV-negative	0
HIV-positive CD4>350	0.053
HIV-positive CD4 200-350	0.221
HIV-positive CD4<200	0.547
HIV-positive on ART	0.053
Dead	1

Table S18. Coverage of adult voluntary medical male circumcision:

Nyanza estimates		Reference
Year	**Male circumcision coverage**	
2012	0.66	Kenya AIDS Indicator Survey[31]

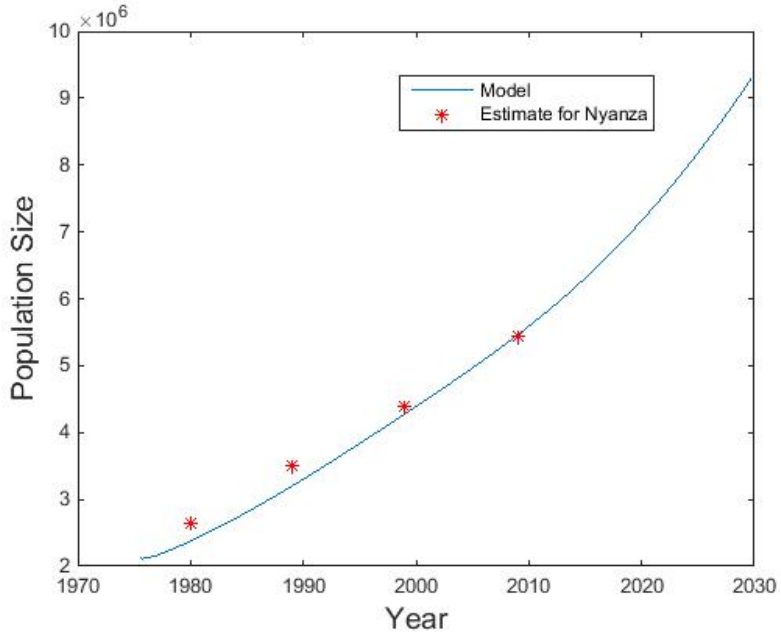
Table S19. Proportion of HIV-positive persons receiving ART

Kenya estimates		Reference
Year	**ART coverage**	
2006	0.10	World Bank Development Indicators[34]
2007	0.14	
2008	0.19	
2009	0.27	
2010	0.33	
2011	0.41	
2012	0.46	
2013	0.49	
2014	0.55	

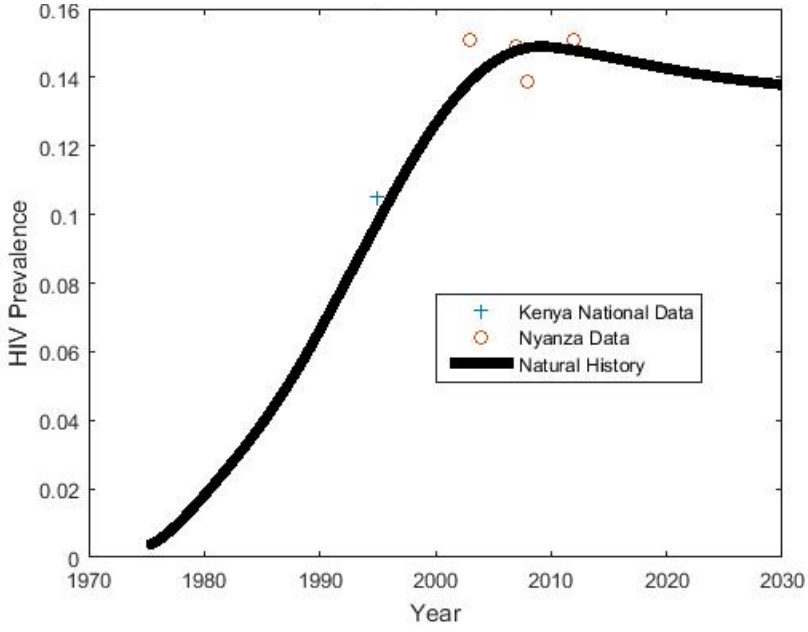
V. Calibration results

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

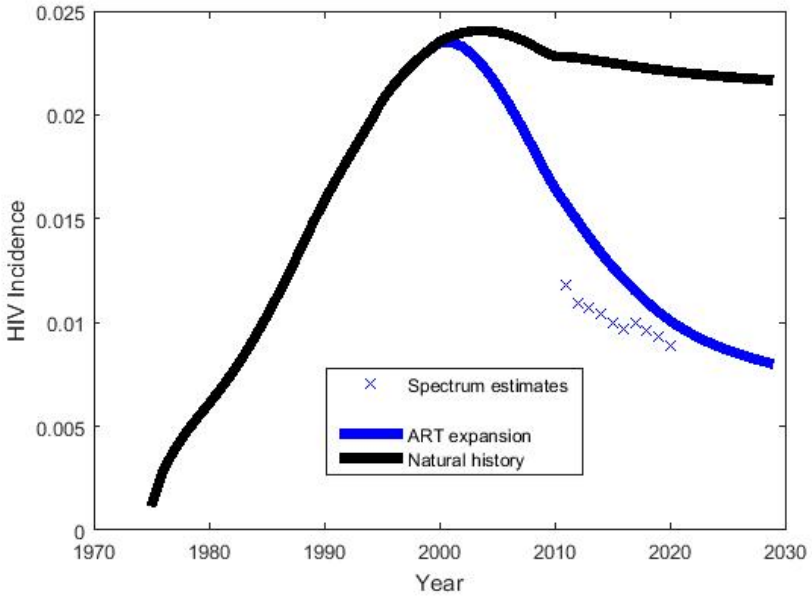
Population size



HIV prevalence over time



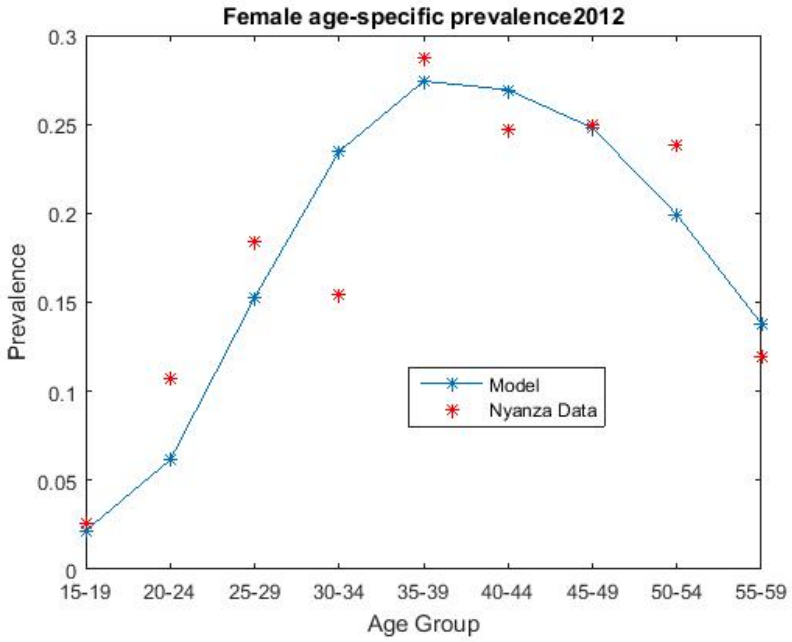
HIV incidence over time*



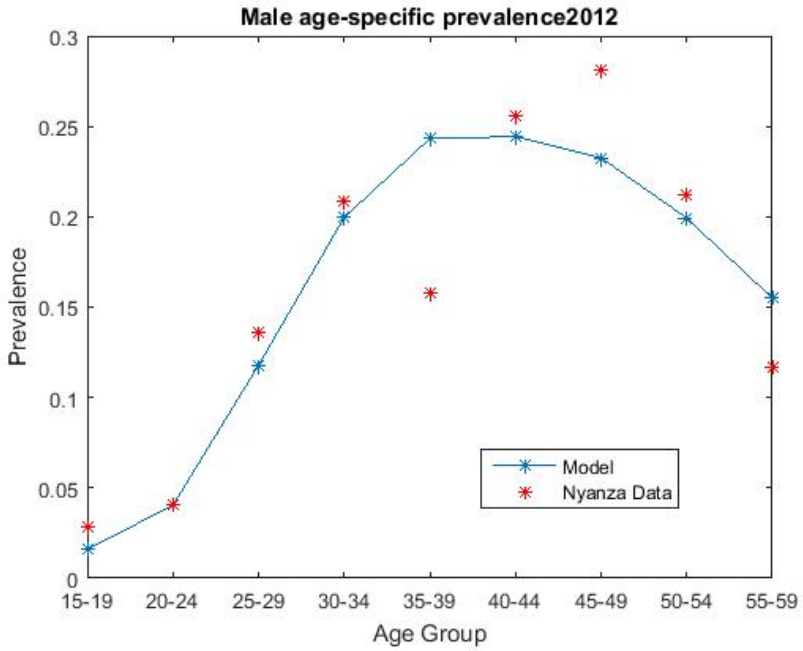
*HIV incidence estimates were obtained from the UNAIDS Spectrum model[2]

Age-specific HIV prevalence

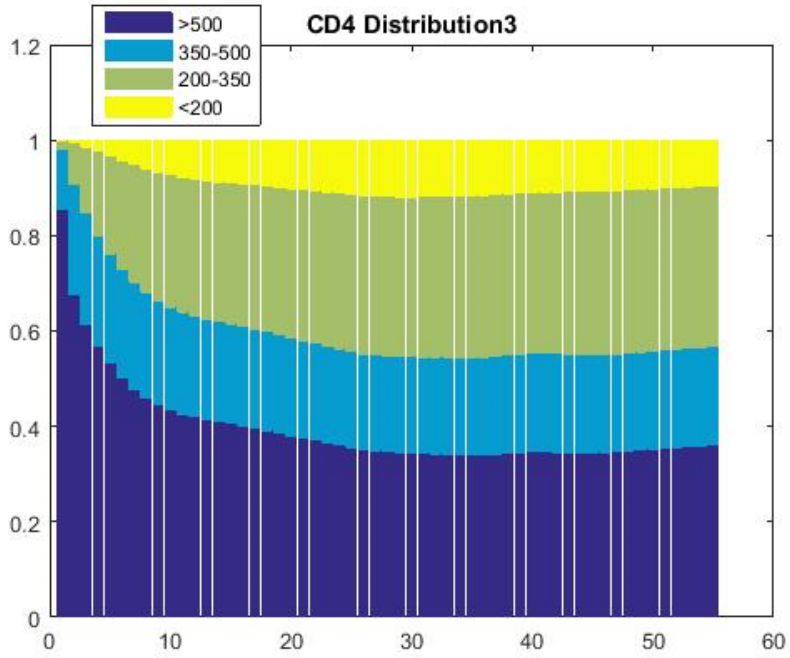
Females:



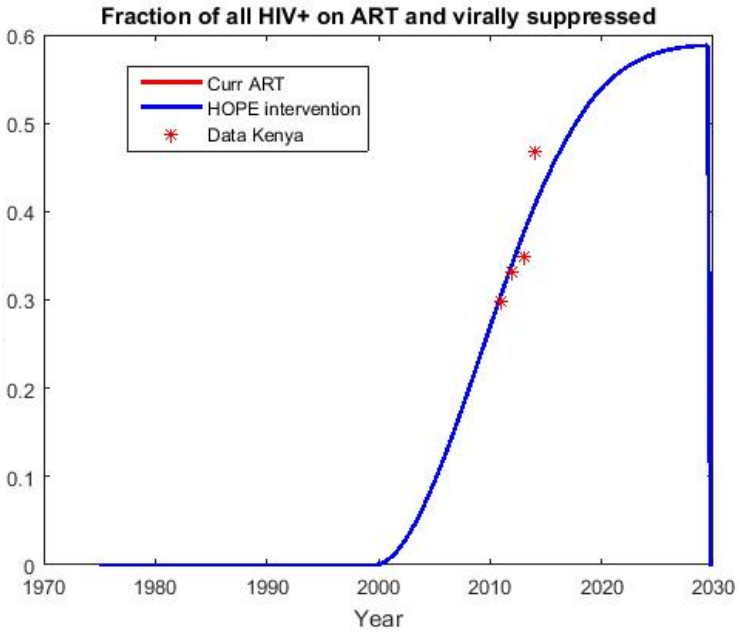
Males:



CD4 Distribution over time



ART Coverage



Primary data on ART coverage reduced by 15% assuming not all persons are virally suppressed.

VI. Additional Results

Cost-effectiveness of the HOPE intervention at lower efficacy (i.e. just 30% increase in likelihood of linking to ART)*

	Current ART scale up	**HOPE intervention with 30% increased probability of ART linkage**
HIV infections averted	--	1,213
DALYs averted	--	5,410
Incremental costs study model (millions)	--	12.2
Incremental costs task shifting model (millions)		6.0
ICER program model ($/DALY averted)	$240	$2,251
ICER task shifting model ($/DALY averted)	$240	$1,105

*Costs and health benefits discounted at 3% annually.

VII. References

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