Abstract (100 Words)

A recent study showed that progestogen-only injectable hormonal contraception (POIHC) doubles the risk of HIV transmission. This may affect contraceptive use and HIV-related outcomes, if women switch away from POIHC. A deterministic compartmental model of individuals aged 15-49 distinguishing gender and HIV status was used to simulate various contraceptive use scenarios. We specifically tracked HIV prevalence, new infections, HIV-related deaths, vertical transmission, and births over a 15-year period for five African countries. Stopping POIHC use will result in a large increase in births and vertical transmission. Switching from POIHC to other contraceptives limits these increases while still improving HIV outcomes.

Keywords: HIV, contraception, mathematical modeling, Sub-Saharan Africa, population level impact

Body (2528 Words)

1. Introduction[1]

Injectable hormonal contraception is the preferred form of contraception in many sub-Saharan countries representing 8.1% to 28.4% of the contraceptive use in the countries we consider [1]. A shot provides two to three months of protection depending on the type. There are two types of progestogen-only injectable hormonal contraception (POIHC): depot-medroxy progesterone acetate (DMPA) and norethisterone enanthate (NET-EN). DMPA is the most widely used progestin-only injectable [2]. More than 12 million women in Africa use DMPA for pregnancy prevention [3]. POIHC is highly effective in preventing pregnancies compared to other methods, and it has a .3% risk of failure with perfect use and a 3% risk with typical use [4].

However, some observational studies (the earliest from 1991[4]) link the use of certain contraceptives with an increased risk of HIV acquisition [2, 5-12]. Most studies focus on combined oral contraceptives (COCs) and/or POIHC (including DMPA and NET-EN). There is limited data on the potential relationship between HIV risks and other hormonal contraceptive methods such as implants, vaginal rings, or intrauterine devices (IUD). Studies involving NET-EN did not conclude any significant relationship between NET-EN use and HIV risk [12-13].

On the other hand, there is evidence that DMPA increases HIV-acquisition and transmission risk. Clinical and laboratory studies suggest several possible biological reasons including vaginal structural changes, higher cervicovaginal HIV shedding and higher number of inflammatory cells in cervicovaginal fluid [14]. A recent study of HIV-1-serodiscordant couples in Africa (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zambia) by Heffron et al. suggests that DMPA may double the risk of HIV infection for women [2]. Subsequent meta-analyses also find increased HIV acquisition risk for

[1] POIHC: progestogen-only injectable hormonal contraception; DMPA: depot-medroxy progesterone acetate; NET-EN: norethisterone enanthate; FC: female condoms; VM: vaginal microbicides, MC; male contraceptives (condoms); OCP: oral contraceptive pills; NON: no contraception; OTH: other forms of contraception

women using DMPA [15-16]. In addition, Heffron et al. is the only study directly looking at the relationship between POIHC and HIV transmission risk, and find that this rate is doubled. They observed increased concentrations of HIV-1 RNA in endocervical secretions from HIV-1 infected women using injectable contraceptives as the potential cause for the increased risk of HIV transmission [2].

Results from this study caused debate among healthcare providers and policy makers. The previous recommendation of the World Health Organization (WHO) did not have any restrictions on the use of hormonal contraceptives [17]. Even though the WHO kept its policy recommendation, it recommended that women using POIHC should get dual protection for HIV and pregnancy by using female or male condoms in addition to POIHC [18-19].

While there is no consensus about the exact effect of POIHC on HIV risk, these studies may lead to changes in public health programs for family planning. Especially, in African countries with high prevalence of both POIHC use and HIV, governments may advise women to quit using POIHC or to switch to other methods. Switching from POIHC to other forms of contraception may reduce HIV infections. On the other hand, decreased use of these contraceptives may cause an increase in unintended pregnancies and higher mother-to-child transmission (vertical transmission) of HIV. This of course depends on the type of contraception because male condoms, for example, are also recognized as a way of controlling the HIV epidemic, preventing HIV infection among adults, and preventing mother-to-child HIV transmission [20].

In this article, we model the population level impact of the potential association of POIHC with increased HIV risk. We predict the effect of potential changes in DMPA use on childbirths, vertical transmission, HIV infections and prevalence in different countries in sub-Saharan Africa for a variety of scenarios of changes in contraceptive use. The remainder of this paper is organized as follows. Section 2 presents the model. Section 3 provides numerical results, and section 4 discusses these results. Section 5 concludes the paper with final remarks.

2. Methods

2.1 Model

The population we consider is adults aged 15-49. We use a deterministic compartmental model of HIV spread. We select Kenya, Zambia, South Africa, Rwanda and Botswana for our study. These are the same countries that Heffron et al. studied except that we omit Uganda and Tanzania as their prevalence is similar to Kenya's (6.5%, 5.6%, and 6.3%, respectively), which we do include. Contraceptive use information was not available for Tanzania and overall contraceptive use was lower in Uganda (23.7%) than in Kenya (45.5%).

The WHO states that the risk of HIV transmission due to POIHC is more important for countries where women have a high risk of acquiring HIV; where hormonal contraceptives (especially POIHC) count for a significant portion of all modern methods used; and where the maternal mortality rate (MMR) is high [17]. These countries are in sub-Saharan Africa where the majority of women with HIV in the world reside [21]; where POHIC represents from 20% to almost 60% of all modern methods of contraception [1]; and where the MMR is mostly higher than the global average. The MMRs of Kenya, Zambia, South Africa, Rwanda, and Botswana are 413, 603, 237, 383 and 513 per 100,000 live births respectively while the global average is 251 per 100,000 live births [22]. In addition, Kenya, Zambia, South Africa, Rwanda, and Botswana display variety in the levels of HIV prevalence and in the usage of different contraceptives.

We assume all transmission is heterosexual and divide the adult population into four compartments by gender and HIV status. We assume that the ratio of women to men is one, since the actual ratio is quite close. We also assume that contraceptive use does not affect the progression of HIV in an HIV-infected female [17]. Fig. 1 illustrates the compartmental model and Table A.1 in the Appendix summarizes the notation used.

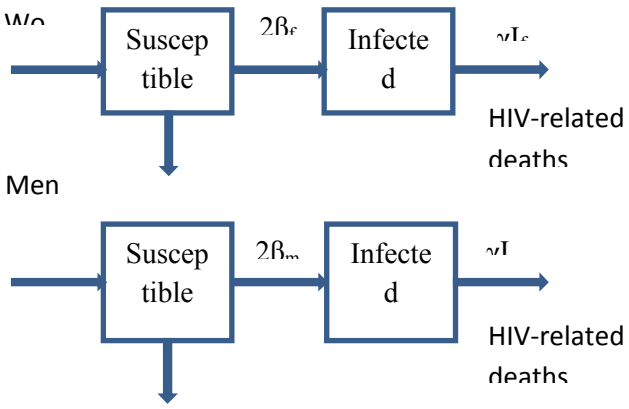


Fig. 1. Compartmental Model

Below are the differential equations (Eq. 1-7) that fully specify the model. Here N is the size of our population; I_f and I_m are the number of infected females and males in the population; and S_f and S_m are the number of susceptible females and males in the population. Note that $I_f + S_f = I_m + S_m = N/2$, $\left(1 - \frac{I_f}{N/2}\right) = S_f / N$, and $\left(1 - \frac{I_m}{N/2}\right) = S_m / N$. The first two equations describe the rate of new infections; the third equation describes the overall population growth; and Eq. 4-6 describe outcomes of interest:

$$\dot{I}_f = -\gamma I_f + \beta_f I_m \left(1 - \frac{I_f}{N/2}\right) \quad (1)$$

$$\dot{I}_m = -\gamma I_m + \beta_m I_f \left(1 - \frac{I_m}{N/2}\right) \quad (2)$$

$$\dot{N} = \alpha N \quad (3)$$

$$\dot{J} = \beta_f I_m \left(1 - \frac{I_f}{N/2}\right) + \beta_m I_f \left(1 - \frac{I_m}{N/2}\right) \quad (4)$$

$$\dot{V} = \delta I_f \quad (5)$$

$$\dot{B} = \phi N \quad (6)$$

The four outcomes we track are the cumulative number of infections since the start of the simulation, J, (not the current number of infected); the cumulative number of cases of vertical transmission (i.e., mother-to-child transmission), V; the cumulative number of births, B; and the HIV prevalence at the end of the simulation. The time horizon we look at, 15 years, is short enough that infants infected vertically do not enter the adult population in our model, allowing us to assume that individuals enter the population uninfected.

2.2 Scenarios of Future Contraceptive Use

To compare different levels of contraceptive use, we track the fraction using POIHC, IUD, female condoms (FC), vaginal microbicides (VM), male contraceptives (condoms) (MC), oral contraceptive pills (OCP), no contraception (NON), and other forms of contraception (such as vaginal barrier methods) (OTH). We include vaginal microbicides even though they do not prevent pregnancy, because they do prevent HIV infection. We assume that OTH do not affect HIV transmission. We do not consider couples using multiple forms of contraception simultaneously because that is not common [23]. Overall, we consider methods only preventing pregnancy (POIHC, IUD, OCP and OTH), methods only preventing HIV (VM), and dual protection methods which refers to methods that prevent both HIV and pregnancy (MC and FC).

We consider various scenarios of future contraceptive use. A scenario P=(p_{POIHC}, p_{IUD}, p_{FC}, p_{VM}, p_{MC}, p_{OCP}, p_{OTH}, p_{NON}) is a vector that tracks the fraction using each type. For example, the scenario (10%, 2%, 1%,

3%, 1%, 5%, 20%, 55%) has 10% of females using POIHC, 2% of females using IUD, 1% of females using FC, 3% of females using VM, 1% of males using MC, 5% of females using OCP, 20% of females using other forms of contraception, and 55% of couples using no contraception. Our sources do not directly give the fraction using other forms of contraception (OTH) so we calculate this from the fact that the components of P sum to 100%.

We consider six different scenarios in addition to a baseline (i.e., status quo) scenario and then look at the various outcomes over a 15-year horizon. We assume that sexual behavior does not change beyond these explicit changes in contraceptive use detailed in the following scenarios. Thus, our analysis does not consider self-selection of one type of contraceptive over another or why people switch from one form to another. The baseline scenario (scenario 0) represents the current situation and corresponds to vector P_0 of contraceptive use and its values are given in Table 1 for various countries. Scenarios 2-6 consider five alternative futures: in each, the population switches to a different distribution of contraceptive use. Since changing behavior takes time [24], whether due to a public health campaign or not, we assume that in scenarios 1-5, the contraceptive use switches from the current levels after one year. Note that in scenarios 2, 5, and 6, the total fraction of the population using any kind of protection does not change. In the other scenarios, the total fraction using protection may be significantly less than in the baseline except for Botswana where the total contraceptive use increases slightly.

Scenario 0 (Baseline): Current contraceptive use. $P_0=(p_{0,POIHC}, p_{0,IUD}, p_{0,FC}, p_{0,VM}, p_{0,MC}, p_{0,OCP}, p_{0,OTH}, p_{0,NON})$,

Scenario 1 (POIHC to NON): After one year, all POIHC users stop using POIHC and switch to NON.

$P_1=(0, p_{0,IUD}, p_{0,FC}, p_{0,VM}, p_{0,MC}, p_{0,OCP}, p_{0,OTH}, p_{0,NON}+p_{0,POIHC})$,

Scenario 2 (POIHC to OTH): After one year, all POIHC users stop using POIHC and switch to OTH.

$P_2=(0, p_{0,IUD}, p_{0,FC}, p_{0,VM}, p_{0,MC}, p_{0,OCP}, p_{0,OTH}+p_{0,POIHC}, p_{0,NON})$,

Scenario 3 (POIHC to IUD & MC): After one year, POIHC use drops 50%, IUD use increases 25%, and MC use increases 25%. The remaining individuals switching from POIHC will not use any form of contraception. P_3=($0.5p_{0,POIHC}$, $1.25p_{0,IUD}$, $p_{0,FC}$, $p_{0,VM}$, $1.25p_{0,MC}$, $p_{0,OCP}$, $p_{0,OTH}$, $p_{0,NON}$+($0.5p_{0,POIHC}$-$0.25p_{0,IUD}$ -$0.25p_{0,MC}$)),

Scenario 4 (POIHC to MC): After one year, POIHC use drops 50% and MC use increases 50%. The remaining individuals switching from POIHC will not use any form of contraception. P_4=($0.5p_{0,POIHC}$, $p_{0,IUD}$, $p_{0,FC}$, $p_{0,VM}$, $1.5p_{0,MC}$, $p_{0,OCP}$, $p_{0,OTH}$, $p_{0,NON}$+($0.5p_{0,POIHC}$-$0.5p_{0,MC}$)),

Scenario 5 (POIHC to FC): After one year, 25% of POIHC users switch to FC. P_5=($0.75p_{0,POIHC}$, $p_{0,IUD}$, $p_{0,FC}$+$0.25p_{0,POIHC}$, $p_{0,VM}$, $p_{0,MC}$, $p_{0,OCP}$, $p_{0,OTH}$, $p_{0,NON}$),

Scenario 6 (POIHC to VM): After five years, 25% of POIHC users switch to VM. P_6=($0.75p_{0,POIHC}$, $p_{0,IUD}$, $p_{0,FC}$, $p_{0,VM}$+$0.25p_{0,POIHC}$, $p_{0,MC}$, $p_{0,OCP}$, $p_{0,OTH}$, $p_{0,NON}$).

We have no basis upon which to predict the future prevention behavior in these countries. We choose these scenarios because they cover a variety of possibilities of what might happen. They allow for the continued use of POIHC; users ceasing to use any contraceptives; and users switching to other contraceptives, including a new HIV prevention method (VM). They also cover the possibility of a net decrease in the number of people using contraception. We should note that these are scenarios rather than explicit interventions. We do not consider costs; the feasibility of achieving a particular scenario using a public health campaign; or try to determine the optimal distribution of contraceptive that such a campaign should aim for. Changing behavior on a national level has all kinds of difficulties that are hard to model [25].

2.3 Parameter Values

For the HIV acquisition risk, Heffron et al. find that DMPA doubles it [2], and subsequent meta-analyses find a 1.5-fold [15] and a 1.4-fold [16] increase. We use 1.5 because [15] surveys 18 studies while [16]

considers only 10 studies. For HIV transmission risk, Heffron et al. is the only study directly measuring the impact of POIHC on it [26], and so we use its finding that the risk is doubled.

We assume that 65% of eligible individuals receive antiretroviral therapy (ART) [27]; that the life expectancy without ART is 11.6 years after HIV infection [28]; and that the life expectancy with ART is 37 years after HIV infection [29]. We obtain the HIV-related mortality rate of the population, γ=35%(1/11.6year)+65%(1/37year), by taking a weighted average of the rates with and without ART. Equations (8-16) below describe how to calculate for a scenario P the four model parameters β_f, β_m, φ, and δ, which are not given directly in Table 1. Here β_f and β_m are the infection rates for females and males, φ is the total birth rate, and δ is the vertical transmission rate.

$$\xi_{ff} = \xi_{IHC}^{f} p_{IHC} + \xi_{VM}^{f} p_{VM} + \xi_{FC}^{f} p_{FC} + 1(p_{IUD} + p_{OTH} + p_{NON}) \quad (7)$$

$$\xi_{mf} = \xi_{MC}^{f} p_{MC} + 1(1 - p_{MC}) \quad (8)$$

$$\beta_f = \beta_{0f} \xi_{ff} \xi_{mf} \quad (9)$$

$$\xi_{mm} = \xi_{MC}^{m} p_{MC} + 1(1 - p_{MC}) \quad (10)$$

$$\xi_{fm} = \xi_{IHC}^{m} p_{IHC} + \xi_{FC}^{m} p_{FC} + 1(1 - p_{IHC} - p_{FC}) \quad (11)$$

$$\beta_m = \beta_{0m} \xi_{mm} \xi_{fm} \quad (12)$$

$$\chi = \sum_i \chi_i p_i \quad (13)$$

$$\varphi = \chi \varphi_0 \quad (14)$$

$$v = p_{ART} \pi + (1 - p_{ART}) \pi' \quad (15)$$

$$\delta = v\varphi \quad (16)$$

We calculate β_f, β_m, and φ by multiplying risk-adjustment factors with the values these parameters take with no contraception, β_{0f}, β_{0m}, and φ_0. Specifically, we calculate the HIV infection rate of women, β_f, in

Eq. (7-9) by multiplying β_{0f} by ξ_{ff} and ξ_{mf}, the risk-adjustment factors for female contraception (POIHC, VM, and FC) and male condoms, respectively. These risk adjustment factors are weighted sums of the risk-reduction for female (male) infection due to each form of contraception, for example the risk reduction of MC for female (male) infection, ξ^f_{MC} (ξ^m_{MC}), weighted by the use of MC, p_{MC}. Similarly, we calculate in Eq. (10-12) the HIV infection rate of men, β_m. In Eq. (13-14), we calculate the birth rate, φ, by multiplying φ_0 with the relative risk of pregnancy, χ. This relative risk is again a weighted sum of the effectiveness of each form of contraception [4]. We calculate the rate of vertical transmission, δ, by multiplying the risk of vertical transmission per birth, v, by the birth rate φ (Eq. (15-16). The risk of vertical transmission is π if the mother is on ART and π' without any treatment or intervention. Thus, we calculate the risk of vertical transmission, v, as a weighted sum of π and π' weighted by the percentage of the HIV+ pregnant females who are on antiretroviral drugs, p_{ART} [30].

We choose the remaining parameters, β_{0f}, β_{0m}, and φ_0, so that the above equations give the current values of β_f, β_m, and φ for the status quo scenario, P_0. We fit the base contact rates β_{0m} and β_{0f} for each country such that (a) the infection rate for females is twice that of males, $\beta_{0f}=2\beta_{0m}$ [31]; and (b) that the ratio of the simulated prevalence at year 5 to the starting prevalence matches the ratio of the prevalence in 2012 to the prevalence in 2007. To determine φ_0, we first calculate the risk of being pregnant, χ, under P_0. We then look up the current birth rate, τ [32], and using Eq. (13-14) set $\phi_0 = \tau / \chi$. Table 1 gives the parameter values and Table A.2 in the Appendix shows the calculated values of the parameters we discussed above for the baseline scenario. To validate the model, Appendix Fig. A.1 compares the relative change in the simulated prevalence over time to the UNAIDS prevalence estimates from 2007 to 2012.

Parameter					Value	Source
	Kenya	**Zambia**	**South Africa**	**Rwanda**	**Botswana**	
Initial female prevalence, $2I_f/N$ (%)	7.15	13.10	21.35	3.22	25.09	[37]
Initial male prevalence, $2I_m/N$ (%)	5.1	12.3	14.4	2.6	20.09	[37]
Annual population growth rate, α (%)	2	2	2	2	2	[30]
Annual mortality rate of HIV+ (deaths per year), γ	.0477	.0477	.0477	.0477	.0477	[27, 28,29]
Contraceptive use in status quo, P_0 (%) *						[1]
POIHC	21.6	8.5	28.4	15.2	8.1	
IUD	1.6	0.1	1	0.2	1.7	
FC	0	0	0	0	0	
VM	0	0	0	0	0	
MC	1.8	4.7	4.6	1.9	15.5	
OCP	7.2	11	0.9	6.4	14.3	
OTH	13.3	16.5	15	12.7	4.8	
NON	54.5	59.2	40.1	63.6	55.6	
Relative risk of contraceptives on female infection rate, ξ_i^f **						[18,33,4,34]
POIHC	1.5	1.5	1.5	1.5	1.5	
IUD	1	1	1	1	1	
FC	.24	.24	.24	.24	.24	
VM	.46	.46	.46	.46	.46	
MC	.2	.2	.2	.2	.2	
OCP	1	1	1	1	1	
OTH	1	1	1	1	1	
NON	1	1	1	1	1	
Relative risk of contraceptives on male infection, ξ_i^m						[2,33,4,34]
POIHC	2	2	2	2	2	
IUD	1	1	1	1	1	
FC	.24	.24	.24	.24	.24	
VM	1	1	1	1	1	
MC	.2	.2	.2	.2	.2	
OCP	1	1	1	1	1	
OTH	1	1	1	1	1	
NON	1	1	1	1	1	
Risk reduction of a birth control method for pregnancy, (1- χ_i) (%)						[4]
POIHC	97	97	97	97	97	
IUD	99.2	99.2	99.2	99.2	99.2	

FC	79	79	79	79	79	
VM	15	15	15	15	15	
MC	85	85	85	85	85	
OCP	92	92	92	92	92	
OTH	70	70	70	70	70	
NON	15	15	15	15	15	
Percentage of pregnant females on ART, p_{ART} (%)	73	69	88	65	95	[27]
Vertical transmission probability (%)						
When HIV+ mother is on ART, π	5	5	5	5	5	[35]
When HIV+ mother is not on ART, π'	26	26	26	26	26	[36]
Current annual birth rate (per 1000), τ	31.93	43.51	19.32	36.14	22.02	[32]

* Acronyms: Progestogen-only injectable hormonal contraception (POIHC), IUD, female condoms (FC), vaginal microbicides (VM), male condoms (MC), oral contraceptive pills (OCP), other forms of contraception (OTH), and no contraception (NON).
** Even though VM is not a contraceptive method, it is included in the study for its protective effect on HIV transmission.
Table 1. Parameters

2.4 Analysis

To better understand the simulation results in the various scenarios, we also conducted a marginal analysis that decomposed the increase in the births and the change in new infections into the change in usage of each contraceptive type and their effectiveness per unit of usage in the population on reducing births and HIV infections. These results are then compared to the simulation results. We should also note that these are linear approximations while the simulation follows the disease dynamics over 15 years.

As discussed in the previous subsection, the degree to which POIHC increases HIV acquisition is uncertain, and so far, Heffron et al. is the only study directly looking at the degree to which POIHC increases HIV transmission [2]. We perform sensitivity analysis focusing on this key factor by varying the risk of HIV male-to-female and female-to-male transmission when using POIHC. Specifically, we investigate the following cases for the impact on POIHC use:

Case 0 (Baseline): 50% increase in HIV acquisition risk, 100% increase in female-to-male transmission risk,

Case 1: 100% increase in HIV acquisition risk, 100% increase in female-to-male transmission risk,

Case 2: 50% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk,

Case 3: 50% increase in HIV acquisition risk, 0% increase in female-to-male transmission risk,

Case 4: 0% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk,

Case 5: 0% increase in HIV acquisition risk, 0% increase in female-to-male transmission risk.

In addition, we conduct a probabilistic sensitivity analysis for five parameters (HIV acquisition and transmission rate with POIHC, birth rate, and initial contraceptive use of POIHC, initial contraceptive use of MC). For each replication in the probabilistic sensitivity analysis, we simultaneously draw each parameter from a uniform distribution ranging from -10% to +10% of its baseline value. We chose this distribution for its simplicity.

3. Results

Fig. 2 compares the simulation outcomes of the various scenarios to the baseline scenario. The absolute magnitude of the outcomes is shown in Table A.4 in the Appendix, and the change in prevalence over time is shown in Fig. A.2 in the Appendix. Compared with the baseline, all scenarios had fewer new infections and lower prevalence. In most scenario-country combinations, the births increased compared with the baseline, while the change in vertical transmission had no clear trend.

Scenarios *POIHC to NON* and *POIHC to OTH* provide the most reduction in terms of new infections and prevalence for all countries except Botswana. These reductions are larger in countries where both the current prevalence and POIHC use are high, such as Kenya and South Africa. Since the initial HIV

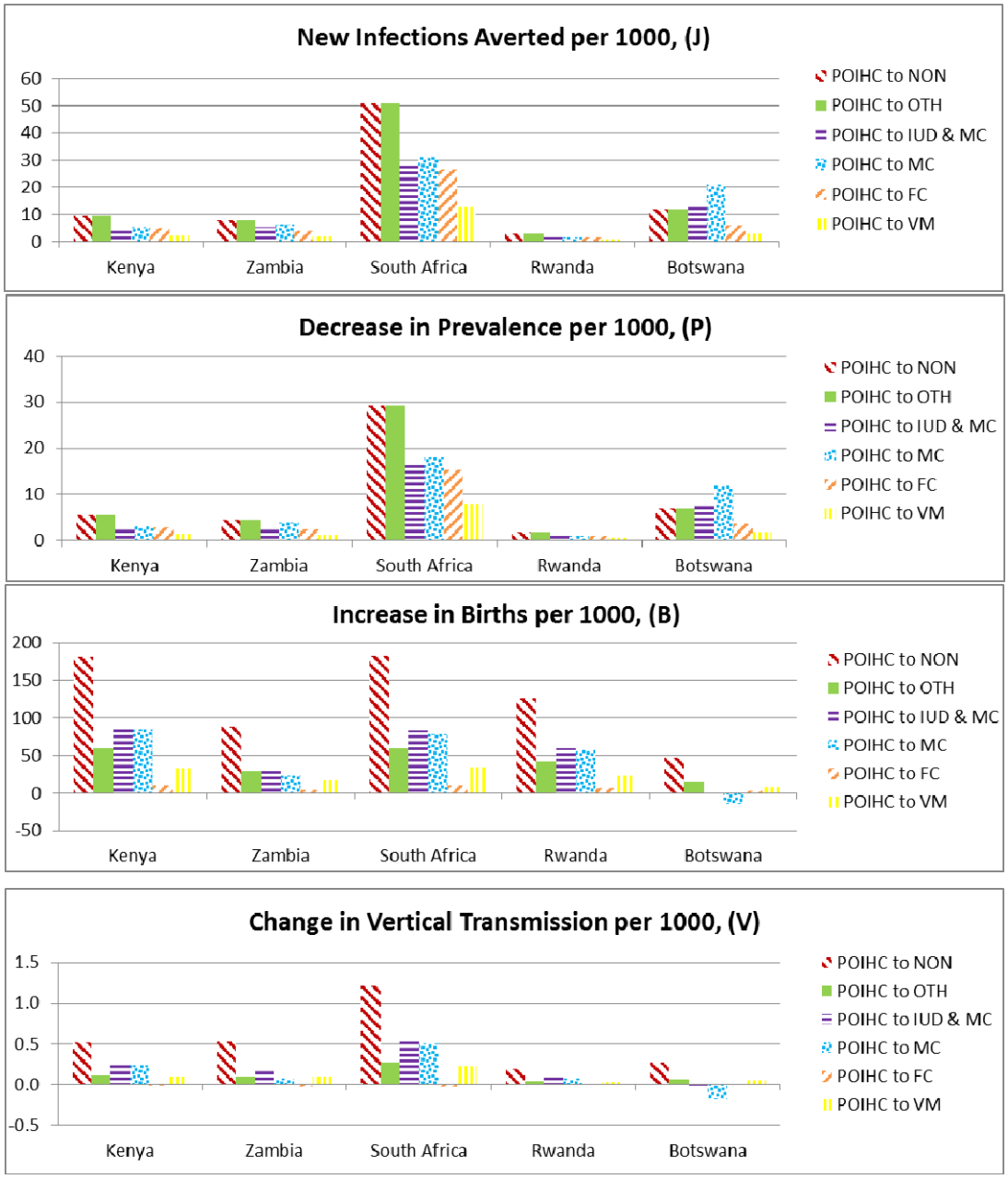


Fig. 2. State in 15 Years: new infections averted, decrease in prevalence, increase in births and change in vertical transmission per 1000. POIHC, NON, OTH, IUD, MC, FC and VM stand for progestogen-only

injectable hormonal contraception, no contraception, other contraception methods, intrauterine device, male condom, female condom and vaginal microbicides, respectively.

prevalence was significantly higher in South Africa than in Kenya, these scenarios lead to correspondingly larger reductions.

In Botswana, *POIHC to MC* followed by *POIHC to IUD & MC* provide the largest reduction in terms of new infections and prevalence. This result is driven by the significant increase in MC use and the fact that the initial contraceptive use of MC is higher in Botswana than in other countries. Thus, as mentioned before, the 25% or 50% increase in MC use outweighs the users switching away from POIHC, resulting in a net increase in the total contraceptive use whereas in all other scenario-country combinations, there is a net decrease in contraceptive use. Additionally, MC has the most protection against HIV. Table A.5 in the Appendix uses marginal analysis to explain in detail such changes for each country.

In Table A.3 of the Appendix we also see the relative reduction in new infections by sex. We find that the benefit for men and women is almost the same except in scenario *POIHC to VM*. Females have a greater decrease in new infections than males in scenario *POIHC to VM* because VM only reduces the risk of HIV infection for women.

We see that births increase for almost all scenarios in all countries except in Botswana where the births decrease in scenario *POIHC to MC*. As before, Botswana is an exception due to the high initial MC use. In all countries, scenario *POIHC to NON* results in the largest increase in births and vertical transmission.

We observe that scenarios with a method preventing both pregnancy and HIV (*POIHC to IUD&MC*, *POIHC to MC*, and *POIHC to FC*) perform better than scenarios focusing on a method preventing only HIV (*POIHC to VM*) for most of the outcomes. This effect is most obvious when comparing scenario *POIHC to FC* to scenario *POIHC to VM* where the exact same number of the women switch to FC in the former and VM in the latter. We see that scenario *POIHC to FC* outperforms scenario *POIHC to VM* in

all outcome measures. This is due to the fact that VM only prevents HIV infection and is not a form of contraception while FC does both.

The marginal analysis is shown in Table 2 below for Kenya and in Table A.4 of the Appendix for all the countries of births and new infections in Table 2 below and Table A.4 in the Appendix. It is reassuring that the marginal analysis, which used a linear approximation, gives results with relative differences that are similar to those of the simulation results. The *POIHC to VM* scenario seems to show larger differences, which can be explained by the fact that in this scenario VM was not in place until five years after other contraceptive changes.

Fig. 3 shows the sensitivity analysis for Kenya. Sensitivity analysis results for all countries are given in Fig. A.3 and Table A.5 in the Appendix. For the new infections averted and the increase in births, Fig. 3 also includes the standard deviation of those outcomes in the probabilistic sensitivity analysis, which can be found in Fig. A.4 of the Appendix. Births (though not cases of vertical transmissions) remain the same for all sensitivity cases since we only consider changes in HIV acquisition and transmission risk. For HIV-related outcomes, all cases show a smaller decrease (some by up to a factor of 2.5) compared to the baseline case where we used the risk numbers provided by Morrison [16] and Heffron et al. [2]. When we compare the cases to Case 1 (rather than Case 0), in which we take risk numbers from Heffron et al., the other sensitivity cases show a smaller decrease for the HIV-related outcomes (some by up to a factor of 3.5). The impact depends on the country. For example, when these parameters decrease, Kenya, South Africa and Rwanda show similar behavior (where *POIHC to FC* is most favorable), different from Zambia and Botswana (where *POIHC to MC* is most favorable).

Contraceptive Type	Change in Each Contraceptive Type per Each Scenario							Change in Relative Risk				Change in New Infections (per 1000)					
	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	FF	MF	MM	FM	NON	OTH	IUD	MC	FC	VM
POIHC	21.6	-21.6	-21.6	-10.8	-10.8	-5.4	-5.4	0.39	0.01	0.01	0.78	2.3	2.3	1.1	1.1	0.6	0.6
IUD	1.6	-	-	0.4	-	-	-	-0.11	0.01	0.01	-0.22	-	-	0.0	-	-	-
FC	-	-	-	-	-	5.4	-	-0.87	0.01	0.01	-0.98	-	-	-	-	0.9	-
VM	-	-	-	-	-	-	5.4	-0.65	0.01	0.01	-0.22	-	-	-	-	-	0.5
MC	1.8	-	-	0.5	0.9	-	-	-0.11	-0.79	-0.79	-0.22	-	-	0.1	0.2	-	-
OCP	7.2	-	-	-	-	-	-	-0.11	0.01	0.01	-0.22	-	-	-	-	-	-
OTH	13.3	-	21.6	-	-	-	-	-0.11	0.01	0.01	-0.22	-	0.5	-	-	-	-
NON	54.5	21.6	-	10.0	9.9	-	-	-0.11	0.01	0.01	-0.22	0.5	-	0.2	0.2	-	-
Any BC	45.5	-21.6	-	-9.9	-9.9	-	-5.4				Total Change	2.8	2.8	1.5	1.6	1.5	1.1
Any BC/HIVp	1.8	-	-	0.5	0.9	5.4	-				Simulation	9.4	9.4	5.0	5.3	4.9	2.3

Contraceptive Type	Contraceptive usage as fraction of the population							Difference in Pregnancy Risk Compared to Average	Increase in Births per 1000					
	Baseline (%)	Change in Percentage Points												
		NON	OTH	IUD & MC	MC	FC	VM		NON	OTH	IUD & MC	MC	FC	VM
POIHC	21.6	-21.6	-21.6	-10.8	-10.8	-5.4	-5.4	-0.49	105.5	105.5	52.7	52.7	26.4	26.4
IUD	1.6	-	-	0.4	-	-	-	-0.51	-	-	-2.0	-	-	-
FC	-	-	-	-	-	5.4	-	-0.31	-	-	-	-	-16.6	-
VM	-	-	-	-	-	-	5.4	0.33	-	-	-	-	-	17.9
MC	1.8	-	-	0.5	0.9	-	-	-0.37	-	-	-1.8	-3.3	-	-
OCP	7.2	-	-	-	-	-	-	-0.44	-	-	-	-	-	-
OTH	13.3	-	21.6	-	-	-	-	-0.22	-	-47.1	-	-	-	-
NON	54.5	21.6	-	10.0	9.9	-	-	0.33	71.7	0.0	33.2	32.8	-	-
Any BC	45.5	-21.6	-	-9.9	-9.9	-	-5.4	Total change	177.1	58.3	82.0	82.3	9.7	44.3
Any BC/HIVp	1.8	-	-	0.5	0.9	5.4	-	Simulation Result	181.4	59.7	84.0	84.2	10.0	33.6

Table 2. Marginal Analysis for Kenya a) Change in New Infections b) Increase in Births. Change in outcomes based on the change in the usage of each contraceptive type and their effectiveness per unit of usage in the population on reducing births and HIV infections. BC refers to birth control while BC/HIVp refers to any form of contraception that also prevents HIV (FC and MC)

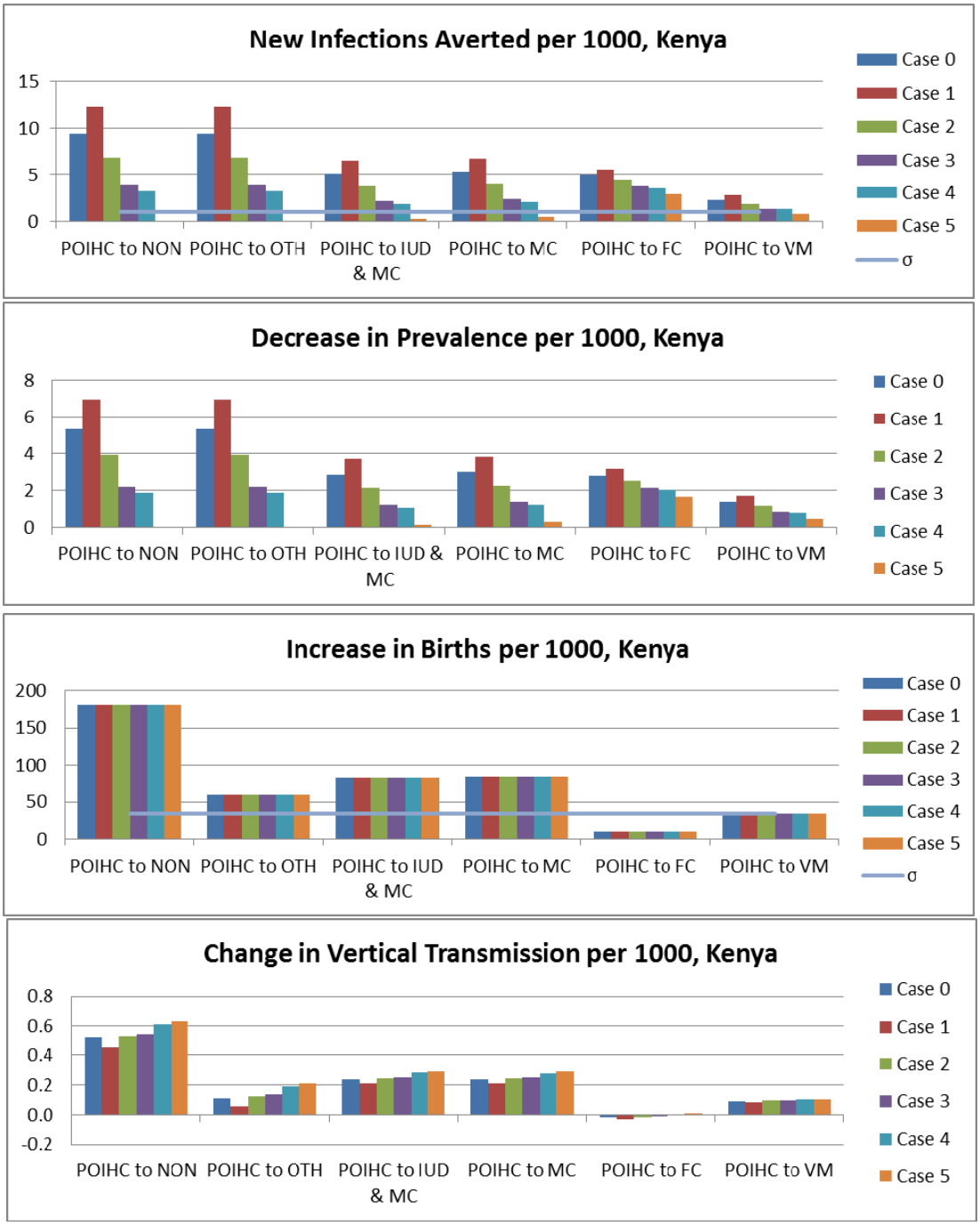


Fig. 3: Sensitivity Analysis of POIHC on HIV Risk for Kenya. Case 0 (Baseline): 50% increase in HIV acquisition risk, 100% increase in female-to-male transmission risk. Case 1: 100% increase in HIV

acquisition risk, 100% increase in female-to-male transmission risk, Case 2: 50% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk, Case 3: 50% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk, Case 4: 50% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk, Case 5: 0% increase in HIV acquisition risk, 0% increase in female-to-male transmission risk. For the panels showing the new infections averted and the increase in births, we show for comparison, σ, the standard deviation of the baseline number of new infections and births, respectively, from the probabilistic sensitivity analysis.

Case 0 and Case 1 have the most dramatic results. Case 1, which uses the HIV risk parameters from Heffron et al. gives the largest decrease in new infections and prevalence and the lowest increase in vertical transmission. Since births are unaffected and since Case 1 has the highest transmission and acquisition risk, these results are expected. As the case number increases, the decrease in the new infections and prevalence slows down while the increase in vertical transmission increases slightly. Case 3 and 4 where the acquisition and transmission risks are increased by 50%, respectively, show similar results with Case 3 being more favorable for HIV outcomes.

Comparing for the new infections averted in Fig. 3, the size of the standard deviation from the probabilistic sensitivity analysis to the size of the differences of the Cases to the baseline case 0, confirms that a key parameter is the HIV acquisition and transmission risk when using POIHC.

4. Discussion

The large increase in births and cases of vertical transmission make scenario *POIHC to NON*, where all POIHC users stop using any form of protection, undesirable. In all other scenarios, HIV-related outcome measures (new infections and prevalence) improve up to 21% while births increase less than 15% with the exception being South Africa where births increase up to 24%. In most scenarios and countries, the change in the level of vertical transmission is small and can go in either direction. In contrast, the *POIHC to OTH* scenario leads to similarly good HIV outcomes, while having a substantially smaller increase in births. However, it is the only scenario that keeps all POIHC users on some form of contraception, making it unfair to compare it to the other scenarios and emphasizing the importance of keeping women

that discontinue POIHC on *some* form of contraception. In the following we compare the remaining four scenarios.

In general, dual protection methods perform the best as expected. Aside from *POIHC to NON*, *POIHC to MC* provides the largest decrease in new infections and prevalence followed by *POIHC to IUD&MC* and *POIHC to FC*. *POIHC to FC* results in the lowest increase in births followed by *POIHC to VM* and *POIHC to MC*. While these different scenarios have similar effects in most of the countries, the magnitudes of the effects are different in each country due to the initial distribution of the contraceptive use. Similar to births, *POIHC to FC* provides the lowest increase in vertical transmission. However, since vertical transmission depends on both birth and new infections, it is hard to identify similar trends for other scenarios as we did for the other metrics. We can also conclude that for Botswana, scenario *POIHC to MC*, which emphasizes male condoms, is the preferred scenario because it provides the greatest reduction in all outcomes (provided of course that the significant increase in MC use is possible in Botswana). Even the births are expected to decrease by 4% for Botswana with this scenario since the current MC use is quite high, and the increase in MC use compensates for their decreased birth-control efficacy as compared to POIHC.

In many cases, scenario *POIHC to FC*, which increases female condom use, may be the preferred outcome because it not only decreases HIV-related outcomes but also decreases vertical transmission. In addition, births increase less than 3% in that scenario. However, female condom use is rare despite being recommended by public health agencies [1]. For that reason we did not consider the even less common scenario involving the simultaneous use of POIHC and either male or female condoms, providing dual protection for birth control and HIV transmission [23].

Some scenarios might be more feasible than others. In addition to FC being very rare, the differences in a specific country's contraceptive use behavior (both the prevalence of all forms of contraception and the distribution among different contraceptive choices) might make some scenario more practical than others.

For example, public officials might need to more marketing effort to change behavior in condom use in Kenya compared to Botswana where prevalence of MC is already high.

There is no consensus about the relationship between POIHC use and increased HIV risk. However, the meta-analysis by Morrison et al. is strong evidence for a relationship between POIHC use and specifically, male-to-female HIV transmission [15]. For female-to-male HIV transmission, Heffron et al. is the only study that finds an association with POIHC [2]. While [26] identified 16 studies that indirectly looked for an association, most of which did not find any, Heffron et al. was the only study identified that directly looked for an association [2]. Sensitivity analysis (comparison of Case 1 with the highest transmission risk values to comparison of Case 5 with the lowest transmission risk values) shows that different assumptions about HIV transmission for POIHC users can have up to a 3.5-fold difference in the magnitude of the results (i.e., the effect of a contraceptive use scenario compared to the baseline). This stresses the need for a more conclusive study of the relationship between POIHC use and HIV transmission. Fig. 3 and Appendix Fig. A.3 also show that the uncertainty in the other parameters as described in the probabilistic sensitivity analysis is of a similar magnitude as the uncertainty explored by the Cases for the POIHC-linked HIV transmission risk.

The limitations of our model are as follows. The rate at which the population will change its contraceptive usage is unknown. We assumed that changes would occur after one year. Slower changes would lessen the differences to the status quo. We made two modeling assumptions that are not true but still reasonably close to reality: we assumed that the ratio of females to males is one and we based our base contact rates on the epidemic dynamics of 2007-2012. We used a simple compartmental model instead of a detailed simulation model. However, this is appropriate since we are studying population-level outcomes over 15 years and have included details (contraception and new HIV infections) important to the factors being studied. We excluded other details such as the different stages of HIV progression or changes to treatment coverage since they affect the role of contraceptives on new infections only very indirectly. In

addition, we do not know the likelihood of the different scenarios occurring or the feasibility of using public health campaigns to achieve them. Currently DMPA is much more common in these countries than NET-EN [2-3]. We assumed that POIHC users would continue to prefer DMPA over NET-EN in the future. If this is not true then the magnitude of changes may be different since there is no reported association between HIV risk and NET-EN use [20] (unlike the case for DMPA [2]). We also assumed that the sexual behavior in a country will not otherwise change when one form of birth control is replaced by another. Currently, differences in fertility characteristics such as birth spacing in various countries and their relation to the use of various contraceptive methods are not well understood. However, we must build our model and base our recommendations on the data available. The most sensible assumption is that POIHC use does not cause short birth intervals but that these fertility characteristics are due to behavioral and cultural factors that merely correlate with the use of POIHC.

5. Conclusion

We observe that switching from POIHC to other types of protection will be beneficial for HIV related outcome measures. Especially for countries where both the POIHC use and the HIV prevalence are high, the HIV-related benefits of switching from POIHC to other protection options are great. For countries with low birth rates, the negative impact of switching from POIHC on births and vertical transmission will be less. Overall, the outcomes depend on the countries and models such as these are useful for tailoring any potential public health intervention to a specific country or population of interest. Especially when combined with analyses of feasibility and costs, our simulations of the various scenarios can form the basis of future public health interventions.

Our results depend highly on the value of the HIV acquisition and transmission risk parameters for those using POIHC, which are currently uncertain. Our analysis explored three major sources of uncertainty: (1) the unknown future sexual behavior of the population in different scenarios; (2) the biological parameter values such as transmission probabilities and risk reductions in different cases and in a probabilistic

sensitivity analysis; and (3) potential limitations and sources of model error in the discussion. The female-to-male and male-to-female transmission risks impact the HIV outcomes but they do not impact the births. Despite the uncertainty of these parameters, even low percentages of dual protection method use can help balancing between HIV and birth related population level outcomes. The simulations in this study show that stopping POIHC use, with those individuals not switching to any other form of contraception, results in the worst outcomes of all the scenarios considered, an important fact public policy decision makers should keep in mind when designing interventions and preparing for the potential population-level changes in sexual behavior due to the link between POIHC and HIV.

Acknowledgments

We have no conflicts of interest to declare. We thank Stéphane Helleringer and Rebecca Wurtz for insightful discussions.

References

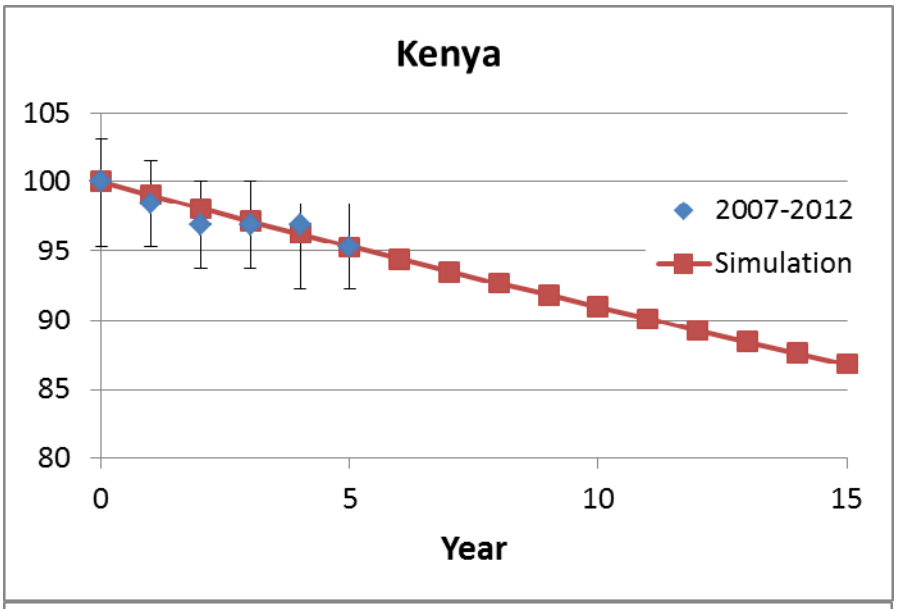
1. United Nations, DESA Population 2011 World Contraceptive Use. Available from: http://www.un.org/esa/population/publications/wcu2010/Main.html Accessed December 12, 2011
2. Heffron R, Donnell D, Rees H.et al. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. Lancet Infect Dis. 2012; 12: 19–26
3. Pelluck P. The New York Times. 2012; 3 October. Contraceptive Used in Africa May Double Risk of H.I.V. Available from: http://www.nytimes.com/2011/10/04/health/04hiv.html?pagewanted=all Accessed October 5, 2011.
4. Agboghoroma CO. Contraception in the Context of HIV/AIDS: A Review. African Journal of Reproductive Health. 2011; 15(3): 15-24.
5. Plummer FA, Simonsen JN, Cameron DW. et al. Cofactors in male-female sexual transmission of human immunodeficiency virus type 1. J Infect Dis. 1991; 163: 233–39.
6. Baeten JM, Benki S, Chohan V, Lavreys L, McClelland RS,Mandaliya K, et al. Hormonal contraceptive use, herpes simplex virus infection, and risk of HIV-1 acquisition among Kenyan women. AIDS 2007; 21:1771–1777.
7. Morrison CS, Turner AN, Jones LB. Highly effective contraception and acquisition of HIV and other sexually transmitted infections. Best Pract Res Clin Obstet Gynaecol. 2009; 23: 263–84.
8. Morrison CS, Chen PL, Kwok C. et al. Hormonal contraception and HIV acquisition: reanalysis using marginal structural modeling. AIDS. 2010; 24: 1778–81.
9. Watson-Jones D, Baisley K, Weiss HA. et al. Risk factors for HIV incidence in women participating in an HSV suppressive treatment trial in Tanzania. AIDS. 2009; 23: 415–22.
10. Lavreys L, Baeten JM, Kreiss JK. et al. Injectable contraceptive use and genital ulcer disease during the early phase of HIV-1 infection increase plasma virus load in women. J Infect Dis. 2004;189:303–11.
11. Stringer EM, Kaseba C, Levy J.et al. A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol. 2007; 197(144):e1–8.
12. Morrison CS, Skoler-Karpoff S, Kwok C, et al. Hormonal contraception and the risk of HIV acquisition among women in South Africa. AIDS, 2012, 26:497-504.
13. Myer L, Denny L, Wright T, et al. Prospective study of hormonal contraception and women's risk of HIV infection in South Africa. Int J Epidemiology 2007;36:166–174.
14. Hel Z, Stringer E, Mestecky J. Sex steroid hormones, hormonal contraception, and the immunobiology of human immunodeficiency virus-1 infection. Endocr Rev 2010; 31: 79‑97.
15. Morrison C, et al. Presented at AIDS 2014. Melbourne, Australia: Jul 20–25, 2014. Hormonal contraception and HIV infection: results from a large individual participant data meta-analysis.
16. Ralph LJ, McCoy SI, Shiu K. et al. Hormonal contraceptive use and women's risk of HIV acquisition: a meta-analysis of observational studies. Lancet Infect Dis 2015;15: 181–89
17. WHO. Medical eligibility criteria for contraceptive use, Fourth edition 2009. A WHO Family Planing Cornerstone. Available from: http://whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf Accessed at February 16, 2012

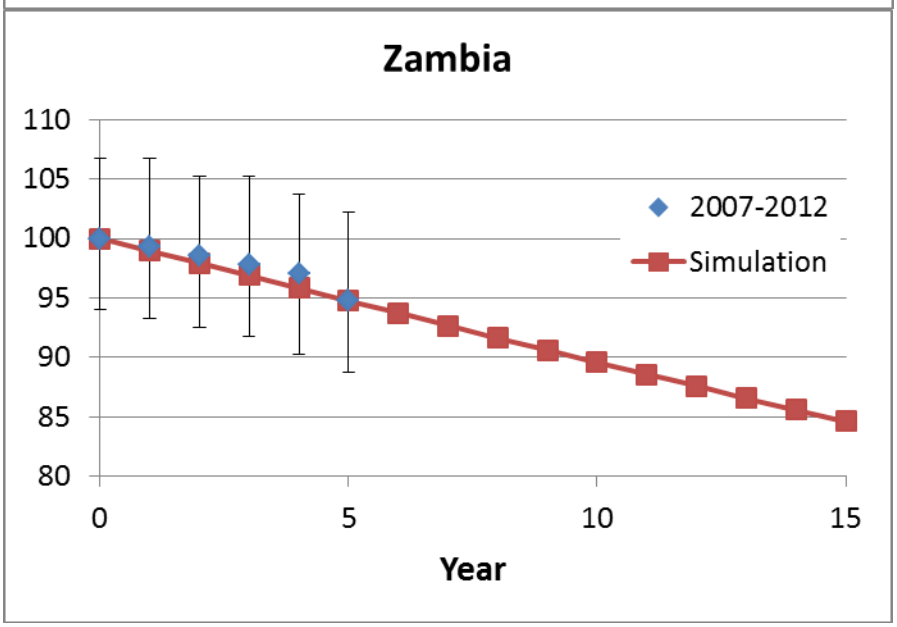
18. WHO. Women need access to dual protection—effective contraceptives and HIV prevention options. 2012, 16 February. Available from: http://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2012/february/20120216pshormonal/ Accessed February 20, 2012
19. WHO. Hormonal Contraception and HIV. Technical Statement. Available from: http://whqlibdoc.who.int/hq/2012/WHO_RHR_12.08_eng.pdf Accessed at February 20, 2012
20. Padian NS, Buve A, Balkus J, et al.. Biomedical interventions to prevent HIV infection: evidence, challenges, and way forward. Lancet. 2008;372:585–599.
21. Abdool Karim Q, Sibeko S, and Baxter C. Preventing HIV Infection in Women: A Global Health Imperative. Clinical Infectious Diseases 2010; 50(S3):S122–S129
22. Hogan, M.C., Foreman, K.J., Naghavi, M. et al. Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5 The Lancet 2010, 375 (9726), pp. 1609-1623
23. Sales J.M., Whiteman M.K., Kottke M.J. et. al. Dual Protection Use to Prevent STIs and Unintended Pregnancy. Infectious Diseases in Obstetrics and Gynecology Volume 2012, Article ID 972689, 2 pages
24. UNAIDS. Guidelines for Behavior Change Interventions to Prevent HIV: Sharing Lessons from an Experience in Bangladesh Based on the Application of Lessons from Sonagachi, Kolkata. Available from http://www.hivpolicy.org/Library/HPP001312.pdf Accessed December 20, 2014.
25. The Global HIV Prevention Working Group. Behavior Change and HIV Prevention: (Re)Considerations for the 21st Century. Available from http://www.malecircumcision.org/advocacy/documents/PWG_behavior_report_FINAL.pdf Accessed December 20, 2014.
26. Haddad et al. Contraceptive Methods and Risk of HIV Acquisition or Female-to-Male Transmission. *Curr HIV/AIDS Rep*. 2014 December ; 11(4): 447–458.
27. UNAIDS. 2010 Report on the global AIDS epidemics. Available from: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2010/20101123_globalreport_en.pdf Accessed January 9, 2012
28. Glynn JR, Sonnenberg P, Nelson G, Bester A, Shearer S, Murray J. Survival from the HIV-1 seroconversion in Southern Africa: a retrospective cohort study in nearly 2000 gold miners over 10 years follow up. AIDS. 2007; 21: 625-632
29. Mills EJ, Bakanda C, Birungi J. et al. Life expectancy of Persons Receiving Combination Antiretroviral Therapy in Low-Income Countries: A Cohort Analysis from Uganda. Ann Intern Med. 2011; 155: 209-216
30. World Bank. Available from: http://www.worldbank.org/depweb/english/modules/social/pgr/datasubs.html Accessed February 20, 2012
31. 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: 118–29.
32. CIA World Factbook 2011. Available from https://www.cia.gov/library/publications/the-world-factbook/rankorder/2054rank.html Accessed at January 16, 2012

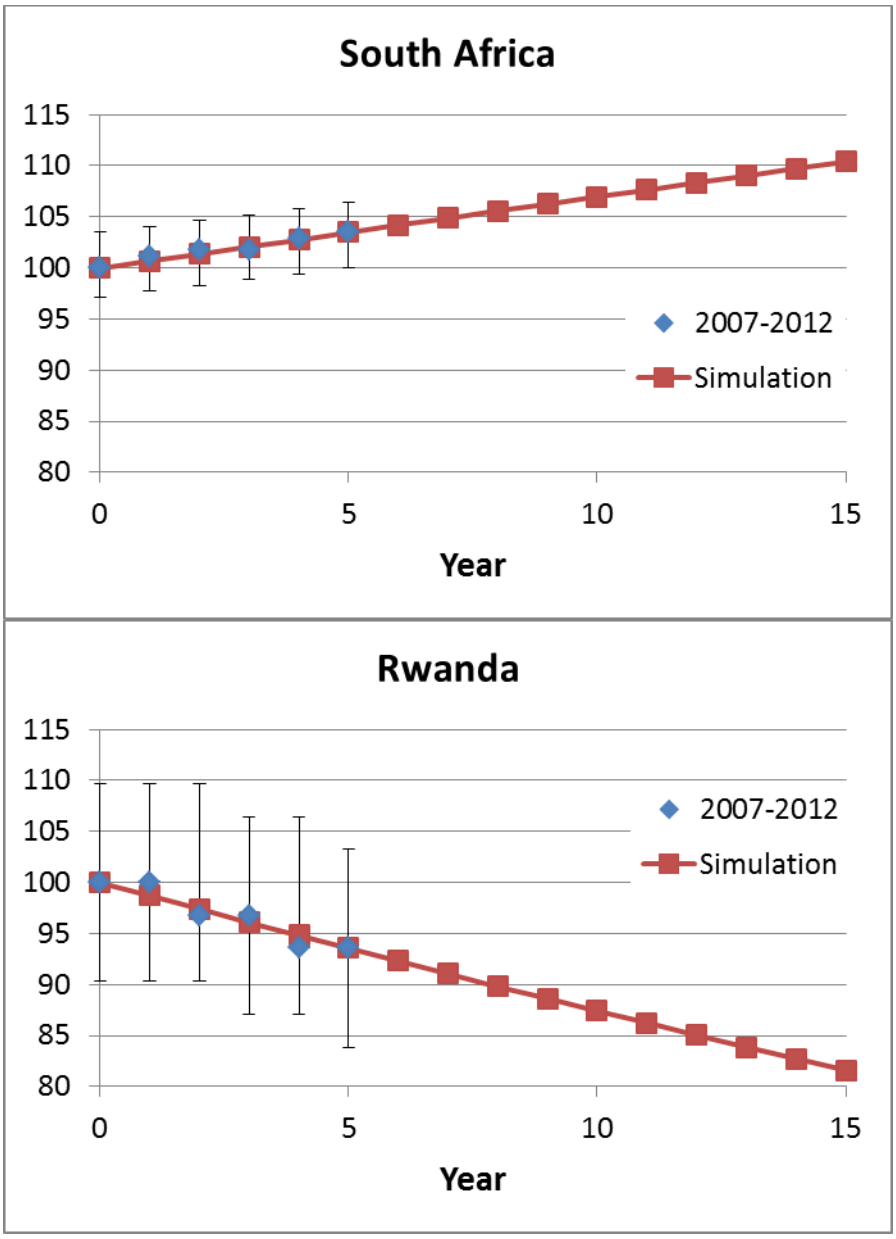
33. Abdool Karim Q, Abdul Karim SS, Frohlich JA. et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010;329:1168-1174.
34. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database Syst Rev. 2002(1):CD003255.
35. PEPFAR Prevention of Mother-to-Child Transmission of HIV: Expert Panel Report and Recommendations to the U.S. Congress and U.S. Global AIDS Coordinator 2010 Available from http://www.pepfar.gov/documents/organization/135465.pdf Accessed at January 16, 2012
36. Soderlund N, Zwi K, Kinghorn A, Gray G. Prevention of vertical transmission of HIC: analysis of cost effectiveness options available in South Africa. BMJ. 1999;318:1651-1656.
37. UNAIDS. UNAIDS Report on the Global AIDS Epidemic - 2013 HIV estimates with uncertainty bounds. Available from www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/GR2013_HIV_Estimates_AnnexTable.xls

Supplementary Appendix

Table of Contents


Kenya
105
100
95
90
85
80
0
5
10
15
Year
2007-2012
Simulation


Zambia
110
105
100
95
90
85
80
0
5
10
15
Year
2007-2012
Simulation


South Africa
115
110
105
100
95
90
85
80
0
5
10
15
Year
2007-2012
Simulation
Rwanda
115
110
105
100
95
90
85
80
0
5
10
15
Year
2007-2012
Simulation

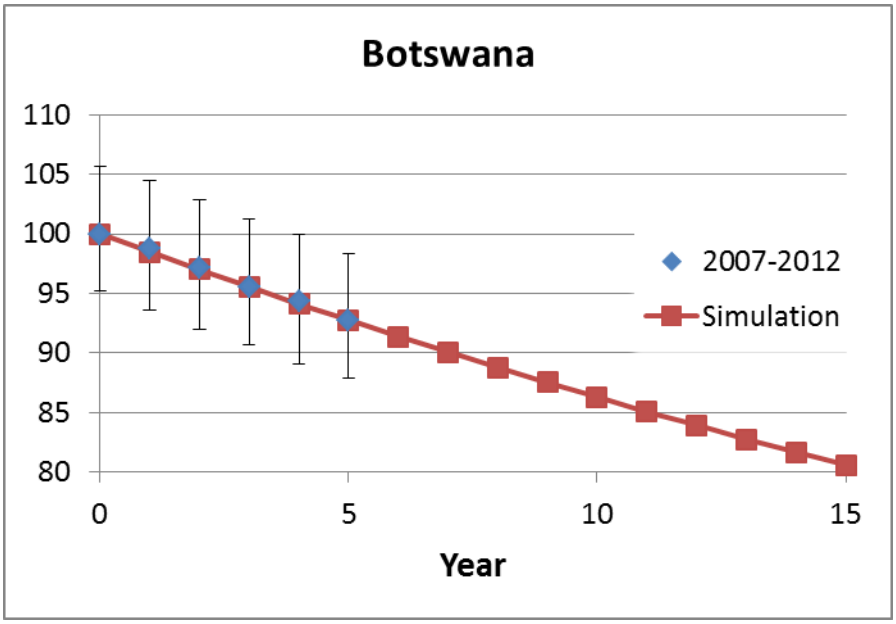


Fig. A.1 Validation. The blue time series are the UNAIDS estimates for adult (age 15-49) prevalence from 2007 to 2012 [37], along with the low and high estimates. The red time series is the simulation. Both have been normalized to start at 100.

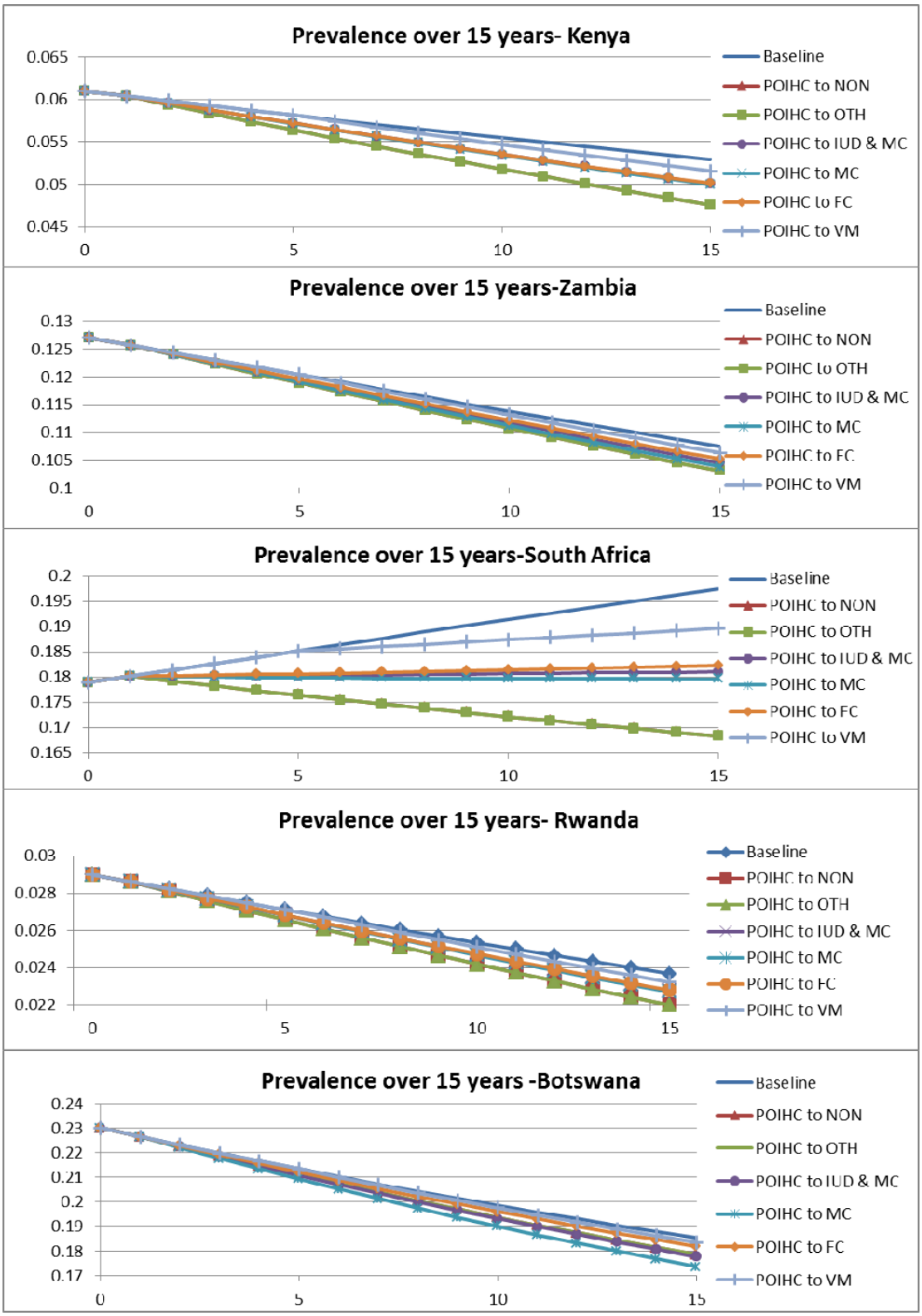
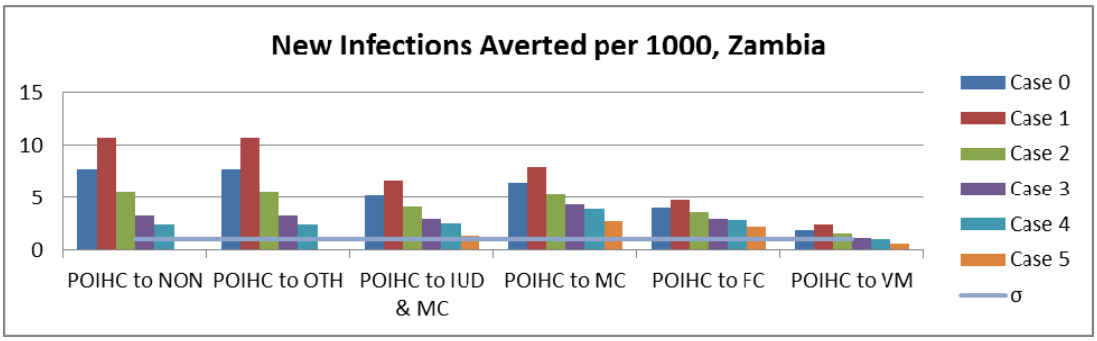
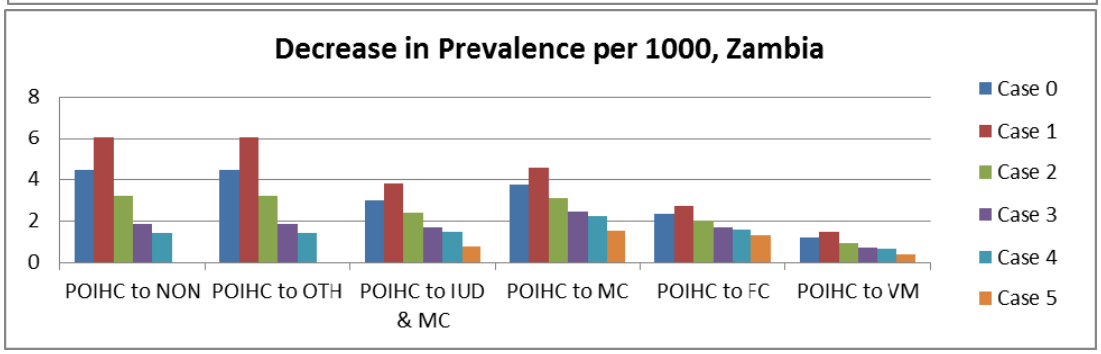
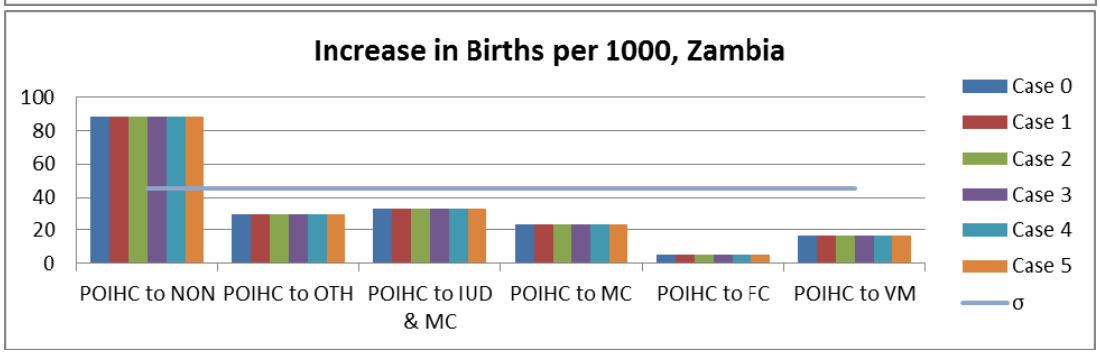
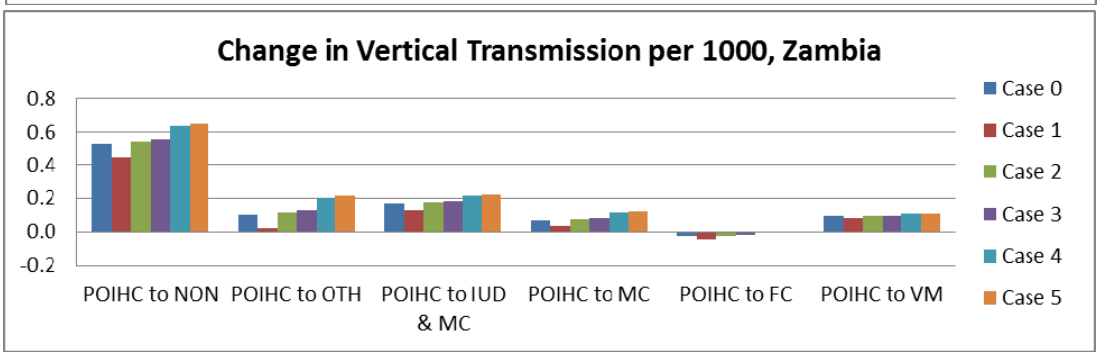


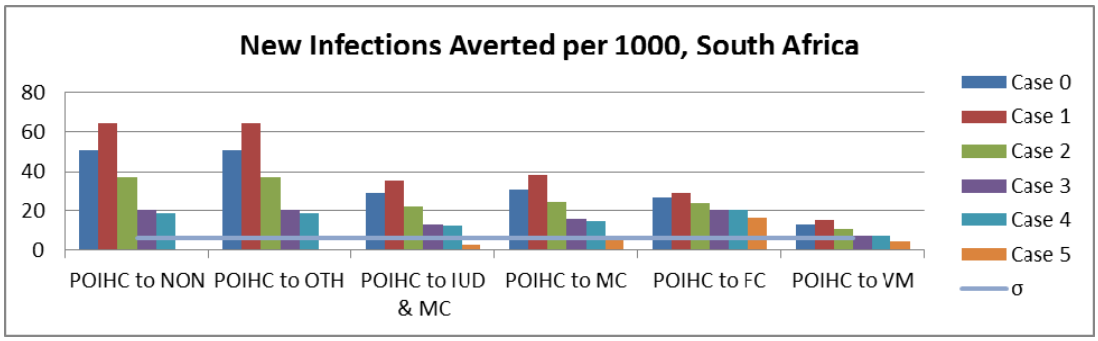
Fig. A.2. Prevalence over 15 years in various countries

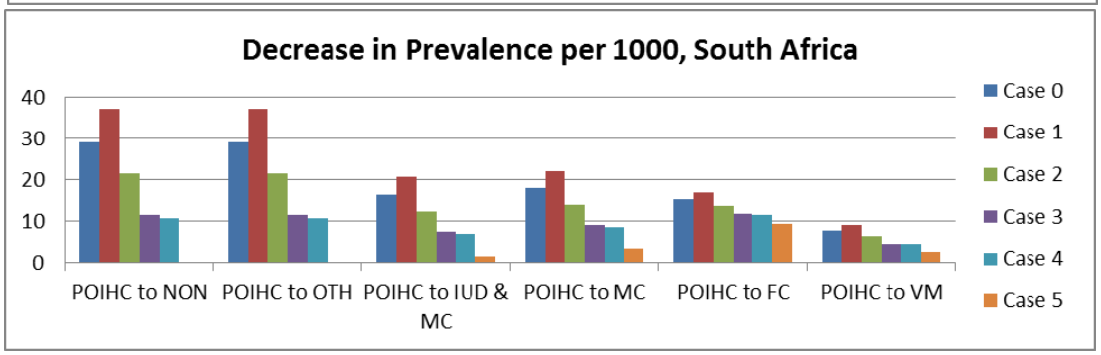

New Infections Averted per 1000, Zambia
15
10
5
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ

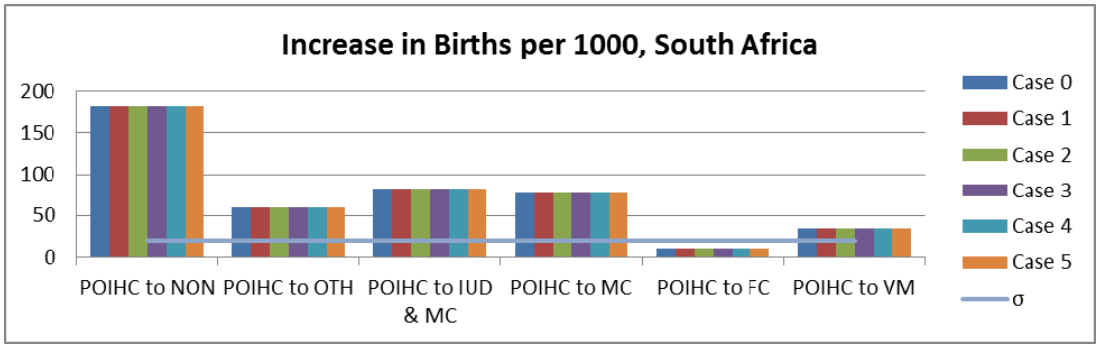

Decrease in Prevalence per 1000, Zambia
8
6
4
2
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5

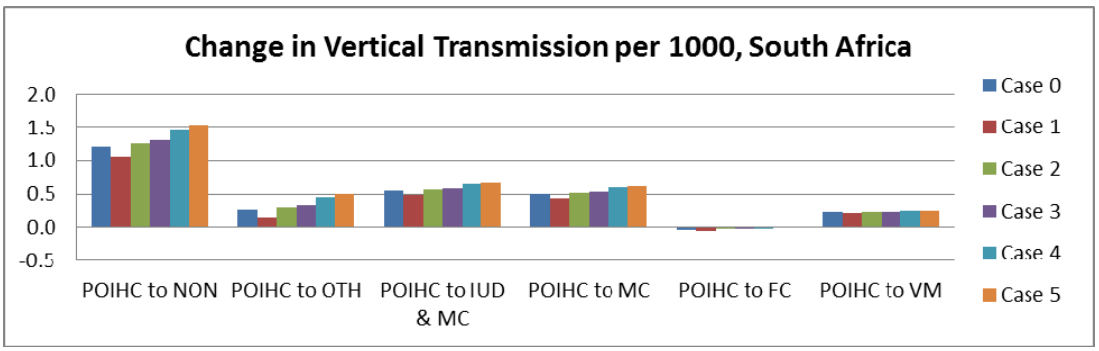

Increase in Births per 1000, Zambia
100
80
60
40
20
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ

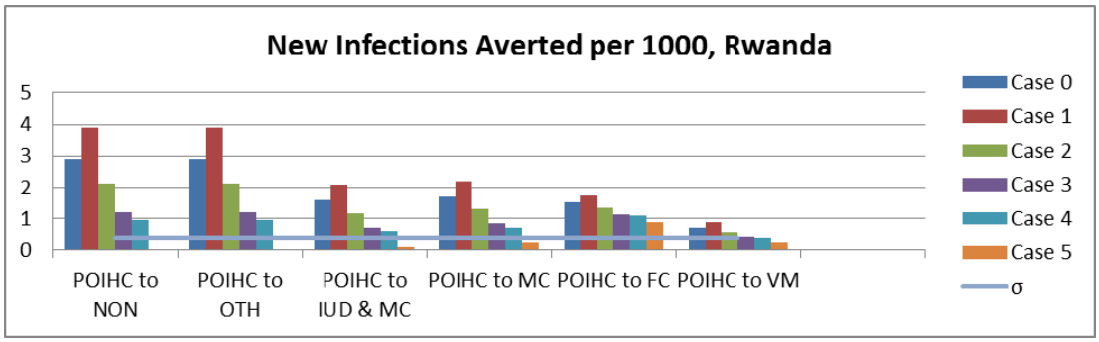

Change in Vertical Transmission per 1000, Zambia
0.8
0.6
0.4
0.2
0.0
-0.2
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5

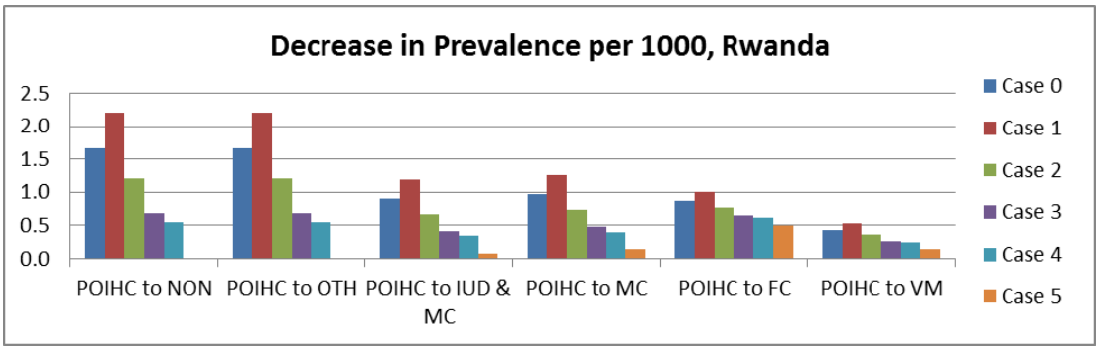

New Infections Averted per 1000, South Africa
80
60
40
20
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ

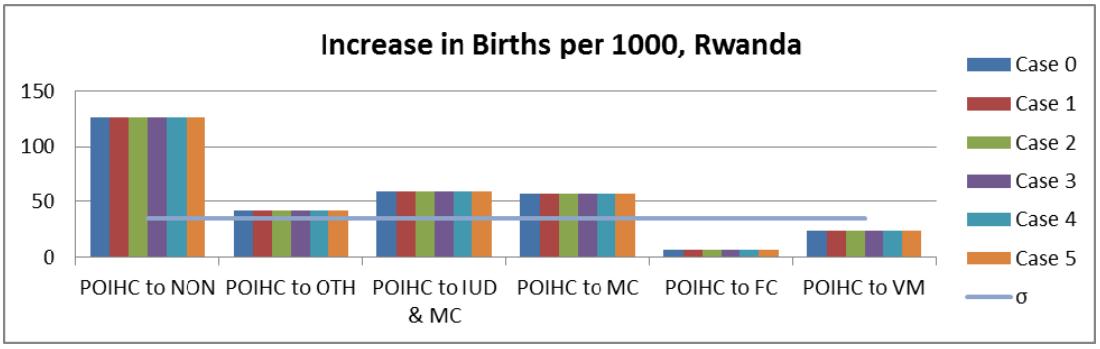

Decrease in Prevalence per 1000, South Africa
40
30
20
10
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5

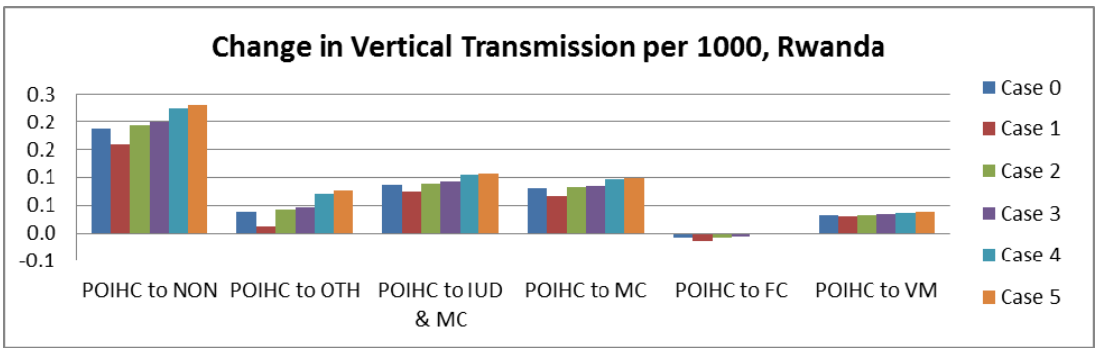

Increase in Births per 1000, South Africa
200
150
100
50
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ


Change in Vertical Transmission per 1000, South Africa
2.0
1.5
1.0
0.5
0.0
-0.5
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5


New Infections Averted per 1000, Rwanda
5
4
3
2
1
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ


Decrease in Prevalence per 1000, Rwanda
2.5
2.0
1.5
1.0
0.5
0.0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5


Increase in Births per 1000, Rwanda
150
100
50
0
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5
σ


Change in Vertical Transmission per 1000, Rwanda
0.3
0.2
0.2
0.1
0.1
0.0
-0.1
POIHC to NON
POIHC to OTH
POIHC to IUD & MC
POIHC to MC
POIHC to FC
POIHC to VM
Case 0
Case 1
Case 2
Case 3
Case 4
Case 5

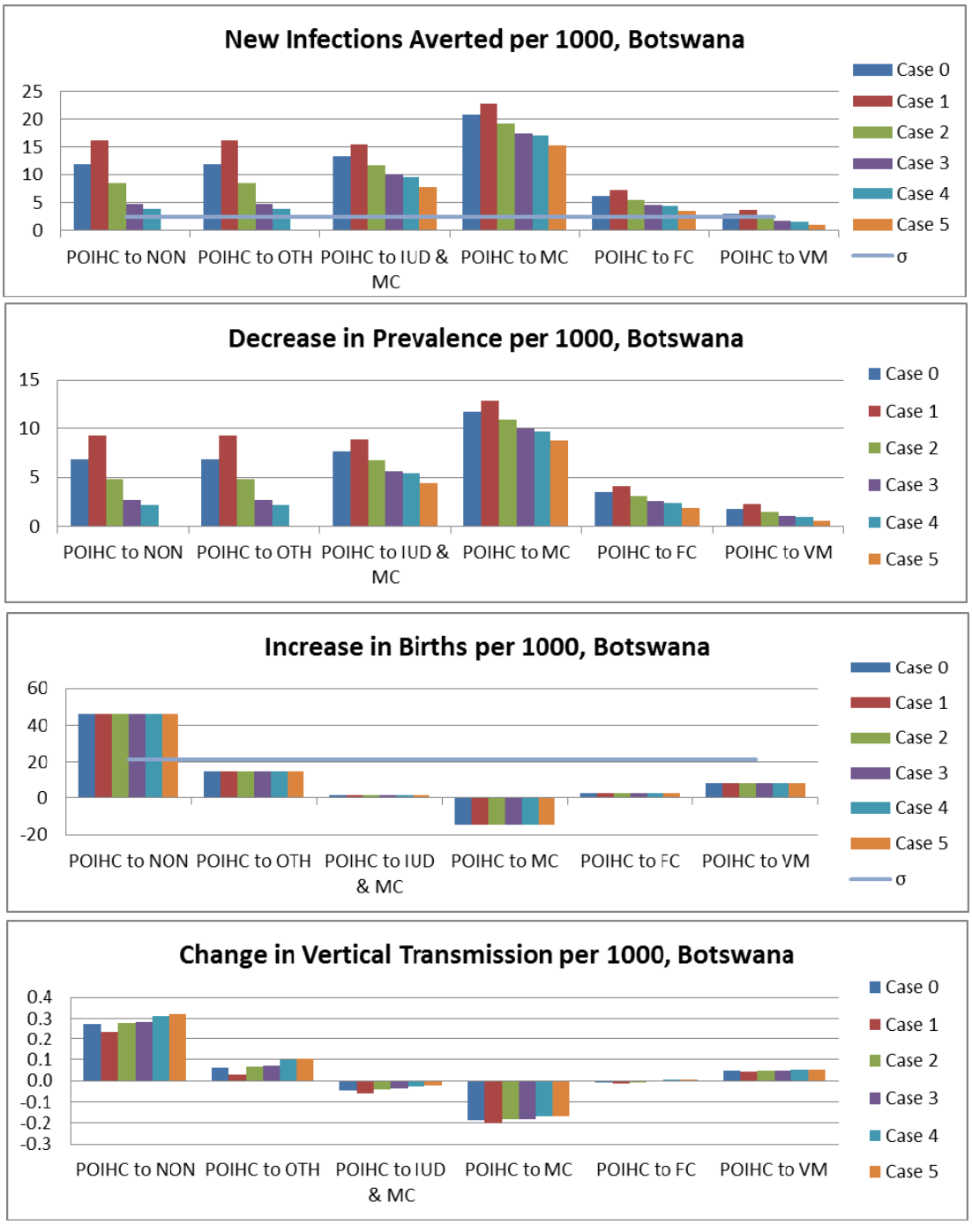
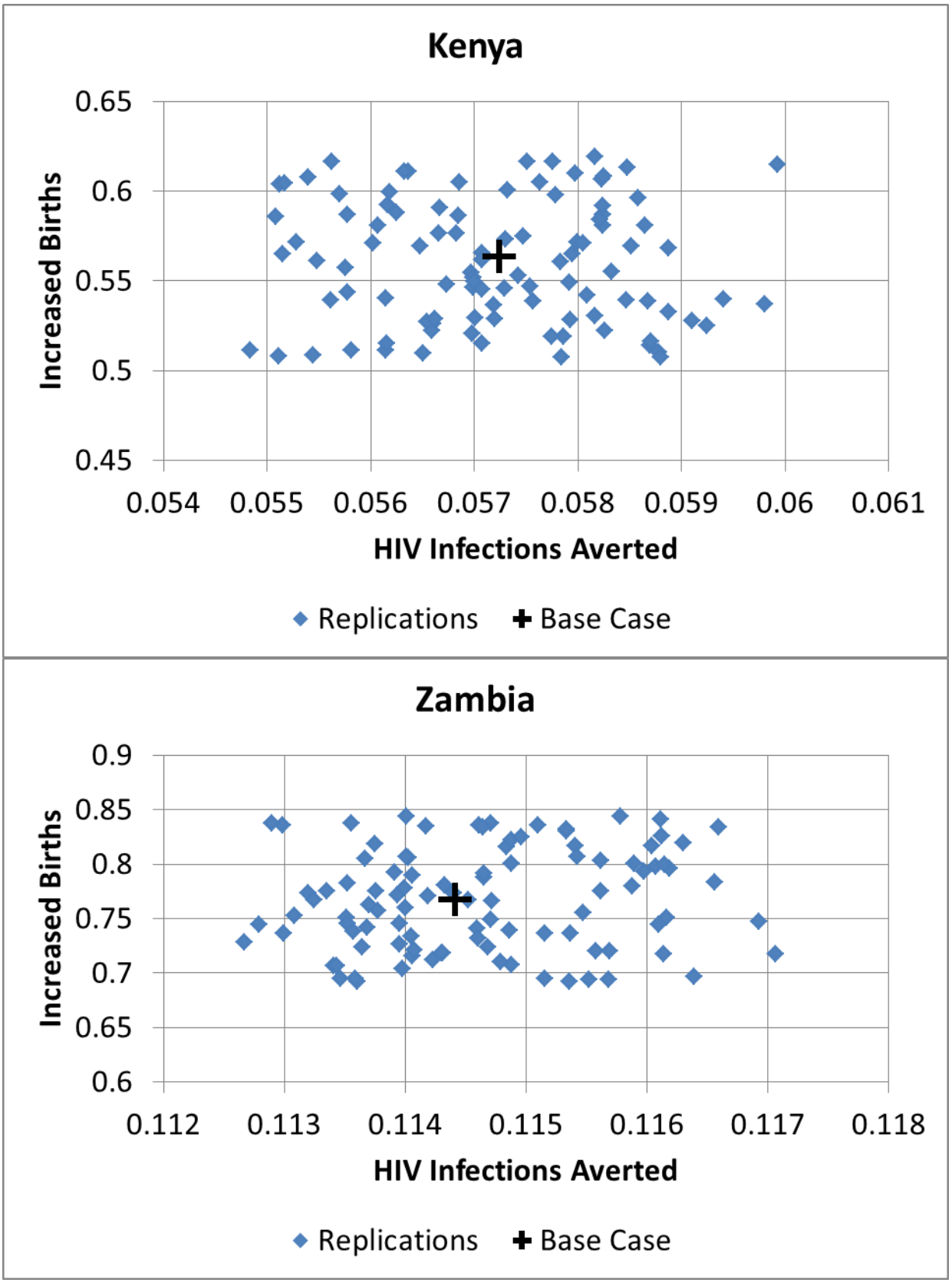
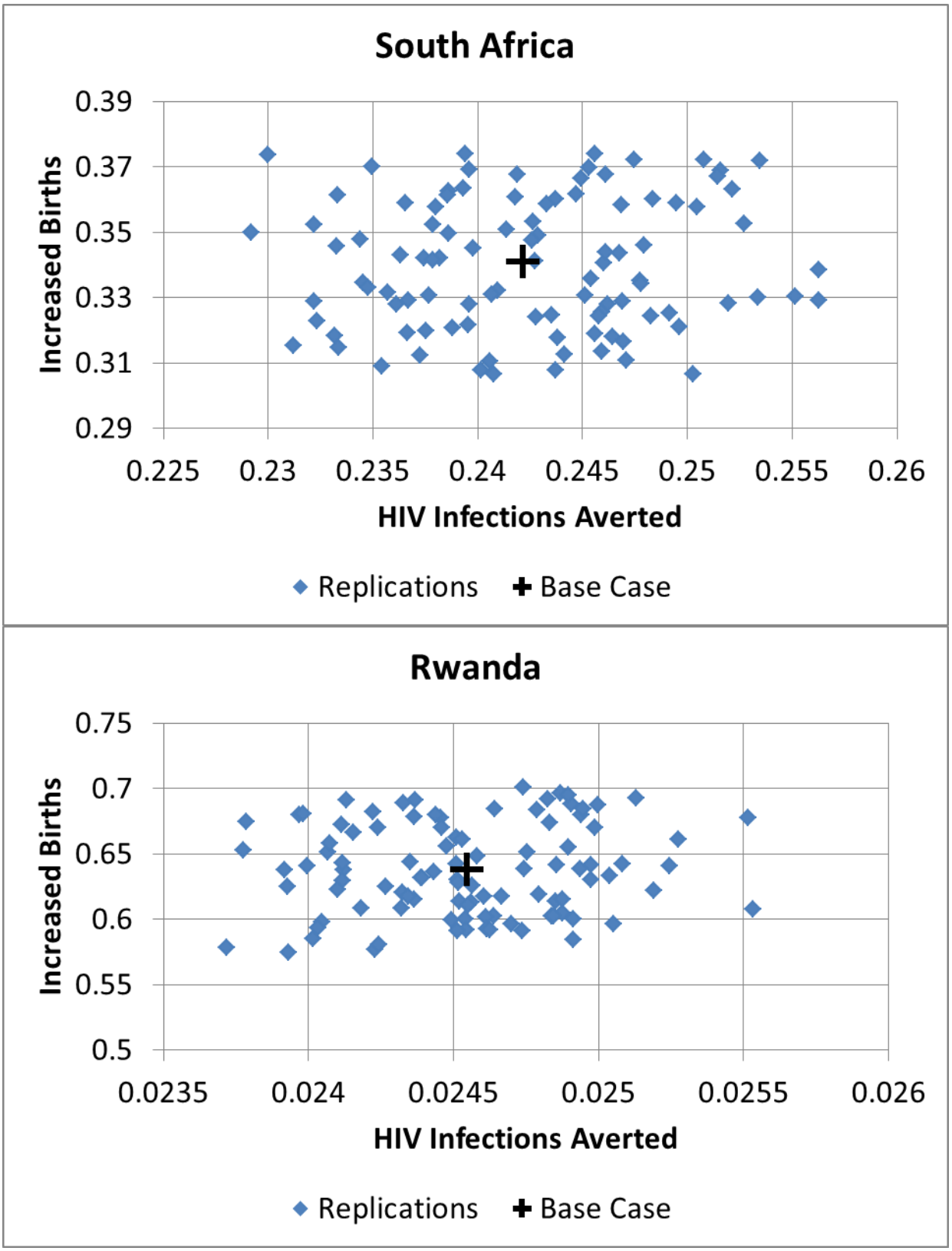


Fig A.3. Sensitivity analysis for each country


Kenya
Increased Births
0.65
0.6
0.55
0.5
0.45
0.054
0.055
0.056
0.057
0.058
0.059
0.06
0.061
HIV Infections Averted
Replications
Base Case
Zambia
Increased Births
0.9
0.85
0.8
0.75
0.7
0.65
0.6
0.112
0.113
0.114
0.115
0.116
0.117
0.118
HIV Infections Averted
Replications
Base Case


South Africa
0.39
0.37
0.35
0.33
0.31
0.29
Increased Births
0.225
0.23
0.235
0.24
0.245
0.25
0.255
0.26
HIV Infections Averted
Replications
Base Case
Rwanda
0.75
0.7
0.65
0.6
0.55
0.5
Increased Births
0.0235
0.024
0.0245
0.025
0.0255
0.026
HIV Infections Averted
Replications
Base Case

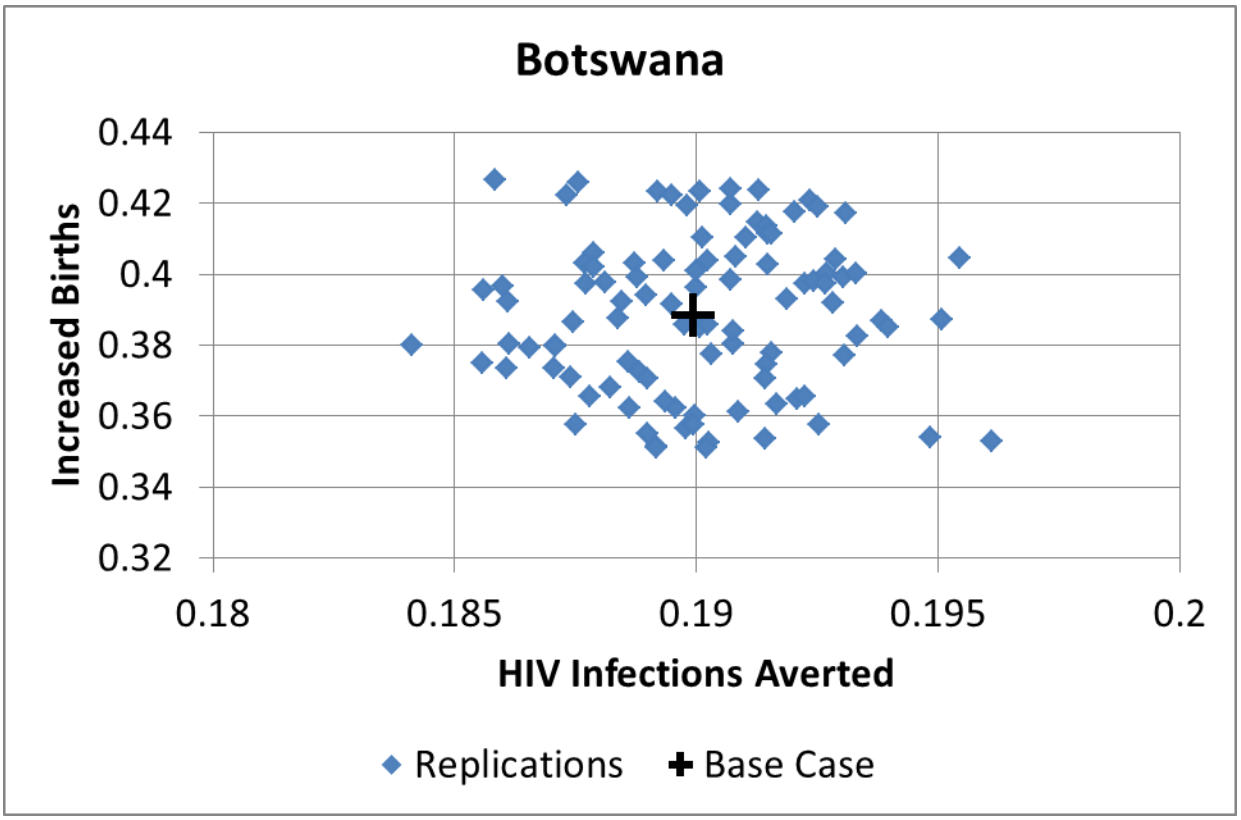


Fig A.4 Probabilistic sensitivity analysis. The figure shows for each country the base case and the 100 replications of a probabilistic sensitivity analysis where some parameters (HIV acquisition and transmission rate with POIHC, birth rate, and initial contraceptive use of POIHC, initial contraceptive use of MC) were independently drawn from a uniform distribution ranging from -10% to +10% of the baseline value.

Notation
Total Population (ages 15-49), $N(t)$
Female and male susceptible population, $S_f(t)$, $S_m(t)$
Female and male infected population, $I_f(t)$, $I_m(t)$
Male-to-female and female-to-male and infection rate, β_f, β_m
Annual population growth rate, α
Annual mortality rate of HIV+ (deaths per year), γ
Annual rate of vertical transmission per infected female, δ
Annual rate of births per capita, φ
Cumulative number of new infections, J
Cumulative number of cases of vertical transmission, V
Cumulative number of births, B
Female, male, and total prevalence, $2I_f/N$, $2I_m/N$, $(I_f+I_m)/N$
Portfolio of contraceptive use, $P=(p_{POIHC},p_{IUD},p_{FC},p_{VM},p_{MC},p_{OTH},p_{NON})$
Female and male infection rates assuming no protection, β_{0f}, β_{0m}
Relative risk of female (male) infection using contraceptive x, ξ_x^f , (ξ_x^m)
Total relative risk of j={m,f} infection using i={m,f} contraceptives in current portfolio, ξ_{ij}
Per capita birth rate assuming no protection, φ_0
Relative risk of pregnancy (compared to no protection), χ
Probability of mother-to-child (vertical) transmission
Overall, with mother on ART, without mother on ART: v, π, π'
Percentage of pregnant females on ART, p_{ART}
Current portfolio of contraceptive use, P_0
Current birth rate, τ

Table A.1. Notation used in the model

Parameter	Value *
N(0)	1, 1, 1, 1, 1
β_f	0.0873, 0.0885, 0.1304, 0.0776, 0.0939
β_m	0.0437, 0.0442, 0.0652, 0.0388, 0.0470
δ	0.0034, 0.0050, 0.0015, 0.0045, 0.0013
φ	0.0319, 0.0435, 0.0193, 0.0361, 0.0220
β_{0f}	0.0799, 0.0882, 0.1185, 0.0732, 0.1030
β_{0m}	0.0364, 0.0424, 0.0527, 0.0342, 0.0496
ξ_{ff}	1.108, 1.043, 1.142, 1.076, 1.041
ξ_{mf}	.9856, .9624, .9632, .9848, .8760
ξ_{mm}	.9856, .9624, .9632, .9848, .8760
ξ_{fm}	1.216, 1.085, 1.284, 1.152, 1.081
φ_0	0.0616, 0.0762, 0.0471, 0.0611, 0.0420
χ	.5182, .5711, .4101, .5912, .5243
ν	.1067, .1151, .0752, .1235, .0605

* Values are in order: Kenya, Zambia, South Africa, Rwanda and Botswana

Table A.2. Values of calculated parameters for the baseline scenario.

	Kenya		Zambia		South Africa		Rwanda		Botswana	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Baseline*	0.02	0.03	0.04	0.07	0.10	0.14	0.01	0.01	0.08	0.11
POIHC to NON **	-19.58	-14.10	-8.72	-5.58	-24.30	-18.38	-14.64	-9.96	-7.96	-5.18
POIHC to OTH	-19.58	-14.10	-8.72	-5.58	-24.30	-18.38	-14.64	-9.96	-7.96	-5.18
POIHC to IUD & MC	-10.38	-7.63	-5.57	-3.91	-13.45	-10.50	-7.87	-5.50	-8.02	-6.46
POIHC to MC	-10.79	-8.04	-6.75	-5.01	-14.50	-11.58	-8.31	-5.94	-11.98	-10.27
POIHC to FC	-9.28	-8.12	-4.10	-3.20	-11.62	-10.45	-6.90	-5.74	-3.71	-2.96
POIHC to VM	-3.85	-4.19	-1.71	-1.65	-4.98	-5.49	-2.84	-2.94	-1.56	-1.55

* Values are a fraction of the initial population.
** Values for scenarios 1-6 are percent changes compared to baseline.

Table A.3a. Cumulative number of new infections over 15 years by sex

	Kenya		Zambia		South Africa		Rwanda		Botswana	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Baseline*	0.02	0.03	0.04	0.07	0.10	0.14	0.01	0.01	0.08	0.11
POIHC to NON **	0.47	0.47	0.38	0.39	2.54	2.53	0.14	0.15	0.61	0.58
POIHC to OTH	0.47	0.47	0.38	0.39	2.54	2.53	0.14	0.15	0.61	0.58
POIHC to IUD & MC	0.25	0.25	0.25	0.28	1.41	1.45	0.08	0.08	0.62	0.73
POIHC to MC	0.26	0.27	0.30	0.35	1.51	1.59	0.08	0.09	0.92	1.16
POIHC to FC	0.22	0.27	0.18	0.22	1.21	1.44	0.07	0.08	0.29	0.33
POIHC to VM	0.09	0.14	0.08	0.12	0.52	0.76	0.03	0.04	0.12	0.18

* Values are a fraction of the initial population.
** Values for scenarios 1-6 are changes compared to baseline (10^{-3}).

Table A.3b. Cumulative number of new infections over 15 years by sex

Marginal Analysis of New Infections in Zambia																	
Contraceptive Type	Change in Each Contraceptive Type per Each Scenario							Change in Relative Risk				Change in New Infections (per 1000)					
	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	FF	MF	MM	FM	NON	OTH	IUD	MC	FC	VM
POIHC	8.5	-8.5	-8.5	-4.2	-4.2	-2.1	-2.1	0.46	0.04	0.04	0.92	5.2	5.2	2.6	2.6	1.3	1.3
IUD	1.0	-	-	-	-	-	-	-0.04	0.04	0.04	-0.09	-	-	0.0	-	-	-
FC	-	-	-	-	-	2.1	-	-0.80	0.04	0.04	-0.85	-	-	-	-	1.5	-
VM	-	-	-	-	-	-	2.1	-0.58	0.04	0.04	-0.09	-	-	-	-	-	0.7
MC	4.7	-	-	1.2	2.4	-	-	-0.04	-0.76	-0.76	-0.09	-	-	1.0	2.0	-	-
OCP	11.0	-	-	-	-	-	-	-0.04	0.04	0.04	-0.09	-	-	-	-	-	-
OTH	16.5	-	8.5	-	-	-	-	-0.04	0.04	0.04	-0.09	-	0.1	-	-	-	-
NON	58.3	8.5	-	2.8	1.9	-	-	-0.04	0.04	0.04	-0.09	0.1	-	0.0	0.0	-	-
Any BC	41.7	-8.5	-	-2.8	-1.9	-	-2.1				Total Change	5.3	5.3	3.6	4.6	2.8	2.0
Any BC/HIVp	4.7	-	-	1.2	2.4	2.1	-				Simulation	7.8	7.8	5.2	6.5	4.1	1.9

Marginal Analysis of Births in Zambia														
	Contraceptive usage as fraction of the population							Difference in Pregnancy Risk Compared to Average	Increase in Births per 1000					
		Change in Percentage Points												
Contraceptive Type	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM		NON	OTH	IUD & MC	MC	FC	VM
POIHC	8.5	-8.5	-8.5	-4.2	-4.2	-2.1	-2.1	-0.53	45.4	45.4	22.4	22.4	11.2	11.2
IUD	1.0	-	-	-	-	-	-	-0.56	-	-	-1.7	-	-	-
FC	-	-	-	-	-	2.1	-	-0.35	-	-	-	-	-7.4	-
VM	-	-	-	-	-	-	2.1	0.29	-	-	-	-	-	6.0
MC	4.7	-	-	1.2	2.4	-	-	-0.41	-	-	-5.0	-9.9	-	-
OCP	11.0	-	-	-	-	-	-	-0.48	-	-	-	-	-	-
OTH	16.5	-	8.5	-	-	-	-	-0.26	-	-22.4	-	-	-	-
NON	58.3	8.5	-	2.8	1.9	-	-	0.29	24.3	-	8.0	5.4	-	-
Any BC	41.7	-8.5	-	-2.8	-1.9	-	-2.1	Total change	69.7	23.0	23.8	17.9	3.8	17.2
Any BC/HIVp	4.7	-	-	1.2	2.4	2.1	-	Simulation Result	88.3	29.1	33.4	23.3	4.8	16.4

Marginal Analysis of New Infections in South Africa																	
Contraceptive Type	Change in Each Contraceptive Type per Each Scenario							Change in Relative Risk				Change in New Infections (per 1000)					
	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	FF	MF	MM	FM	NON	OTH	IUD	MC	FC	VM
POIHC	28.4	-28.4	-28.4	-14.2	-14.2	-7.1	-7.1	0.36	0.04	0.04	0.72	27.6	27.6	13.7	13.7	6.9	6.9
IUD	1.0	-	-	-	-	-	-	-0.14	0.04	0.04	-0.28	-	-	0.1	-	-	-
FC	-	-	-	-	-	7.1	-	-0.90	0.04	0.04	-1.04	-	-	-	-	11.8	-
VM	-	-	-	-	-	-	7.1	-0.68	0.04	0.04	-0.28	-	-	-	-	-	6.6
MC	4.6	-	-	1.2	2.3	-	-	-0.14	-0.76	-0.76	-0.28	-	-	2.5	4.8	-	-
OCP	0.9	-	-	-	-	-	-	-0.14	0.04	0.04	-0.28	-	-	-	-	-	-
OTH	15.0	-	28.4	-	-	-	-	-0.14	0.04	0.04	-0.28	-	7.4	-	-	-	-
NON	50.1	28.4	-	12.8	11.9	-	-	-0.14	0.04	0.04	-0.28	7.4	-	3.4	3.1	-	-
Any BC	49.9	-28.4	-	-12.8	-11.9	-	-7.1				Total Change	35.0	35.0	19.7	21.7	18.7	13.5
Any BC/HIVp	4.6	-	-	1.2	2.3	7.1	-				Simulation	50.7	50.7	28.5	31.1	26.5	12.8

Marginal Analysis of Births in South Africa														
	Contraceptive usage as fraction of the population							Difference in Pregnancy Risk Compared to Average	Increase in Births per 1000					
		Change in Percentage Points												
Contraceptive Type	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM		NON	OTH	IUD & MC	MC	FC	VM
POIHC	28.4	-28.4	-28.4	-14.2	-14.2	-7.1	-7.1	-0.46	129.8	129.8	64.9	64.9	32.5	32.5
IUD	1.0	-	-	-	-	-	-	-0.48	-	-	-1.4	-	-	-
FC	-	-	-	-	-	7.1	-	-0.28	-	-	-	-	-19.7	-
VM	-	-	-	-	-	-	7.1	0.36	-	-	-	-	-	25.8
MC	4.6	-	-	1.2	2.3	-	-	-0.34	-	-	-4.0	-7.8	-	-
OCP	0.9	-	-	-	-	-	-	-0.41	-	-	-	-	-	-
OTH	15.0	-	28.4	-	-	-	-	-0.19	-	-53.1	-	-	-	-
NON	50.1	28.4	-	12.8	11.9	-	-	0.36	103.1	-	46.5	43.2	-	-
Any BC	49.9	-28.4	-	-12.8	-11.9	-	-7.1	Total change	232.9	76.7	105.9	100.3	12.8	58.2
Any BC/HIVp	4.6	-	-	1.2	2.3	7.1	-	Simulation Result	182.3	60.0	83.2	78.6	10.0	33.8

Marginal Analysis of New Infections in Rwanda																	
Contraceptive Type	Change in Each Contraceptive Type per Each Scenario							Change in Relative Risk				Change in New Infections (per 1000)					
	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	FF	MF	MM	FM	NON	OTH	IUD	MC	FC	VM
POIHC	15.2	-15.2	-15.2	-7.6	-7.6	-3.8	-3.8	0.42	0.02	0.02	0.85	0.3	0.3	0.2	0.2	0.1	0.1
IUD	0.2	-	-	-	-	-	-	-0.08	0.02	0.02	-0.15	-	-	0.0	-	-	-
FC	-	-	-	-	-	3.8	-	-0.84	0.02	0.02	-0.91	-	-	-	-	0.1	-
VM	-	-	-	-	-	-	3.8	-0.62	0.02	0.02	-0.15	-	-	-	-	-	0.1
MC	1.9	-	-	0.5	1.0	-	-	-0.08	-0.78	-0.78	-0.15	-	-	0.0	0.0	-	-
OCP	6.4	-	-	-	-	-	-	-0.08	0.02	0.02	-0.15	-	-	-	-	-	-
OTH	12.7	-	15.2	-	-	-	-	-0.08	0.02	0.02	-0.15	-	0.0	-	-	-	-
NON	63.6	15.2	-	7.1	6.7	-	-	-0.08	0.02	0.02	-0.15	0.0	-	0.0	0.0	-	-
Any BC	36.4	-15.2	-	-7.1	-6.6	-	-3.8				Total Change	0.4	0.4	0.2	0.2	0.2	0.1
Any BC/HIVp	1.9	-	-	0.5	1.0	3.8	-				Simulation	2.9	2.9	1.6	1.7	1.5	0.7

Marginal Analysis of Births in Rwanda														
	Contraceptive usage as fraction of the population								Increase in Births per 1000					
		Change in Percentage Points												
Contraceptive Type	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	Difference in Pregnancy Risk Compared to Average	NON	OTH	IUD & MC	MC	FC	VM
POIHC	15.2	-15.2	-15.2	-7.6	-7.6	-3.8	-3.8	-0.56	85.3	85.3	42.7	42.7	21.3	21.3
IUD	0.2	-	-	-	-	-	-	-0.58	-	-	-0.6	-	-	-
FC	-	-	-	-	-	3.8	-	-0.38	-	-	-	-	-14.5	-
VM	-	-	-	-	-	-	3.8	0.26	-	-	-	-	-	9.8
MC	1.9	-	-	0.5	1.0	-	-	-0.44	-	-	-2.2	-4.4	-	-
OCP	6.4	-	-	-	-	-	-	-0.51	-	-	-	-	-	-
OTH	12.7	-	15.2	-	-	-	-	-0.29	-	-44.3	-	-	-	-
NON	63.6	15.2	-	7.1	6.7	-	-	0.26	39.3	-	18.4	17.3	-	-
Any BC	36.4	-15.2	-	-7.1	-6.6	-	-3.8	Total change	124.6	41.0	58.2	55.6	6.8	31.2
Any BC/HIVp	1.9	-	-	0.5	1.0	3.8	-	Simulation Result	126.6	41.7	59.5	56.6	6.9	23.5

Marginal Analysis of New Infections in Botswana																	
Contraceptive Type	Change in Each Contraceptive Type per Each Scenario							Change in Relative Risk				Change in New Infections (per 1000)					
	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM	FF	MF	MM	FM	NON	OTH	IUD	MC	FC	VM
POIHC	8.1	-8.1	-8.1	-4.0	-4.0	-2.0	-2.0	0.46	0.12	0.12	0.92	17.7	17.7	8.7	8.7	4.3	4.3
IUD	1.7	-	-	-	-	-	-	-0.04	0.12	0.12	-0.08	-	-	-0.1	-	-	-
FC	-	-	-	-	-	2.0	-	-0.80	0.12	0.12	-0.84	-	-	-	-	3.8	-
VM	-	-	-	-	-	-	2.0	-0.58	0.12	0.12	-0.08	-	-	-	-	-	1.5
MC	15.5	-	-	3.9	7.8	-	-	-0.04	-0.68	-0.68	-0.08	-	-	9.7	19.4	-	-
OCP	14.3	-	-	-	-	-	-	-0.04	0.12	0.12	-0.08	-	-	-	-	-	-
OTH	4.8	-	8.1	-	-	-	-	-0.04	0.12	0.12	-0.08	-	-2.2	-	-	-	-
NON	55.6	8.1	-	-	-3.7	-	-	-0.04	0.12	0.12	-0.08	-2.2	-	0.1	1.0	-	-
Any BC	44.4	-8.1	-	-	3.7	-	-2.0				Total Change	15.5	15.5	18.3	29.1	8.1	5.9
Any BC/HIVp	15.5	-	-	3.9	7.8	2.0	-				Simulation	12.0	12.0	13.5	20.8	6.2	3.0

Marginal Analysis of Births in Botswana														
	Contraceptive usage as fraction of the population							Difference in Pregnancy Risk Compared to Average	Increase in Births per 1000					
		Change in Percentage Points												
Contraceptive Type	Baseline (%)	NON	OTH	IUD & MC	MC	FC	VM		NON	OTH	IUD & MC	MC	FC	VM
POIHC	8.1	-8.1	-8.1	-4.0	-4.0	-2.0	-2.0	-0.49	40.0	40.0	19.8	19.8	9.9	9.9
IUD	1.7	-	-	-	-	-	-	-0.52	-	-	-2.1	-	-	-
FC	-	-	-	-	-	2.0	-	-0.31	-	-	-	-	-6.3	-
VM	-	-	-	-	-	-	2.0	0.33	-	-	-	-	-	6.5
MC	15.5	-	-	3.9	7.8	-	-	-0.37	-	-	-14.6	-29.2	-	-
OCP	14.3	-	-	-	-	-	-	-0.44	-	-	-	-	-	-
OTH	4.8	-	8.1	-	-	-	-	-0.22	-	-18.2	-	-	-	-
NON	55.6	8.1	-	-	-3.7	-	-	0.33	26.4	0.0	-0.7	-12.1	-	-
Any BC	44.4	-8.1	-	-	3.7	-	-2.0	Total change	66.4	21.9	2.5	-21.5	3.6	16.4
Any BC/HIVp	15.5	-	-	3.9	7.8	2.0	-	Simulation Result	46.4	15.3	1.7	-14.7	2.5	8.6

Table A.4 Marginal Analysis a) Change in New Infections b) Increase in Births. Change in outcomes based on the change in the usage of each contraceptive type and their effectiveness per unit of usage in the population on reducing births and HIV infections. BC refers to birth control while BC/HIVp refers to any form of contraception that also prevents HIV (FC and MC).

a) New Infections Averted								
Country	**Case**	**Baseline**	**POIHC to NON**	**POIHC to OTH**	**POIHC to IUD**	**POIHC to MC**	**POIHC to FC**	**POIHC to VM**
Kenya	**Case 0**	0.06	9.38	9.38	5.02	5.26	4.92	2.32
	Case 1	0.06	12.25	12.25	6.52	6.75	5.56	2.78
	Case 2	0.06	6.89	6.89	3.74	3.99	4.39	1.89
	Case 3	0.06	3.84	3.84	2.18	2.43	3.74	1.37
	Case 4	0.06	3.23	3.23	1.88	2.13	3.61	1.31
	Case 5	0.06	0.00	0.00	0.27	0.53	2.95	0.79
Zambia	**Case 0**	0.11	7.77	7.77	5.21	6.50	4.06	1.92
	Case 1	0.11	10.68	10.68	6.67	7.94	4.75	2.40
	Case 2	0.11	5.61	5.61	4.13	5.44	3.55	1.55
	Case 3	0.11	3.26	3.26	2.96	4.29	2.99	1.14
	Case 4	0.11	2.40	2.40	2.54	3.87	2.79	1.02
	Case 5	0.11	0.00	0.00	1.35	2.70	2.24	0.62
South Africa	**Case 0**	0.24	50.70	50.70	28.51	31.08	26.53	12.76
	Case 1	0.24	64.70	64.70	35.85	38.32	29.47	15.06
	Case 2	0.24	37.38	37.38	21.70	24.37	23.85	10.42
	Case 3	0.24	20.30	20.30	12.95	15.76	20.40	7.41
	Case 4	0.24	18.44	18.44	12.04	14.85	20.04	7.44
	Case 5	0.24	0.00	0.00	2.96	5.91	16.54	4.39
Rwanda	**Case 0**	0.02	2.90	2.90	1.58	1.69	1.52	0.71
	Case 1	0.02	3.89	3.89	2.09	2.20	1.75	0.87
	Case 2	0.02	2.12	2.12	1.18	1.30	1.35	0.58
	Case 3	0.02	1.22	1.22	0.72	0.84	1.14	0.42
	Case 4	0.02	0.95	0.95	0.59	0.70	1.08	0.39
	Case 5	0.02	0.00	0.00	0.12	0.24	0.88	0.24
Botswana	**Case 0**	0.19	11.98	11.98	13.47	20.83	6.20	2.95
	Case 1	0.19	16.28	16.28	15.55	22.81	7.22	3.68
	Case 2	0.19	8.52	8.52	11.82	19.26	5.38	2.36
	Case 3	0.19	4.78	4.78	10.03	17.56	4.50	1.71
	Case 4	0.19	3.81	3.81	9.56	17.10	4.27	1.57
	Case 5	0.19	0.00	0.00	7.75	15.39	3.38	0.93

b) Decrease in Prevalence								
Country	**Case**	**Baseline**	**POIHC to NON**	**POIHC to OTH**	**POIHC to IUD**	**POIHC to MC**	**POIHC to FC**	**POIHC to VM**
Kenya	**Case 0**	0.05	5.37	5.37	2.88	3.01	2.82	1.42
	Case 1	0.05	6.99	6.99	3.73	3.86	3.18	1.71
	Case 2	0.05	3.94	3.94	2.14	2.28	2.51	1.16
	Case 3	0.05	2.19	2.19	1.24	1.39	2.14	0.84
	Case 4	0.05	1.86	1.86	1.08	1.23	2.07	0.81
	Case 5	0.05	0.00	0.00	0.15	0.30	1.69	0.48
Zambia	**Case 0**	0.11	4.44	4.44	2.97	3.71	2.31	1.18
	Case 1	0.11	6.07	6.07	3.80	4.52	2.71	1.47
	Case 2	0.11	3.19	3.19	2.35	3.10	2.02	0.95
	Case 3	0.11	1.84	1.84	1.68	2.43	1.70	0.70
	Case 4	0.11	1.39	1.39	1.45	2.21	1.60	0.63
	Case 5	0.11	0.00	0.00	0.77	1.54	1.27	0.38
South Africa	**Case 0**	0.20	29.24	29.24	16.47	17.95	15.32	7.88
	Case 1	0.20	37.23	37.23	20.68	22.09	17.01	9.30
	Case 2	0.20	21.55	21.55	12.53	14.07	13.77	6.43
	Case 3	0.20	11.69	11.69	7.46	9.08	11.77	4.57
	Case 4	0.20	10.71	10.71	6.98	8.60	11.58	4.59
	Case 5	0.20	0.00	0.00	1.71	3.41	9.55	2.71
Rwanda	**Case 0**	0.02	1.66	1.66	0.90	0.97	0.87	0.44
	Case 1	0.02	2.21	2.21	1.19	1.25	1.00	0.54
	Case 2	0.02	1.21	1.21	0.67	0.74	0.77	0.35
	Case 3	0.02	0.69	0.69	0.41	0.48	0.65	0.26
	Case 4	0.02	0.54	0.54	0.34	0.40	0.62	0.24
	Case 5	0.02	0.00	0.00	0.07	0.13	0.50	0.15
Botswana	**Case 0**	0.19	6.81	6.81	7.65	11.81	3.52	1.81
	Case 1	0.19	9.23	9.23	8.82	12.92	4.10	2.25
	Case 2	0.19	4.83	4.83	6.70	10.91	3.05	1.44
	Case 3	0.19	2.69	2.69	5.68	9.95	2.55	1.04
	Case 4	0.19	2.18	2.18	5.43	9.71	2.43	0.96
	Case 5	0.19	0.00	0.00	4.40	8.73	1.92	0.56

c) Increase in Births								
Country	**Case**	**Baseline**	**POIHC to NON**	**POIHC to OTH**	**POIHC to IUD**	**POIHC to MC**	**POIHC to FC**	**POIHC to VM**
Kenya	**Case 0**	0.56	181.37	59.72	84.01	84.23	9.95	33.64
	Case 1	0.56	181.37	59.72	84.01	84.23	9.95	33.64
	Case 2	0.56	181.37	59.72	84.01	84.23	9.95	33.64
	Case 3	0.56	181.37	59.72	84.01	84.23	9.95	33.64
	Case 4	0.56	181.37	59.72	84.01	84.23	9.95	33.64
	Case 5	0.56	181.37	59.72	84.01	84.23	9.95	33.64
Zambia	**Case 0**	0.77	88.25	29.06	33.44	23.30	4.84	16.37
	Case 1	0.77	88.25	29.06	33.44	23.30	4.84	16.37
	Case 2	0.77	88.25	29.06	33.44	23.30	4.84	16.37
	Case 3	0.77	88.25	29.06	33.44	23.30	4.84	16.37
	Case 4	0.77	88.25	29.06	33.44	23.30	4.84	16.37
	Case 5	0.77	88.25	29.06	33.44	23.30	4.84	16.37
South Africa	**Case 0**	0.34	182.34	60.04	83.22	78.57	10.01	33.82
	Case 1	0.34	182.34	60.04	83.22	78.57	10.01	33.82
	Case 2	0.34	182.34	60.04	83.22	78.57	10.01	33.82
	Case 3	0.34	182.34	60.04	83.22	78.57	10.01	33.82
	Case 4	0.34	182.34	60.04	83.22	78.57	10.01	33.82
	Case 5	0.34	182.34	60.04	83.22	78.57	10.01	33.82
Rwanda	**Case 0**	0.64	126.62	41.69	59.50	56.55	6.95	23.49
	Case 1	0.64	126.62	41.69	59.50	56.55	6.95	23.49
	Case 2	0.64	126.62	41.69	59.50	56.55	6.95	23.49
	Case 3	0.64	126.62	41.69	59.50	56.55	6.95	23.49
	Case 4	0.64	126.62	41.69	59.50	56.55	6.95	23.49
	Case 5	0.64	126.62	41.69	59.50	56.55	6.95	23.49
Botswana	**Case 0**	0.39	46.36	15.27	1.75	-14.69	2.54	8.60
	Case 1	0.39	46.36	15.27	1.75	-14.69	2.54	8.60
	Case 2	0.39	46.36	15.27	1.75	-14.69	2.54	8.60
	Case 3	0.39	46.36	15.27	1.75	-14.69	2.54	8.60
	Case 4	0.39	46.36	15.27	1.75	-14.69	2.54	8.60
	Case 5	0.39	46.36	15.27	1.75	-14.69	2.54	8.60

d) Increase in Vertical Transmission								
Country	**Case**	**Baseline**	**POIHC to NON**	**POIHC to OTH**	**POIHC to IUD**	**POIHC to MC**	**POIHC to FC**	**POIHC to VM**
Kenya	**Case 0**	0.00	0.52	0.11	0.24	0.24	-0.02	0.09
	Case 1	0.00	0.45	0.06	0.21	0.21	-0.03	0.09
	Case 2	0.00	0.53	0.12	0.25	0.24	-0.01	0.09
	Case 3	0.00	0.55	0.14	0.25	0.25	-0.01	0.10
	Case 4	0.00	0.62	0.19	0.28	0.28	0.00	0.10
	Case 5	0.00	0.63	0.21	0.29	0.29	0.00	0.10
Zambia	**Case 0**	0.01	0.53	0.10	0.17	0.07	-0.03	0.09
	Case 1	0.01	0.45	0.02	0.13	0.03	-0.05	0.08
	Case 2	0.01	0.54	0.11	0.17	0.08	-0.03	0.09
	Case 3	0.01	0.56	0.13	0.18	0.08	-0.02	0.10
	Case 4	0.01	0.63	0.20	0.22	0.12	-0.01	0.10
	Case 5	0.01	0.65	0.21	0.22	0.12	0.00	0.11
South Africa	**Case 0**	0.00	1.21	0.27	0.55	0.50	-0.03	0.23
	Case 1	0.00	1.06	0.15	0.49	0.44	-0.05	0.21
	Case 2	0.00	1.25	0.30	0.57	0.52	-0.03	0.23
	Case 3	0.00	1.31	0.34	0.59	0.54	-0.02	0.24
	Case 4	0.00	1.46	0.45	0.65	0.60	0.00	0.25
	Case 5	0.00	1.52	0.50	0.68	0.62	0.01	0.26
Rwanda	**Case 0**	0.00	0.19	0.04	0.09	0.08	-0.01	0.03
	Case 1	0.00	0.16	0.01	0.07	0.07	-0.01	0.03
	Case 2	0.00	0.19	0.04	0.09	0.08	-0.01	0.03
	Case 3	0.00	0.20	0.05	0.09	0.08	-0.01	0.03
	Case 4	0.00	0.22	0.07	0.10	0.10	0.00	0.04
	Case 5	0.00	0.23	0.08	0.11	0.10	0.00	0.04
Botswana	**Case 0**	0.00	0.27	0.06	-0.04	-0.19	-0.01	0.05
	Case 1	0.00	0.24	0.03	-0.06	-0.20	-0.01	0.04
	Case 2	0.00	0.28	0.07	-0.04	-0.18	-0.01	0.05
	Case 3	0.00	0.28	0.07	-0.04	-0.18	-0.01	0.05
	Case 4	0.00	0.31	0.10	-0.03	-0.17	0.00	0.05
	Case 5	0.00	0.32	0.11	-0.02	-0.17	0.00	0.05

Table A.4. Sensitivity Analysis a) New Infections, b) Prevalence, c) Births d) Vertical Transmission: Case 0 (Baseline): 50% increase in HIV acquisition risk, 100% increase in female-to-male transmission risk. Case 1: 100% increase in HIV acquisition risk, 100% increase in female-to-male transmission risk. Case 2: 50% increase in HIV acquisition risk, 50% increase in female-to-male transmission risk. Case 3: 50% increase in HIV acquisition risk, 0% increase in female-to-male transmission risk. Case 4: 0%

increase in HIV acquisition risk, 50% increase in female-to-male transmission risk. Case 5: 0% increase in HIV acquisition risk, 0% increase in female-to-male transmission risk.