Modeling the Impact of Male Circumcision HIV Intervention Strategies

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Introduction

Being uncircumcised was first suggested as a risk factor for male HIV acquisition by Alfred Fink in 1986 in light of research suggesting that some STDs are more common in more uncircumcised men and the observation that female to male HIV transmission was much more common in Africa, where men are more likely to be uncircumcised, than in the United States (Fink 1986). Over the next fifteen years, a multitude of observational studies assessed the possibility of a relationship between circumcision and HIV incidence (Siegfried, Muller et al. 2005). Out of 18 studies of high risk populations – truck drivers, sex workers, STD clinic attendees, and tuberculosis patients – all reported an odds ratio (OR) less than 1, and 13 out of the 18 studies found an OR significantly different from 1 (95% CI). Population based surveys conducted in a variety of rural and urban African settings were not nearly so conclusive. Eight such studies found an odds ratio greater than 1, while eleven found an odds ratio less than 1. However, only eight of the 19 studies found an odds ratio significantly different from 1.

Several biological mechanisms have been proposed to explain decreased HIV acquisition in circumcised males. The most plausible appears to be that the inner mucosal surface of the male foreskin has a high density of $CD4^+$ T cells, with the surface of the adult male's foreskin having many times the number of target cells as cervical tissue, the known site of HIV-1 acquisition in females (Patterson, Landay et al. 2002). One early hypothesis proposed by STD research speculated that the keratinisation of the exposed glans of the circumcised penis provided a protective barrier against the HIV virus, but was cast into doubt based on a study of 13 cadavers that found no difference in the keratin layer covering the glans of a circumcised and uncircumcised penis (Szabo and Short 2000).

While the results of early observational studies and laboratory studies of HIV susceptibility were promising, evidence for causation was needed; randomized, controlled intervention trials were planned and implemented to assess the impact of male circumcision on male HIV acquisition. The first of these trials amongst a general population sample of 3274 uncircumcised males ages 18-24 years in South Africa recorded 20 HIV infections in 2354 follow-up person-years amongst the intervention group and 49 HIV infections in 2339 person-years for the control group (Auvert, Taljaard et al. 2005). These results correspond to a raw reduced risk of 0.40, which lowered to 0.39 after controlling for several sexual and behavioral factors. Two other randomized trials are currently underway in Kenya and Uganda with results expected in 2007 and 2008 respectively.

HIV Epidemic Intervention

The substantial effect shown by the lone completed randomized trial certainly adds male circumcision to the list of strategies to be considered in trying to intervene in and control the heterosexual HIV epidemic in Africa. However, a few concerns must be addressed:

1. Is widespread male circumcision socially and culturally acceptable in African communities?
2. Is there a safe and affordable surgical procedure for performing a high volume of circumcisions?
3. Is the *population level effect* substantial enough to merit a widespread intervention?

To address the question of acceptability and efficacy, several acceptability studies have been conducted throughout sub-Saharan Africa, with nearly all finding a majority of men interested in becoming circumcised if it will reduce their risk of contracting HIV. In a survey conducted in Botswana, where circumcision was prevalent historically but now uncommon, 67% of respondents indicated that they would probably or definitely circumcise a male child if the procedure were offered free of charge in a hospital setting, and this proportion increased to 90% after an informational session about the risks and benefits of circumcision was provided (Kebaabetswe, Lockman et al. 2003). In addition, 81% of uncircumcised men agreed that they would become circumcised if the procedure were offered free in a hospital setting, and 71% of women reported that they preferred a circumcised partner after the information session.

In a survey of men entering beer halls in Harare, Zimbabwe, Halperin et al. (2005) find that while just 14% of respondents were circumcised, 43% reported positive health benefits and 45% of uncircumcised men agreed that they would like to become circumcised if circumcision could be provided safely and affordably and if it would reduce the risk of contracting HIV and other STIs. Further, circumcised men and men who were willing to become circumcised were younger, suggesting that circumcision will be even more acceptable in Zimbabwe in the future.

Amongst a rural population of KwaZulu-Natal in South Africa, 51% of uncircumcised men said they would become circumcised if the procedure could be provided safely and affordably and 50% would circumcise their sons while two-thirds of women preferred a circumcised partner and 72% would circumcise their sons (Scott, Weiss et al. 2005). In a survey conducted in townships near Johannesburg, Lagarde et al. (2003) report that 72.5% of uncircumcised men would prefer to become circumcised if male circumcision proved protective against HIV.

Amongst the traditionally non-circumcising Luo population in western Kenya, 60% of uncircumcised men responded that they would prefer to be circumcised and 69% of women would prefer a circumcised partner (Mattson, Bailey et al. 2005). About 80% of both men and women reported that it was easier for uncircumcised men to contract STIs, with 60% of women and 43% of men reporting that it was easier for uncircumcised men to get AIDS.

Through focus group discussions conducted amongst the Luo, Bailey, Muga et al. (2002) find substantial interest in male circumcision for its perceived hygienic benefits and widespread perception that circumcised men are less susceptible to HIV infection. The researchers conclude that “male circumcision is becoming more of a personal decision as ethnicity and religious preference are increasingly disassociated from circumcision status” (Bailey, Muga et al. 2002).

A study of 368 infants in Tanzania found a complication rate of only 2% for those circumcised between 7 and 14 days after birth when using the Plastibell device, a complication rate similar to that found in western countries (Manji 2000). The overall cost of the procedure was equivalent to 15 to 20 US dollars per circumcision. Additionally, a recent study in Kisumu District, Kenya developed an efficient method for circumcising males aged 18 to 24 (Krieger, Bailey et al. 2005). The procedure was performed on 479 men as part of the ongoing clinical trial there, and 17 complications were reported, corresponding to a low 3.5% complication rate. There were no fatalities or disabilities and 99% of men reported being happy with the procedure one month later.

Finally, to address the question of the overall population level effect of a male circumcision intervention, mathematical modeling is needed. While randomized trials are necessary to establish causality of an individual level protective effect, they monitor only a small subset of the population (a *sample* of young adult, uncircumcised males who are HIV negative) for a short period of time, and hence can say little about the broader epidemic. Indeed the larger scale impact of such an intervention is to be debated. As pointed about by Michelle Garenne:

> "For persons who are highly exposed to risk of HIV infection…a 60% reduction in annual risk will ultimately protect only a smaller proportion. Basic probability calculations show that in discordant couples exposed for 30 years, some 74% will contract the HIV virus if circumcised, compared with 97% if uncircumcised—a small reduction indeed if compared with a highly efficacious vaccine." [Garenne 2006]

While Garenne's assumption of 30 year long discordant relationships is undoubtedly unrealistic, and he fails to consider the effect of delaying the age of HIV infection by several years, possibly from the early twenties to the mid thirties, the point is well made that further work needs to be done before rolling out an intervention.

Methods

We use the Structured Population Event History Simulator (SPEHS) to model an HIV epidemic in a sub-Saharan African population [Clark 2001]. SPEHS is a two-sex individual level model that specifically models fertility and mortality, nuptiality, non-marital unions, sexual intercourses, and vertical and horizontal HIV transmission. Even two decades after the beginning of the real HIV epidemic in much of Africa, there are still many pieces of missing data that would be needed to create a realistic transmission model that precisely matches the epidemic in an observed population [Garnett & Anderson, 1993]. Instead, SPEHS strives to model a realistic demography that is plausible for any number of sub-Saharan African populations by simulating individuals participating in birth, death, union formation and separation, and sexual intercourses. The time step is one month. HIV is introduced into the population through a 15 per 10,000 random incidence and transmitted vertically and horizontally to create a relatively large HIV epidemic.

Model parameters dictating fertility, mortality and nuptiality are calculated directly using 40 years of demographic data collected between 1956 and 2005 from the Tonga tribe in the Gwembe Valley of southeastern Zambia [Thayer & Scudder]. Per sex act HIV transmission parameters are calculated from data observed by Gray et al. in Uganda [Gray]. The male and female HIV prevalence curves for the resulting epidemic are shown in Figure 1.

In order analyze the impact of male circumcision on the HIV epidemic, circumcisions are added to the model, with 25 percent of males being circumcised at birth accounting for traditional circumcision practices. Twenty five percent is a high estimate for current circumcision prevalence in most African populations, and should hence give a conservative estimate for the impact of interventions on the HIV epidemic. Males who are circumcised have a 59.9 percent lower monthly probability of acquiring HIV than if they had not been circumcised, calculated using the results from the completed randomized clinical trial (Auvert, Taljaard et al. 2005).

Several different intervention scenarios are tested by introducing male circumcisions into a target age group 30 years after the beginning of the HIV epidemic. Circumcisions are carried out in the target age group at the target intervention level for the remaining duration of the simulation. The three target age groups for intervention are circumcising males at birth, teenagers between the ages of 10-13y, and young adults between the ages of 18-24y. A fourth scenario is considered as well, referred to as the 'mixed' intervention: circumcising young adults for the first 15 years of intervention, and at birth for the duration of the intervention. The four intervention levels are circumcising 10 percent, 25 percent, 50 percent, and 75 percent of the uncircumcised male population in the target age groups. The results shown are the average over three simulation runs of each scenario.

Results

Figure 2 shows the impact of male circumcision intervention on male HIV prevalence when circumcising at birth. As the graph shows, when circumcising only ten percent of the otherwise uncircumcised male infants, the impact of the intervention appears to be negligible. But when circumcising 50 to 75 percent of the otherwise uncircumcised infants, the intervention has a strong impact, decreasing endemic male HIV prevalence by as much as 25 percent (from roughly 19 percent to 14 percent).

Another important question is how the intervention, targeted directly only at males, will impact HIV in females. Figure 3 shows, intuitive when considering HIV transmission dynamics, that male circumcision intervention has a similar positive, although possibly slightly delayed affect on female HIV prevalence.

The final question is in which target age group the intervention will be the most effective. Figures 4, 5, and 6 shows the impact of circumcision when targeted at teenage, adult, and mixed age group respectively. Figure 7 shows the absolute difference between prevalence in the control scenario and HIV prevalence at the 50 percent intervention level for each of the target age groups. Here it is important to notice that the impact of the epidemic is observed most rapidly (almost immediately after the year 30 intervention point) when the adult population is targeted. However, the long term impact of the intervention is less because some sexual activity, and hence HIV transmission, has already begun prior to circumcision. Alternately the greatest long term benefit is through targeting the infant or teenage population. The ‘mixed age’ intervention retains the best of both of these strategies by circumcising adults at the beginning of the intervention and thus providing immediate protection for sexually active males, and circumcising infants long term, thus providing protection throughout sexual activity for future population.

Discussion

Male circumcision intervention programs may have a substantial impact on the heterosexual HIV epidemic in Africa, including HIV in females and children, but alone such an intervention will not end the epidemic. Furthermore, in order to be effective, intervention programs will need to reach a large proportion of the uncircumcised population, ideally 50 percent or greater. The decrease in HIV prevalence does not appear to be linearly related to the intervention level. The ideal intervention strategy to provide the greatest both immediate and long term benefit should be to circumcise young teenagers, just before they enter ages of sexual activity, or to implement a ‘mixed’ intervention strategy that targets young adults initially but in the long term circumcises infant males.

There is at least on major and several minor caveats to these results. Currently no disinhibition in sexual behavior is modeled accompanying the perceived protective effect of becoming circumcised. This assumption may be severe considering several previous publications have highlighted the danger and likelihood of said disinhibition (Bailey, Neema et al. 1999). In the completed trial in South Africa, disinhibtion was in fact observed in the form of increased risky behavior after recovering from circumcision, but *in spite* of this, male circumcision was still found to have a strong protective effect. Also, targeting younger populations of males, such as infants and possible pre-sexually active teenagers may decrease some disinhibition by avoiding the psychological switch that “I am now protected.” No matter what the situation this concern highlights the need for education and individual counseling to accompany any intervention program.

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Figures

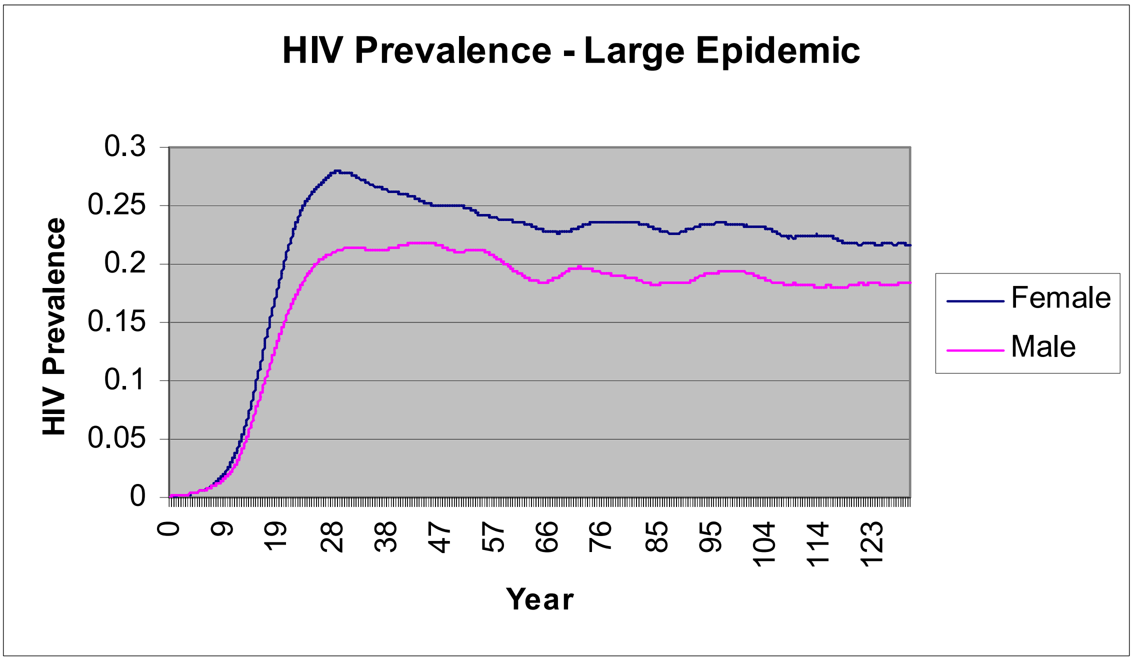

Figure 1: HIV prevalence in control epidemic

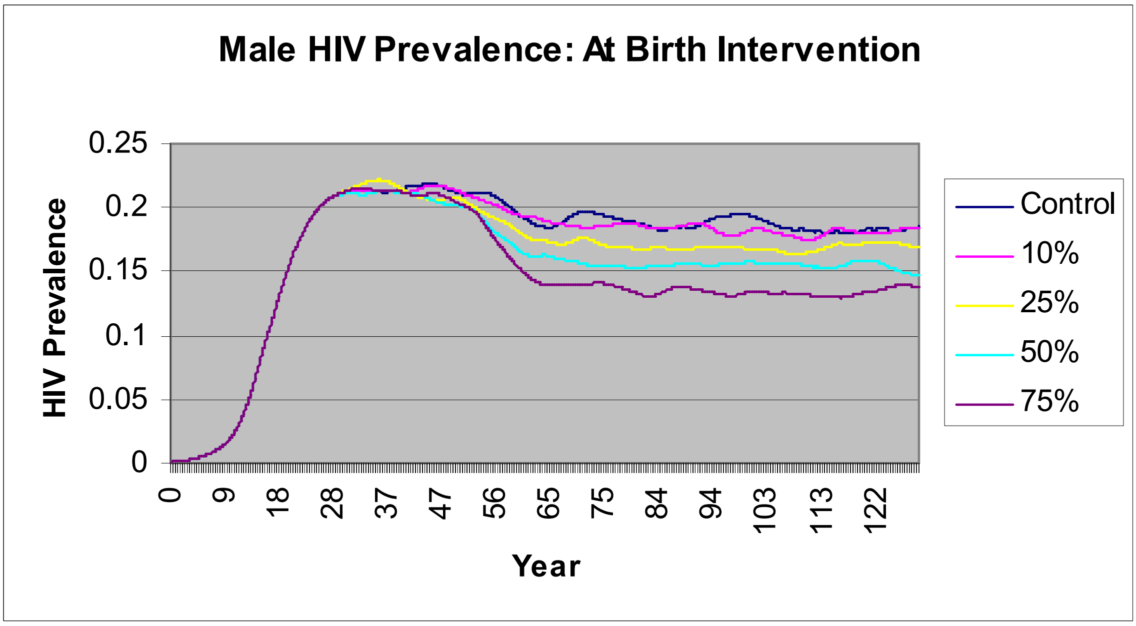

Figure 2: Impact of male circumcision intervention on male HIV prevalence when circumcision occurs at birth.

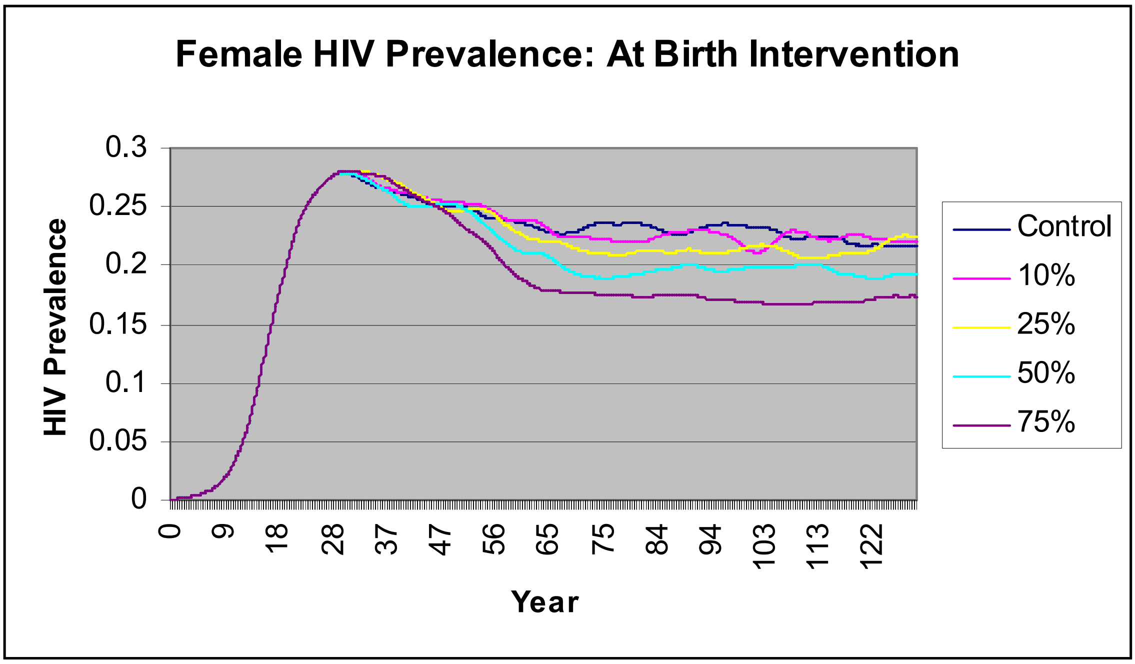

Figure 3: Impact of male circumcision intervention on female HIV prevalence when circumcision occurs at birth.

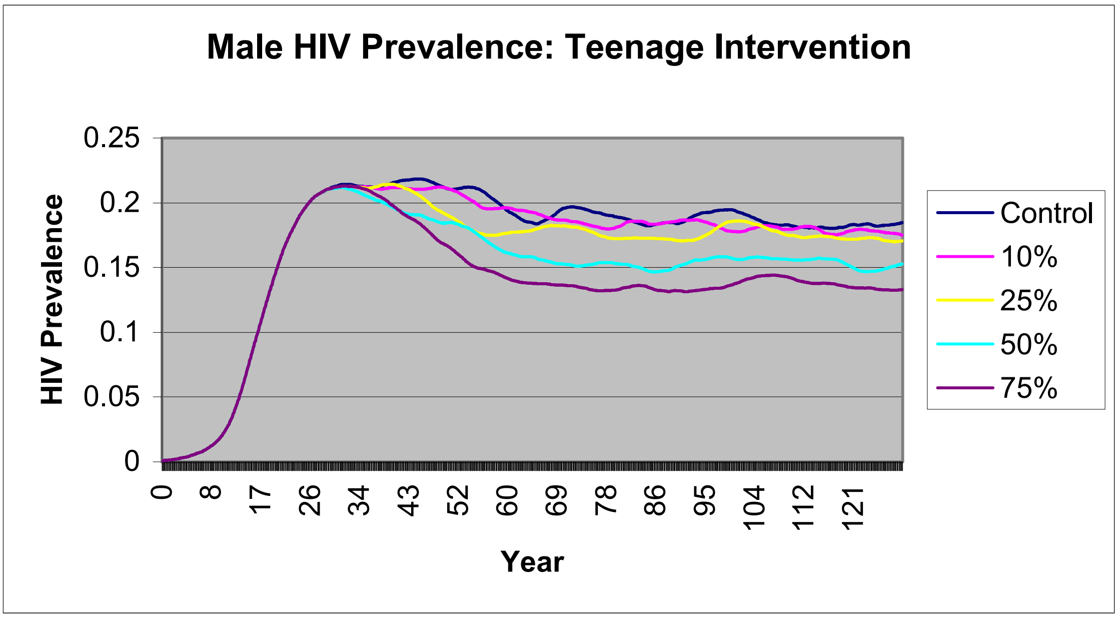

Figure 4: Impact of male circumcision intervention on male HIV prevalence for age 10-13y target population

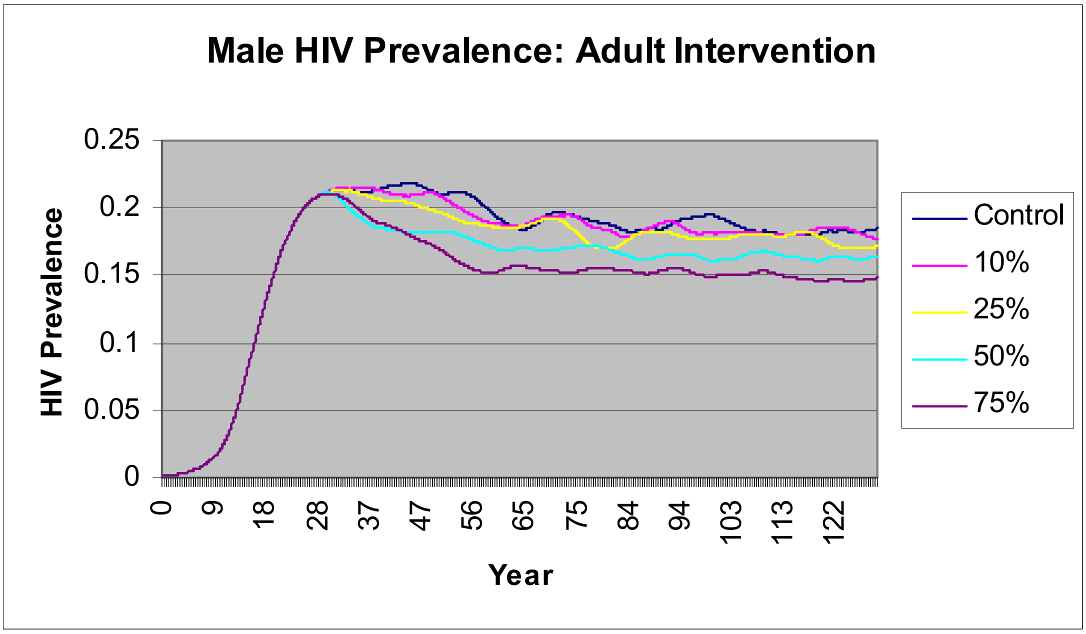

Figure 5: Impact of male circumcision intervention on male HIV prevalence for age 18-24y target population

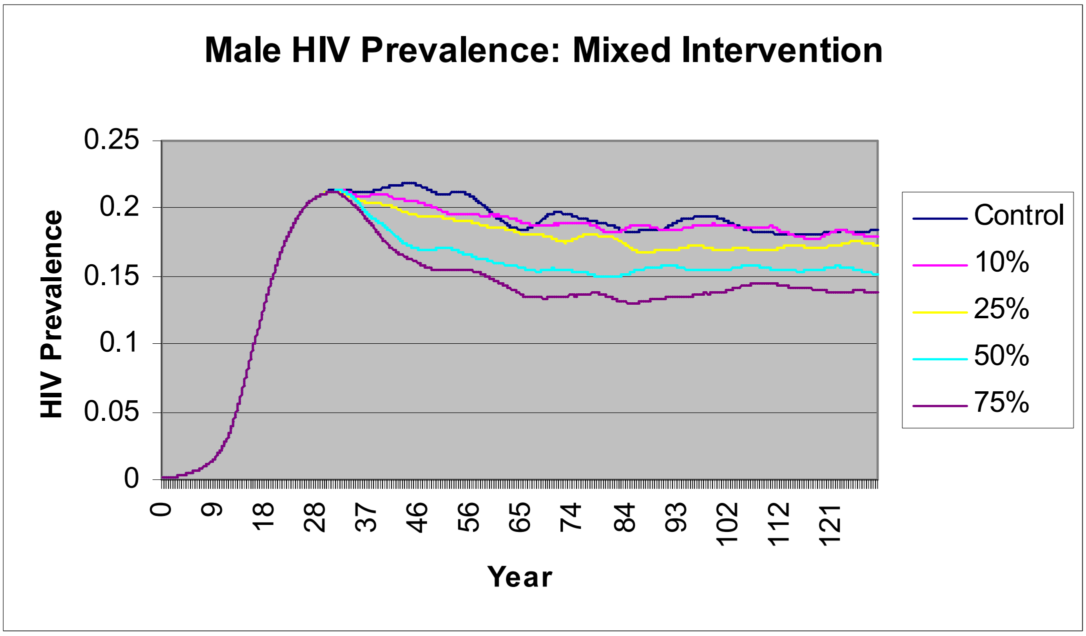

Figure 6: Impact of male circumcision intervention on male HIV prevalence for mixed age target population (18-24y for 15 years and at birth for duration).

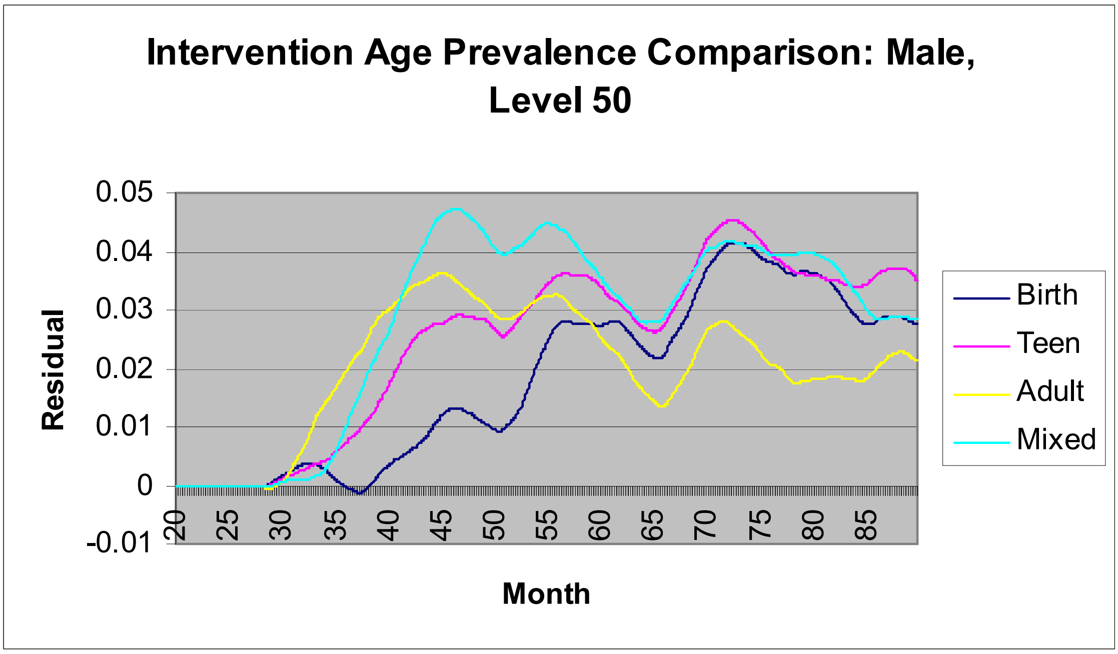

Figure 7: Absolute difference between male HIV prevalence in control and intervention scenarios to compare the effectiveness of each intervention scenario.