Supplemental Digital Content

1 Methodology for estimating the contribution of identifiable HIV incidence among stable HIV-1 sero-discordant couples to total HIV population-level incidence

We based our model for estimating the contribution of identifiable HIV incidence among stable HIV-1 sero-discordant couples (SDCs) to total HIV population-level incidence, on an approach that uses a framework of repeated cross-sectional surveys. The framework was designed to conceptualize HIV-1 transmission within stable couples using a commonly implemented approach in HIV prevention interventions.

Among couples that have been identified as HIV-1 sero-discordant during a baseline screening cross-sectional survey, HIV-1 sero-conversions within SDCs are those where the sero-positive partner transmits the infection to the sero-negative partner over the course of the year before the next cross-sectional survey. These transmissions define the *identifiable HIV incidence among SDCs* since they occurred in couples that have already been identified as discordant before the sero-conversion of the negative partner, and before these couples become concordant positive.

The probability of HIV-1 transmission per partnership from the HIV sero-positive to the HIV sero-negative partner in an SDC using the binomial (Bernoulli) model [1] is given by

$$t_1 = 1-\left(1-p\right)^{\left(1-f_{condom}\right)n\tau_{follow-up}}\left(1-\left(1-E_{condom}\right)p\right)^{f_{condom}n\tau_{follow-up}}$$

Here p is the HIV-1 transmission probability per heterosexual coital act (which can be influenced by male circumcision if the susceptible partner is male and circumcised), f_{condom} is the fraction of coital acts protected by condom use among stable couples, n is the frequency of coital acts per month, $\tau_{follow-up}$ is the duration between the two cross-sectional surveys, and

E_{condom} is the efficacy of condoms in preventing HIV-1 transmission. To account for the effect of male circumcision, the average country-specific probability of HIV transmission per partnership from the HIV sero-positive to the HIV sero-negative partner in an SDC (t_{w1}) was determined as a weighted average of the probability of HIV transmission per partnership among SDCs with and without male circumcision, and depending on whether the infected partner is male or female. A description of the parameters of this methodology and their values can be found in Table S1 and Table 1 of the main text.

The number of new identifiable HIV infections arising from sero-conversions within SDCs is then calculated as $N_{couples}P_{all}t_{w1}$, where $N_{couples}$ is the number of stable couples identified in the baseline screening cross-sectional survey a year earlier, and P_{all} is the prevalence of HIV-1 sero-discordancy among stable sexual couples (that is the proportion of SDCs out of all stable sexual couples). The parameter values of this expression can be found in Table 1 of the main text.

The contribution of identifiable HIV incidence among SDCs to total HIV population-level incidence is then estimated by

$$F_{\text{Incidence-discordant}} = \frac{N_{couples}P_{all}t_{w1}}{N_{reproductive\ age}(1-P)\varphi}$$

Here, $N_{reproductive\ age}$ is the number of individuals in the reproductive age in the population, P is the prevalence of HIV-1 infection in the population, and φ is the HIV population-level incidence rate. The parameter values of this expression can be found in Tables 1 and 2 of the main text.

2 Model parameterization

Multiple data sources were used to parameterize our model (Fig. S1). Countries were considered for analysis based on the availability of the Demographic and Health Survey (DHS) HIV serological biomarker survey. For each country, we analyzed only the most recent DHS survey where HIV data were collected. Consequently, a total of 20 countries in sub-Saharan Africa were included in our analysis: Burkina Faso (2003), Cameroon (2004), Democratic Republic of Congo (2007), Cote d'Ivoire (2005), Ethiopia (2005), Ghana (2003), Guinea (2005), Kenya (2008-2009), Lesotho (2009), Liberia (2007), Malawi (2010), Mali (2006), Niger (2006), Rwanda (2005), Senegal (2005), Sierra Leone (2008), Swaziland (2006-07), Tanzania (2007-08), Zambia (2007), and Zimbabwe (2005-06).

DHSs are nationally representative household surveys that collect individual-level demographic and health data for men and women which are then used to form couple databases [2]. We merged the country-specific DHS couple database with the corresponding HIV sero-status database to analyze the epidemiology of HIV among stable sexual couples in sub-Saharan Africa. We excluded from our analyses couples where one or both partners did not test for HIV. Missing HIV information among all couples ranged from 2.2-28.1% (mean of 13.0%) across countries. Where couple databases could not be identified, we matched individual databases for men and women with the corresponding HIV sero-status database, before merging both databases using the husband line number as an identifier per established methodology [3] to form a couple database with HIV sero-status information.

Country-specific DHS data [2], along with the United Nations Population Division Database [4], were used to derive the size of the population in reproductive age ($N_{reproductive\ age}$), the fraction of the population in reproductive age engaged in stable couples ($f_{in\ stable\ couples}$), the number of

stable couples in the population ($N_{couples}$), HIV-1 prevalence (P), the prevalence of HIV-1 sero-discordancy (P_{all}), the fraction of HIV-1 infected females in SDCs (f_{index}), the fraction of circumcised males in SDCs with HIV-1 infected females (f_{mc}), and the fraction of coital acts protected by condom use (f_{condom}). The latter was based on the measure of condom use at last sex act among stable couples. Values for these country-specific variables can be found in Table 1 of the main text.

Our calculations are based on the empirical measures of HIV-1 transmission probability per heterosexual coital act as available from the Rakai Study [5] and the Partners in Prevention HSV/HIV Transmission Study (Partners in Prevention Study) [6-8] (Table S1). These studies are considered the state of the art studies for estimating HIV-1 transmission probability per coital act and were conducted among SDCs in sub-Saharan Africa.

HIV population-level incidence rate (φ) for each country, for the specific year in which the DHS survey was conducted, was obtained from the UNAIDS SPECTRUM model predictions [9, 10]. For countries where estimates from SPECTRUM were not available or where the bounds of the 95% confidence interval were not precisely specified, φ was derived from the DHS HIV-1 prevalence in the population assuming a stable HIV epidemic and using the relation:

$$\varphi = \frac{P}{Duration\ of\ \ infection}$$

Here, the duration of HIV infection is estimated at 11 years [11]. It bears notice that for the vast majority of countries, including those where SPECTRUM estimates are available, estimates predicted by SPECTRUM or derived using the DHS data were either similar or within the confidence intervals of each other.

Figure S1: Schematic diagram of the different data sources used to estimate the contribution of stable discordant couples to total HIV incidence in the population.

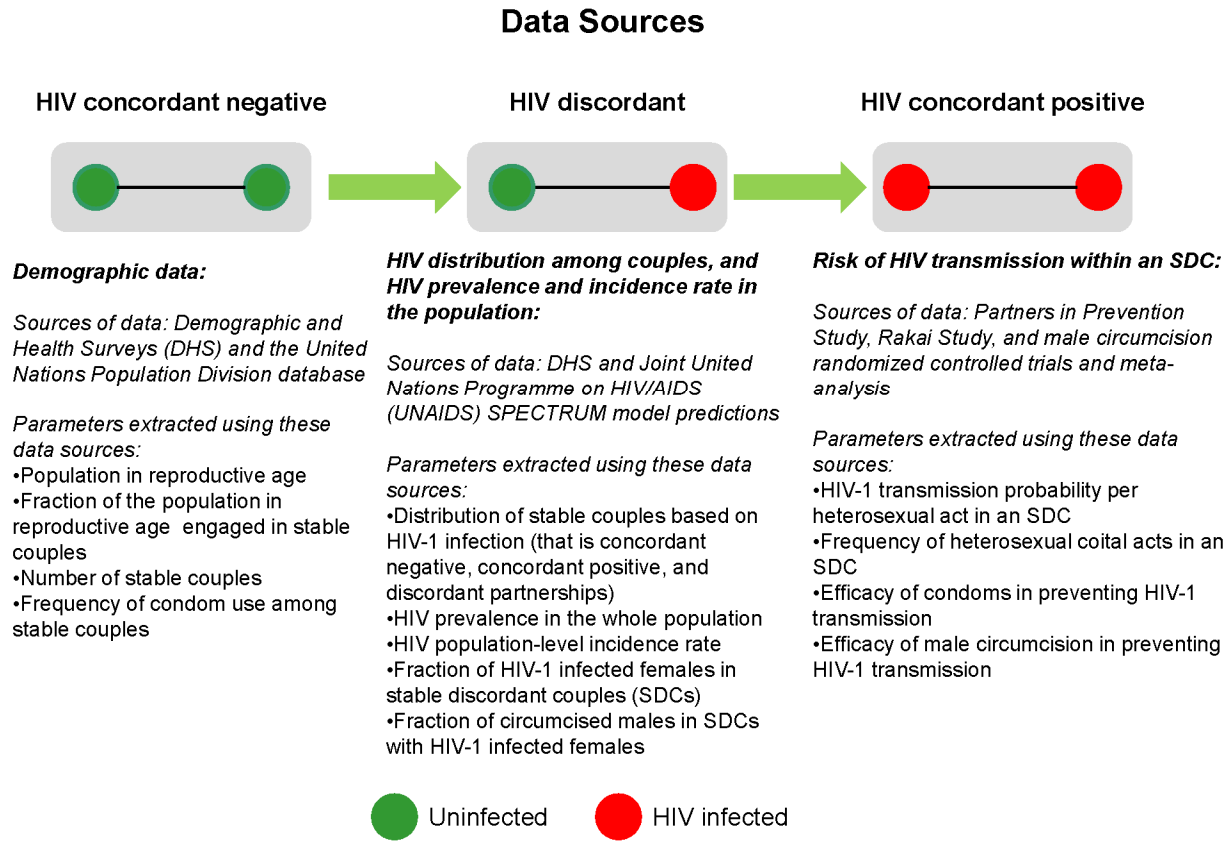


Table S1: Model assumptions related to different model parameters.

Assumptions	Parameter values	Source
HIV-1 transmission probability per coital act		
Average (p) using the Rakai Study	0.0012	[5]
Average (p) using the Partners in Prevention Study	0.0011	[6-8]
Average (p) using the Rakai and the Partners in Prevention studies	0.00115	Derived
Frequency of coital acts (n)	8.3 acts per month	[5]
Duration between each round of the cross-sectional survey ($\tau_{follow-up}$)	1 year	Assumption
Efficacy of condoms in preventing HIV-1 transmission (E_{condom})	80%	[8, 12]
Efficacy of male circumcision in preventing HIV-1 acquisition	58%	[13-16]

3 Uncertainty analyses

Uncertainty analyses were performed for the estimates of the contribution of SDCs to total HIV population-level incidence for each country using Monte Carlo sampling from uniform distributions for the specified ranges of uncertainty of the model parameters (Fig. S2). For 200,000 runs of the model, random values were selected at each run from the specified ranges of uncertainty for the HIV-1 transmission probability per heterosexual coital act, the country-specific fraction of the population in the reproductive age, the country-specific fraction of the population in reproductive age engaged in stable couples, the country-specific HIV-1 prevalence, the country-specific HIV population-level incidence rate, the country-specific prevalence of HIV-1 sero-discordancy among stable couples, the country-specific fraction of HIV-1 infected females in SDCs, the country-specific fraction of circumcised males in SDCs with HIV-1 infected females, the efficacy of male circumcision in preventing HIV-1 acquisition, the frequency of coital acts, the country-specific frequency of condom use among stable couples, and the efficacy of condoms in preventing HIV-1 transmission.

The uncertainty uniform distribution ranges were determined using either the confidence intervals around the empirical measures of these parameters or plausibility ranges as suggested by available empirical evidence. Country-specific ranges for the fraction of the population that are in the reproductive age were extracted from the DHS using the minima and maxima values of the proportions of men and women in the reproductive age. Similarly, country-specific ranges for the fraction of the population in reproductive age engaged in stable couples were extracted from the DHS using the minima and maxima values of the proportions of men and women reporting being in stable sexual couples. Meanwhile, ranges of uncertainty for the HIV population-level incidence rate were determined by the lower and upper bounds of the 95% confidence interval around this measure as provided by the SPECTRUM model for each country. In the absence of SPECTRUM estimates, or in instances where the bounds of the 95% confidence interval around this measure were not precisely specified, the ranges of uncertainty were derived using the confidence intervals around HIV-1 prevalence measures from the DHSs. Table S2 displays the ranges of uncertainty for the uniform distributions of the different model parameters.

Table S2: Model assumptions in terms of the ranges of uncertainty for the key parameters in the model. For parameters describing country-specific values, countries are shown in order of increasing HIV-1 prevalence.

Assumptions	**Parameter Range**	**Source**
HIV-1 transmission probability per heterosexual coital act		
Average (p)	0.0009-0.0015	[5]
Fraction of the population in the reproductive age		
Senegal	45.7-46.2%	[2]
Niger	34.6-38.5%	[2]
Mali	42.3-42.3%	[2]
Congo	44.1-46.5%	[2]
Ethiopia	42.7-44.5%	[2]
Sierra Leone	37.0-39.7%	[2]
Liberia	39.5-44.3%	[2]

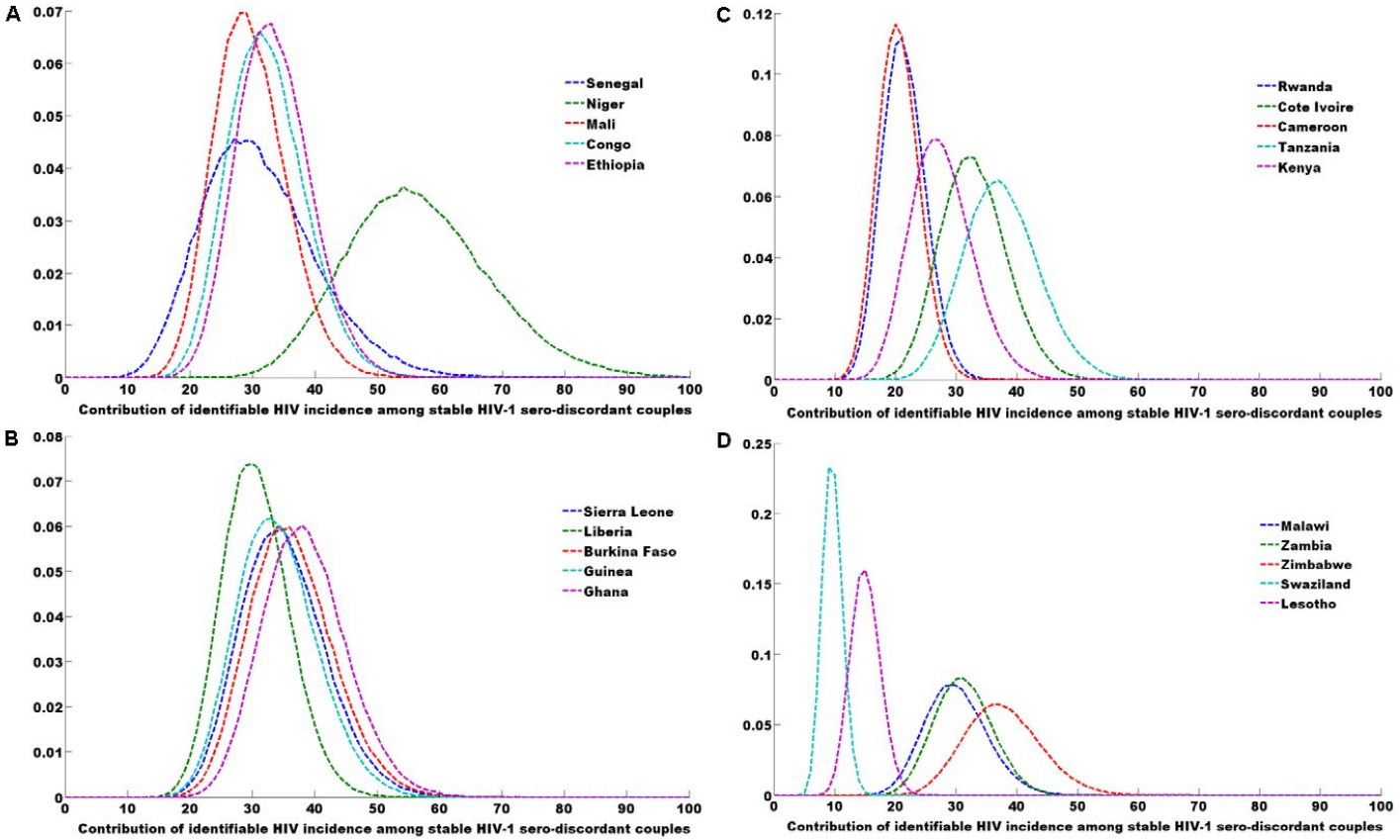
Burkina Faso	38.8-49.6%	[2]
Guinea	40.4-42.5%	[2]
Ghana	44.7-45.5%	[2]
Rwanda	46.2-46.7%	[2]
Cote d'Ivoire	46.6-49.2%	[2]
Cameroon	45.1-48.1%	[2]
Tanzania	39.9-43.5%	[2]
Kenya	45.4-45.9%	[2]
Malawi	40.8-43.4%	[2]
Zambia	42.1-44.3%	[2]
Zimbabwe	44.7-46.0%	[2]
Swaziland	44.2-45.8%	[2]
Lesotho	42.7-48.4%	[2]
Fraction of the population in reproductive age engaged in stable couples		
Senegal	49.62-67.56%	[2]
Niger	66.50-86.11%	[2]
Mali	65.05-84.79%	[2]
Congo	56.49-66.26%	[2]
Ethiopia	56.75-64.44%	[2]
Sierra Leone	63.32-74.93%	[2]
Liberia	56.83-64.02%	[2]
Burkina Faso	55.90-77.38%	[2]
Guinea	59.20-79.10%	[2]
Ghana	53.27-62.36%	[2]
Rwanda	48.67-51.86%	[2]
Cote d'Ivoire	44.42-58.99%	[2]
Cameroon	50.73-67.25%	[2]
Tanzania	53.06-64.03%	[2]
Kenya	51.36-58.36%	[2]
Malawi	58.78-67.45%	[2]
Zambia	55.76-61.60%	[2]
Zimbabwe	47.65-57.74%	[2]
Swaziland	29.32-41.34%	[2]
Lesotho	42.68-53.11%	[2]
HIV-1 prevalence		
Senegal	0.37-0.77%	[2]
Niger	0.51-0.91%	[2]
Mali	0.96-1.50%	[2]
Congo	1.01-1.60%	[2]
Ethiopia	1.18-1.74%	[2]
Sierra Leone	1.16-1.84%	[2]

Liberia	1.28-1.78%	[2]
Burkina Faso	1.24-1.90%	[2]
Guinea	1.27-1.95%	[2]
Ghana	1.76-2.37%	[2]
Rwanda	2.69-3.35%	[2]
Cote d'Ivoire	4.03-5.52%	[2]
Cameroon	4.91-5.83%	[2]
Tanzania	5.27-6.23%	[2]
Kenya	5.60-7.22%	[2]
Malawi	10.00-11.38%	[2]
Zambia	13.50-14.96%	[2]
Zimbabwe	17.35-18.96%	[2]
Swaziland	18.19-19.61%	[2]
Lesotho	21.82-24.16%	[2]
HIV population-level incidence rate (per 100 person-years)		
Senegal	0.03-0.07	[2]
Niger	0.05-0.08	[2]
Mali	0.09-0.14	[2]
Congo	0.09-0.15	[2]
Ethiopia	0.11-0.16	[2]
Sierra Leone	0.11-0.17	[2]
Liberia	0.12-0.16	[2]
Burkina Faso	0.11-0.17	[2]
Guinea	0.12-0.18	[2]
Ghana	0.14-0.21	[9, 10]
Rwanda	0.24-0.30	[2]
Cote d'Ivoire	0.37-0.50	[2]
Cameroon	0.49-0.67	[9, 10]
Tanzania	0.37-0.60	[9, 10]
Kenya	0.36-0.71	[9, 10]
Malawi	0.67-1.23	[9, 10]
Zambia	1.01-1.40	[9, 10]
Zimbabwe	0.86-1.48	[9, 10]
Swaziland	2.56-3.40	[9, 10]
Lesotho	2.18-3.04	[9, 10]
Prevalence of HIV-1 sero-discordancy among stable couples		
Senegal	0.14-0.97%	[2]
Niger	0.60-1.51%	[2]
Mali	0.79-1.68%	[2]
Congo	1.14-2.26%	[2]
Ethiopia	1.33-2.42%	[2]

Sierra Leone	1.13-2.48%	[2]
Liberia	1.35-2.51%	[2]
Burkina Faso	1.21-2.36%	[2]
Guinea	1.05-2.24%	[2]
Ghana	2·01-3.56%	[2]
Rwanda	1.62-2.91%	[2]
Cote d'Ivoire	4.41-7.02%	[2]
Cameroon	4.15-6.12%	[2]
Tanzania	5.53-7.38%	[2]
Kenya	4.69-7.42%	[2]
Malawi	7.47-9.37%	[2]
Zambia	9.79-12.40%	[2]
Zimbabwe	11.54-14.67%	[2]
Swaziland	13.64-19.44%	[2]
Lesotho	14.72-20.03%	[2]
Fraction of HIV-1 infected females in stable HIV-1 sero-discordant couples		
Senegal	9.90-81.59%	[2]
Niger	21.10-56.31%	[2]
Mali	49.82-86.25%	[2]
Congo	47.18-78.80%	[2]
Ethiopia	41.33-69.53%	[2]
Sierra Leone	36.35-79.29%	[2]
Liberia	46.38-75.49%	[2]
Burkina Faso	25.63-56.72%	[2]
Guinea	22.66-59.40%	[2]
Ghana	30.17-59.88%	[2]
Rwanda	23.14-50.20%	[2]
Cote d'Ivoire	49.83-73.71%	[2]
Cameroon	42.03-61.57%	[2]
Tanzania	37.32-54.71%	[2]
Kenya	42.83-65.69%	[2]
Malawi	38.84-50.98%	[2]
Zambia	34.42-46.55%	[2]
Zimbabwe	33.62-62.32%	[2]
Swaziland	42.99-62.32%	[2]
Lesotho	35.91-52.61%	[2]
Fraction of circumcised males in stable HIV-1 sero-discordant couples with HIV-1 infected females		
Senegal	15.81-100%	[2]
Niger	58.72-99.77%	[2]
Mali	73.97-99.87%	[2]
Congo	84.56-100%	[2]

Ethiopia	81.03-99.91%	[2]
Sierra Leone	76.84-100%	[2]
Liberia	87.66-100%	[2]
Burkina Faso	75.13-99.87%	[2]
Guinea	58.72-99.77%	[2]
Ghana	83.16-100%	[2]
Rwanda	11.89-54.28%	[2]
Cote d'Ivoire	17.18-46.13%	[2]
Cameroon	93.84-100%	[2]
Tanzania	40.12-66.02%	[2]
Kenya	62.39-89.44%	[2]
Malawi	26.07-44.40%	[2]
Zambia	5.82-18.44%	[2]
Zimbabwe	3.79-16.25%	[2]
Swaziland	8.44-28.97%	[2]
Lesotho	49.51-74.30%	[2]
Efficacy of male circumcision in preventing HIV-1 acquisition	43-69%	[13-16]
Frequency of coital acts (n)	4-12 acts per month	[5, 17]
Fraction of coital acts protected by condom use (f_{condom})		
Senegal	0.87-2.36%	[2]
Niger	0.05-0.50%	[2]
Mali	0.44-1.17%	[2]
Congo	1.37-2.62%	[2]
Ethiopia	0.07-0.48%	[2]
Sierra Leone	0.51-1.72%	[2]
Liberia	1.90-3.31%	[2]
Burkina Faso	3.26-5.26%	[2]
Guinea	0.44-1.49%	[2]
Ghana	2.54-4.37%	[2]
Rwanda	0.61-1.51%	[2]
Cote d'Ivoire	3.49-5.92%	[2]
Cameroon	3.96-5.98%	[2]
Tanzania	4.17-5.83%	[2]
Kenya	239-4.50%	[2]
Malawi	4.74-6.32%	[2]
Zambia	5.59-7.68%	[2]
Zimbabwe	2.28-3.90%	[2]
Swaziland	20.59-27.27%	[2]
Lesotho	21.18-27.34%	[2]
Efficacy of condoms in preventing HIV-1 transmission (E_{condom})	70-95%	[12]

Figure S2: Uncertainty analyses for the contribution of identifiable HIV incidence among stable HIV-1 sero-discordant couples to total HIV population-level incidence. The likelihood distribution of outcome was generated by Monte Carlo sampling from uniform distributions for the specified ranges of uncertainty of the demographic, biological, and epidemiological parameters of the model and using 200,000 runs of the model. Each panel displays the likelihood distribution for 5 countries. Countries are shown in order of increasing HIV-1 prevalence.



REFERENCES

1. Rottingen JA, Garnett GP. The epidemiological and control implications of HIV transmission probabilities within partnerships. *Sex Transm Dis* 2002,**29**:818-827.
2. Demographic and health surveys. In: *MEASURE DHS*. Calverton: ICF Macro.
3. Rutstein S., Rojas G. Guide to DHS statistics. In. Calverton, Maryland; 2006.
4. United Nations Population Division. World Population Prospects: the 2008 Revision Population Database. http://esa.un.org/unpp/index.asp?panel=2.
5. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O*, et al.* Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005,**191**:1403-1409.
6. Hughes JP. Personal communication. In; 2010.
7. Celum C, Wald A, Lingappa JR, Magaret AS, Wang RS, Mugo N*, et al.* Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. *N Engl J Med* 2010,**362**:427-439.
8. Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G*, et al.* Determinants of Per-Coital-Act HIV-1 Infectivity Among African HIV-1-Serodiscordant Couples. *J Infect Dis* 2012,**205**:358-365.
9. Gouws E, Joint United Nations Programme on HIV/AIDS (UNAIDS). Personal Communication. 2011.
10. UNAIDS. HIV estimates with uncertainty bounds 1990-2009. In; 2010.
11. UNAIDS. UNAIDS Reference Group on Estimates, Modelling and Projections. 2007.
12. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2001:CD003255.
13. Weiss HA, Halperin D, Bailey RC, Hayes RJ, Schmid G, Hankins CA. Male circumcision for HIV prevention: from evidence to action? *Aids* 2008,**22**:567-574.
14. 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. *PLoS Med* 2005,**2**:e298.
15. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN*, et al.* Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *The Lancet* 2007,**369**:643-656.
16. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F*, et al.* Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *The Lancet* 2007,**369**:657-666.
17. Brown MS. Coitus, the proximate determinant of conception: inter-country variance in sub-Saharan Africa. *J Biosoc Sci* 2000,**32**:145-159.