Male Circumcision Health Impact Estimation Model for Prevention of Heterosexual Transmission of HIV, HSV-2 and HPV

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Research & Metrics
Population Services International

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For more information or the latest model updates, contact Hongmei Yang at hyang@psi.org.

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Male Circumcision Health Impact Estimation Model for Prevention of Heterosexual Transmission of HIV, HSV-2 and HPV

Background

Population Services International (PSI) is a social marketing organization that promotes healthy behaviors in low-income and vulnerable populations. PSI has programs in 65 countries (www.psi.org) and covers a wide range of health areas including medical male circumcision (MC) to prevent HIV infection and other sexually transmitted infections. PSI uses the disability-adjusted life year (DALY)\(^1\) as the metric for measuring the health impact of interventions in health areas. A DALY model has been developed for each of PSI’s product/services and behavior change communications (BCC) interventions. The DALY model presented here is the male circumcision model for prevention of heterosexual transmission of HIV and other sexually transmitted infections.

Research has shown that male circumcision (MC) is effective in reducing the likelihood of female-to-male sexual transmission of HIV. According to three randomized control trials, male circumcision provides approximately 60% protection against HIV transmission at each high-risk exposure (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007). Recently, a few studies have indicated that male circumcision also provides some protection against other sexually transmitted infections (STIs) such as herpes simplex virus type 2 (HSV-2) and human papillomavirus (HPV) (see references under Tables 1 and 2). Some of the studies focused on the effect of male circumcision of HIV-negative men on the incidence/prevalence of specific STIs among these men and their female partners, while others focused on the effect of male circumcision of HIV-positive men. The study findings on the protective efficacy of male circumcision in the heterosexual transmission of HIV and other sexually transmitted infections, for men and their female partners, are summarized below for HIV-negative men (Table 1) and for HIV-positive men (Table 2).

\(^1\) A DALY is defined as one healthy year of life lost due to premature death and/or disability from a disease. It measures the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability. In our model, a global standard life expectancy at birth of 81.25 years was used to calculate the number of years of life lost (YLL) due to premature death. A 3% time discounting was applied for future years but no age weighting was applied in the modeling (i.e., DALY(0.03,0)).
Table 1. Protective efficacy of male circumcision in heterosexual transmission of HIV and other STIs (incidence and prevalence), HIV-negative men and their female partners

<table>
<thead>
<tr>
<th>Sexually transmitted infections (incidence and prevalence)</th>
<th>Protective efficacy of male circumcision in heterosexual transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (HIV-negative)</td>
</tr>
<tr>
<td>HSV-2 incidence</td>
<td>0.28 (0.08-0.44)(^b) ; 0.3 (0.09-0.45)(^b)</td>
</tr>
<tr>
<td>HR-HPV incidence</td>
<td>0.33 (0.21-0.49)(^c)</td>
</tr>
<tr>
<td>HR-HPV prevalence</td>
<td>0.35 (0.1-0.54)(^a) ; 0.34 (0.14-0.49)(^e)</td>
</tr>
<tr>
<td>Syphilis incidence</td>
<td>No(^a)</td>
</tr>
<tr>
<td>Trichomoniasis prevalence</td>
<td></td>
</tr>
<tr>
<td>Bacterial vaginitis prevalence</td>
<td></td>
</tr>
<tr>
<td>HIV incidence</td>
<td>0.6 (0.32-0.76)(^g) ; 0.6 (0.32-0.77)(^l) ; 0.6 (0.3-0.7)(^l)</td>
</tr>
</tbody>
</table>

Note: HSV-2 = Herpes simplex virus type 2. HR-HPV = High-risk human papillomavirus. 
\(^a\) Tobian et al., 2009a; \(^b\) Tobian et al., 2009b; \(^c\) Gray et al., 2010; \(^d\) Wawer et al., 2011; \(^e\) Auvert et al., 2009; \(^f\) Gray et al., 2009; \(^g\) Auvert et al., 2005; \(^h\) Bailey et al., 2007; \(^i\) Gray et al., 2007; \(^j\) Turner et al., 2007; \(^k\) Serwadda et al., 2010; \(^l\) Tobian et al., 2011; \(^m\) Wawer et al., 2009; \(^n\) Tobian et al., 2012.

Table 2. Protective efficacy of male circumcision in heterosexual transmission of HIV and other STIs (incidence and prevalence), HIV-positive men and their female partners

<table>
<thead>
<tr>
<th>Sexually transmitted infection (incidence and prevalence)</th>
<th>Protective efficacy of male circumcision in heterosexual transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (HIV-positive)</td>
</tr>
<tr>
<td>HSV-2 incidence</td>
<td>0.3 (0.09-0.45)(^b)</td>
</tr>
<tr>
<td>HR-HPV incidence</td>
<td>No(^k)</td>
</tr>
<tr>
<td>HR-HPV prevalence</td>
<td>0.34 (0.14-0.49)(^e) ; 0.23 (0.03-0.38)(^k)</td>
</tr>
<tr>
<td>HIV incidence</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: HSV-2 = Herpes simplex virus type 2. HR-HPV = High-risk human papillomavirus. 
\(^b\) Tobian et al., 2009b; \(^e\) Auvert et al., 2009; \(^k\) Serwadda et al., 2010; \(^l\) Tobian et al., 2011; \(^m\) Wawer et al., 2009.

Currently, PSI has male circumcision programs in five countries – Lesotho, South Africa, Swaziland, Zambia and Zimbabwe. It is expected that similar programs will be implemented in other countries. The PSI office in each of the five countries provides medical circumcision procedures to adult males (age 15+) at PSI clinics or partners’ clinics. Pre- and post-circumcision counseling is provided to help clients understand 1) the steps involved in the surgical procedure, 2) the importance of avoiding sexual intercourse during healing, and 3) the limits of the partial protection against HIV and other STIs provided by circumcision.
The male circumcision (MC) DALY model developed by PSI provides an estimate of DALYs averted per MC procedure (i.e., MC DALY coefficient). The model is used to measure the impact of social marketing programs that deliver male circumcision services to prevent heterosexual transmission of HIV and other sexually transmitted infections. This report 1) describes the principles and structure of a simple deterministic model (in Excel) that estimates the health impact of the male circumcision program in DALYs averted per MC procedure delivered, and 2) identifies the parameters and assumptions used in the model.

Section 1: Principles and Structure of the Model

The MC DALY model does not estimate burden of disease (BOD) because the BOD for HIV and other sexually transmitted infections has already been estimated by other PSI DALY models. Instead, the MC DALY model estimates the health impact of the PSI male circumcision program. The impact is measured by the number of new infections averted, deaths averted, and DALYs averted per circumcision procedure.

Medical male circumcision has been observed to reduce the incidence of HIV, HSV-2, and high-risk human papillomavirus (HR-HPV) infection and to reduce the prevalence of HR-HPV, trichomoniasis, and bacterial vaginitis (see Tables 1 and 2). Findings on the effect of male circumcision on HR-HPV infection however indicate that a reduction of the prevalence of an infection does not necessarily equate to a reduction of the incidence of the infection. We therefore are excluding trichomoniasis and bacterial vaginitis from the modeling because there is no reported evidence of reduced incidence of these STIs associated with male circumcision. The MC model presented here focuses on the health impact of male circumcision on:

1. Reducing HIV/AIDS cases and deaths by reducing the heterosexual transmission of HIV,
2. Reducing genital herpes by reducing transmission of HSV-2, and
3. Reducing cervical cancer and other HPV-associated anogenital cancers by reducing transmission of HR-HPV.

1.1 Reducing Heterosexual Transmission of HIV

1.1.1 Estimating the health impact of male circumcision

To measure the health impact of male circumcision in the heterosexual transmission of HIV, the model estimates the reduction in risk of HIV infection that occurs as a result of implementation of the PSI MC program. The program is expected to reduce the per-act female-to-male infectivity of HIV during heterosexual intercourse, while other factors (the epidemic and sexual behaviors) remain the same. Research studies looking at the protective efficacy of male circumcision (MC) in preventing female partners from becoming infected with HIV, and whether people who are circumcised are more likely to engage in risky sexual behaviors, have reported mixed results (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007; Turner et al., 2007). Therefore, for purposes of this DALY model, it is assumed that male circumcision has no protective effect against the spread of HIV from a man to his female partner and that there is no increase in the prevalence of risky sexual behaviors after circumcision. Further, it is assumed that the protective efficacy of circumcision is the same for all men regardless of age at circumcision, as long as the procedure takes place prior to HIV (or STI) exposure.

According to Bernoulli probability theory (Gray et al., 2001; Mastro et al., 1994; Satten et al., 1994), the probability of an HIV-negative man being infected through heterosexual contact during the study period (one year) is modeled as:
where $p$ is the probability of each man having sexual intercourse with a female partner who is HIV positive and $m$ represents the number of female partners in a year; $\lambda$, the probability of HIV transmission within a discordant partnership, is equal to $1-(1-\gamma)^n$, where $\gamma$ refers to per-act infectivity for HIV in unprotected vaginal intercourse and $n$ represents the number of sexual contacts with each partner.

Substituting $1-(1-\gamma)^n$ into the equation, results in

$$P = 1 - (1 - p \times (1 - (1-\gamma)^n))^m,$$

which shows that the probability of infection through heterosexual contact is associated both with the number of sexual partners and the number of contacts with each partner.

Because it is probable that these behaviors are affected by type of sexual partner, the equation is modified to consider three types of sexual partners: regular, casual, and commercial (sex workers). The partner categories need to be exclusive and exhaustive and can be modified at the country level to be culture- or context-specific. The modified full equation estimating the probability of infection through heterosexual contact is expressed as follows:

$$P = 1 - \prod_{i=\text{regular}}(1 - P_i) = 1 - \prod_{i=\text{regular}}(1 - p_i \times (1 - (1-\gamma_i)^n)^m_i)$$

It is assumed that the probability of being infected during each sexual contact and the probability of being infected by each sexual partner are independent. It is also assumed that the probability of each man having sexual contact with a female partner who is HIV positive is equal to the prevalence of HIV in the general female population of reproductive age (15-49 years).

A number of factors can influence the per-act infectivity of HIV transmission, including the following:

- STD-infection status within the partnership,
- HIV-infection stage of the HIV-positive female partner,
- Circumcision status of the male partner, and
- Condom use during sexual intercourse.

Per-act infectivity is therefore adjusted by considering the effects of such cofactors in various probabilistic combinations that a man who is HIV negative may encounter while having sexual intercourse with a woman who is HIV positive.

Because of the diversity of sexual behaviors associated with HIV transmission during heterosexual intercourse, the study population is divided into five risk groups (population categories) defined by the total number of partners in the past year. The cut-off points for the five risk groups were determined based on the distribution of the data. The health impact is estimated for each risk group. The five risk groups are as follows:

- Low Risk (total partners in the past year = 1)
- Medium Risk (total partners in the past year = 2)
High Risk (total partners in the past year = 3-4)

Very High Risk (total partners in the past year = 5-9)

Highest Risk (total partners in the past year ≥ 10)

For each of the five risk groups, the model runs a scenario in which a man has x partners, y sexual contacts with each type of partner, and z sexual contacts protected by a condom. To obtain an estimate of the reduced risk of HIV transmission per person per year when a man has been circumcised during a PSI program, the likelihood of HIV transmission for the circumcised man is subtracted from the likelihood of HIV transmission for the uncircumcised man. Deaths averted per person per year are estimated by assuming that all new HIV infections will die of AIDS-related diseases.

The estimated number of new infections averted per male circumcision per year is translated into an equivalent figure measured in DALYs averted per MC per year. In this step, the model assumes that a man contracts HIV at different ages, according to the five risk categories:

- Age 26 if he is in the low, medium, or high risk categories,
- Age 25 if he is in the very high category, and
- Age 24 if he is in the highest risk category.

On average, a man infected with HIV lives 10 years with HIV and another two years with AIDS, before death. This means that an HIV-positive man loses 19.3 to 19.7 healthy life years. The calculation is made by summing the years of life lost due to disease (i.e., not feeling well during the 10 years of infection with HIV and the two years living with AIDS) and the years of life lost due to premature death (i.e., number of years of life lost, discounted at 3% for future years), compared with a man who is HIV negative.

1.1.2 Estimating the lifetime benefit of male circumcision

An adult man who is circumcised and engages in unprotected sex is at lower risk of contracting HIV than an uncircumcised man, not only at the year of circumcision but also for the rest of his sexually active life. The DALY model assumes that the “lifetime” of a circumcision is 20 years (i.e., a circumcised man is partially protected from HIV for an average of 20 years). Therefore, the lifetime benefit of a male circumcision procedure in terms of new infections averted and DALYs averted can be calculated by summing the protective benefit at the year of circumcision (current year benefit) and the protective benefit throughout the man’s sexually active life (20-year lasting benefit). However, because the circumcision conveys only partial protection, it is possible for a circumcised man to contract HIV through sexual transmission during the 20-year period. The dynamic aspect of the model requires further steps to obtain a more complete picture of the benefits of circumcision in preventing sexual transmission of HIV. First, the likelihood of contracting HIV each year over the 20-year period (with and without circumcision) is estimated for men who are still at risk (HIV negative) at the beginning of each year. Then, the protective benefits of years 2-20 are summed to obtain the 20-year lasting benefit of male circumcision, discounted at 3% for future years.

1.2 Reducing Heterosexual Transmission of HSV-2

Men who are circumcised have lower risk of infection with HSV-2 than those who are uncircumcised (Tobian et al., 2009a; Tobian et al., 2009b). Additionally, as seen in Tables 1 and 2 above, the protective efficacy of male circumcision on the incidence of HSV-2 is almost the same for men who are HIV negative (0.28) as for those who are HIV positive (0.3). For the female partners of circumcised men, however, existing studies have
not yet identified any protective effect of male circumcision (Tobian et al., 2012). We therefore consider here only the effect of male circumcision on reducing HSV-2 infections in men.

### 1.2.1 Estimating the health impact of male circumcision

People infected with HSV-2 can develop genital herpes and the herpes virus stays in the human body for the rest of a person’s life. Symptoms can recur, but usually recurrences are less severe than the original symptoms. Genital herpes is a disease that rarely causes death.

The health impact of reducing HSV-2 infection through male circumcision comes from reducing the number of genital herpes cases.

Genital herpes cases averted in year one by male circumcision are estimated as follows:

$$\text{Herpes cases averted in year one} = \text{herpes incidence rate} \times \text{protective efficacy of male circumcision on HSV-2 infection}.$$  

Since genital herpes does not cause death, no deaths are averted. Therefore, DALYs averted is simply the product of the number of herpes cases averted and the number of years of life lost due to sickness, as follows:

$$\text{DALYs averted per male circumcision} = \text{herpes cases averted} \times \text{years of life lost due to disability (YLD)}.$$  

### 1.2.2 Estimating the lifetime benefit of male circumcision

To estimate the lifetime benefit of male circumcision in preventing HSV-2 infection, we assume that a circumcised man is partially protected from HSV-2 for an average of 20 years, as we did for the HIV model. Therefore, the lifetime benefit can be calculated by summing the protective benefit at the year of circumcision (current year benefit or year-one benefit) and the protective benefit throughout the man’s sexually active life (20-year lasting benefit), as follows:

$$\text{Lifetime benefit of male circumcision in preventing HSV-2 infections} = \text{year one benefit} + \text{year 2-20 benefit, discounted at 3\% for future years}.$$  

However, because circumcision conveys only partial protection against HSV-2, it is possible for a circumcised man to contract HSV-2 through sexual transmission during the 20-year period. Once he is infected, he is no longer part of the at-risk population (or suspect population). We therefore estimate the probability of being a person at risk of HSV-2 infection at the beginning of each year, over the 20-year period, as follows:

$$\text{Probability of being a suspect person at the beginning of each year, over 20-year period} = \text{Probability of being a suspect person at the beginning of the year before - herpes incidence rate} \times (1 - \text{protective efficacy of male circumcision on HSV-2 infection}).$$  

Year 2-20 benefit is then estimated as follows:

$$\text{Year 2-20 benefit of male circumcision in preventing HSV-2 infection} = \text{herpes incidence rate} \times \text{protective efficacy of male circumcision on HSV-2 infection} \times \text{probability of being a suspect person at the beginning of each year}.$$  

### 1.3 Reducing Heterosexual Transmission of High-risk Human Papillomavirus (HR-HPV)

The circumcision of men who are HIV-negative is known to reduce the incidence of high-risk human papillomavirus (HR-HPV) infection among both men and their female partners. The protective efficacy is reported to be 0.33 (95% CI: 0.21-0.49) for men (Gray et al., 2010) and 0.23 (95% CI: 0.07-0.37) for women (Wawer et al., 2011). The circumcision of HIV-positive men, however, does not appear to protect the men or
their female partners from infection with HR-HPV (Serwadda et al., 2010; Tobian et al., 2011). Therefore, this health impact model on the effect of male circumcision on heterosexual transmission of HR-HPV focuses on men who are HIV-negative or whose HIV status at the time of circumcision was unknown.

### 1.3.1 Health impact of male circumcision

HPV infection is associated with genital warts. Genital warts are not curable and frequently recur. While genital warts can be visible, in many cases they do not cause any negative symptoms, and therefore are often not a concern of people who are infected with HPV. This lack of awareness of the health impact of HPV infection is a major public health problem and it is important to reduce the heterosexual transmission of HPV.

HR-HPV infection is associated with high-grade squamous lesions and the development of cervical and other anogenital cancers. Almost all cervical cancers are caused by HR-HPV (Boshart et al., 1984; Parkin, 2002). Additionally, 40% for vulvar and vaginal cancers, 40% for penile cancers, and 90% for anal cancers are attributable to HR-HPV infection (Parkin, 2002). These four cancers – cervical, vulvar and vaginal, penile, and anal cancer – are considered in the modeling of the health impact of male circumcision on reducing HR-HPV infection.

When an HIV-negative man is circumcised, new anogenital cancer cases averted in year one is the sum of cancer cases averted in year one from his female partners (including cervical, vulvar, vaginal, and anal cancer) and from himself (including penile and anal cancer). Anogenital cancer cases averted in year one by male circumcision are estimated, as follows:

\[
\text{Cancer cases averted in year one by male circumcision} = \text{cancer cases averted in year one from female partners (cervical, vulvar, vaginal, and anal cancer)} + \text{cancer cases averted in year one from man (penile and anal cancer)}
\]

The number of cancer cases averted from each female anogenital cancer is estimated by multiplying the number of partners a man has by the incidence rate of each anogenital cancer among women by the attributable fraction, by the protective efficacy of male circumcision on HR-HPV infection, as follows:

\[
\text{Cancer cases averted from each female anogenital cancer} = \text{number of female partners per man} \times \text{incidence rate of each anogenital cancer in women} \times \text{attributable fraction} \times \text{protective efficacy of male circumcision on HR-HPV infection}
\]

The number of cases averted for each male anogenital cancer is estimated by multiplying the incidence rate of each anogenital cancer among men by the attributable fraction, by the protective efficacy of male circumcision on HR-HPV infection, as follows:

\[
\text{Cancer cases averted from each male anogenital cancer} = \text{incidence rate of each anogenital cancer among men} \times \text{attributable fraction} \times \text{protective efficacy of male circumcision on HR-HPV infection}
\]

Deaths averted are estimated by multiplying the cases averted by case fatality rate, which is the ratio of cumulative death rate to cumulative case rate.

\[
\text{Deaths averted by MC} = \text{cancer cases averted} \times \text{cancer case fatality rate (cumulative death rate/cumulative case rate)}
\]

DALYs averted per male circumcision are estimated as follows:

\[
\text{DALYs averted per MC} = \text{cases averted} \times \text{years of life lost due to disability (YLD)} + \text{deaths averted} \times \text{years of life lost due to premature death (YLL)}
\]
A woman with cervical cancer is assumed to go through four stages of the disease – over a period averaging six years (Goldie et al., 2008) – before dying of cervical cancer at age 55 (Jamison et al., 2006). The overall disability weight of cervical cancer is estimated by weighting the disability weight of each stage by the duration of each stage.

*Overall disability weight of cervical cancer = disability weight of each stage \times duration of each stage, weighted*

Years of life lost due to disability (YLD) is then calculated by multiplying the overall duration by overall disability weight. Years of life lost due to premature death (YLL) is discounted at 3% for future years. Because the anogenital cancers occur many years after HR-HPV infection and male circumcision – assuming age at circumcision is 26 – the YLDs and YLLs due to HR-HPV-associated anogenital cancers are discounted at 3% per year for a number of years after the HR-HPV infection but before the diagnosis of cancer (i.e., age at diagnosis minus age at circumcision).

*Years of life lost due to disability (YLD) = first discount at 3% for number of years equivalent to (age at diagnosis – age at circumcision), then overall duration \times overall disability weight, discounted at 3% for future years*

*Years of life lost due to premature death (YLL) is discounted at 3% for future years*

### 1.3.2 Estimating the lifetime benefit of male circumcision

The *lifetime benefit of male circumcision in preventing HR-HPV infection* is calculated by summing the protective benefit at the year of circumcision (current-year benefit or year-one benefit) and the protective benefit throughout the man’s sexually active life (20-year lasting benefit). Because most HPV infections are self-limiting, and people can become infected multiple times, we assume that people are still at risk of infection each year over the 20-year period. Because the cancer incidence rates are low, we did not modify the probability of being a person at risk by considering the likelihood of being a cancer patient. The 20-year benefit is therefore estimated by applying the year-one benefit to the following 19 years, discounting future years at 3%.

*Lifetime benefit of male circumcision in preventing HR-HPV infection = year one benefit \times sum of discounted years over 20-year period*
Section 2: Parameters and Data Sources

This section presents information on the deterministic data points for the parameters used in the male circumcision (MC) DALY model, and their sources.

2.1 Protective Efficacy

**Protective efficacy of condoms:** 90% (Pinkerton et al., 1997)

**Protective efficacy of male circumcision in heterosexual transmission of HIV and other STIs, HIV-negative men and their female partners:** Please refer to Tables 1 and 2 in the text.

2.2 Reducing Heterosexual Transmission of HIV

2.2.1 Risk group sexual activity data

The sexual behavior data presented in the table below were determined using the combined data from three PSI TRaC surveys of the general population age 15-49 in Angola, Zambia and Zimbabwe. The table shows the proportion of sexually active men in each of the five risk groups, the average number of sexual partners the men had in the past year by type of partner, and the average number of sexual contacts the men had with each type of partner.

<table>
<thead>
<tr>
<th>Percent sexually active</th>
<th>Risk group</th>
<th>Percent among those sexually active</th>
<th>Type of partner</th>
<th>Average no. of partners/year</th>
<th>Average no. of sexual contacts/partners/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>82.2% 5297/7135</td>
<td>Low risk (1 partner)</td>
<td>77.3%</td>
<td>regular</td>
<td>0.854</td>
<td>58.75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>casual</td>
<td>0.139</td>
<td>43.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>commercial</td>
<td>0.0072</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Med risk (2 partners)</td>
<td>11.2%</td>
<td>regular</td>
<td>0.958</td>
<td>70.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>casual</td>
<td>0.931</td>
<td>40.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>commercial</td>
<td>0.1112</td>
<td>24.0</td>
</tr>
<tr>
<td></td>
<td>High risk (3-4 partners)</td>
<td>5.3%</td>
<td>regular</td>
<td>0.997</td>
<td>69.78</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>casual</td>
<td>1.763</td>
<td>25.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>commercial</td>
<td>0.5015</td>
<td>24.0</td>
</tr>
<tr>
<td></td>
<td>Very high risk (5-9 partners)</td>
<td>3.7%</td>
<td>regular</td>
<td>1.054</td>
<td>55.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>casual</td>
<td>2.769</td>
<td>21.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>commercial</td>
<td>2.269</td>
<td>25.2</td>
</tr>
<tr>
<td></td>
<td>Highest risk (10+ partners)</td>
<td>2.5%</td>
<td>regular</td>
<td>4.092</td>
<td>31.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>casual</td>
<td>4.74</td>
<td>18.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>commercial</td>
<td>9.315</td>
<td>36.0</td>
</tr>
</tbody>
</table>
Condom usage

Condom use rates by type of partner are as follows: regular partner (10%), casual partner (40%), and commercial sex partner (60%). These rates apply to all PSI countries.

2.2.2 Epidemic data

HIV prevalence rates for the general population of adults were obtained from the UNAIDS Report on the Global AIDS epidemic (UNAIDS, 2010). Adult STD and HIV prevalence among commercial sex workers (CSWs) were obtained based on adjusted functions of adult HIV prevalence.

Male circumcision rate

Male circumcision rates were obtained from Williams et al., (2006). The male circumcision rate in Swaziland (8.2%) was obtained from 2006-07 DHS data (CSO and Macro International, 2008).

2.2.3 Biological information

In Europe and North America, studies of serodiscordant couples have typically reported a per-act infectivity of 0.001 (range: 0.0001-0.0015) (Boily et al., 2009; De Vincenzi, 1994; Downs and De Vincenzi, 1996; Leynaert et al., 1998; Peterman et al., 1988; Royce et al., 1997; Wiley et al., 1989). A study of monogamous couples in Rakai, Uganda found that the average per-act infectivity was 0.0011 (Gray et al., 2001).

Therefore, 0.0005 was selected as the transmission probability per sexual contact during the asymptomatic stage of HIV, with both partners negative for other STIs; and, 0.0047 was selected as the transmission probability per sexual contact during the acute infection stage of HIV, with both partners negative for other STIs (Hollingsworth et al., 2008; Pilcher et al., 2004; Wawer et al., 2005).

The effect of STD infection on HIV transmission is 5 (Rottingen et al., 2001 and Satten et al., 1994)

2.2.4 Disease-related information

Acute period of infection: 54 days (Pilcher et al., 2004)

Duration of HIV: 10 years; YLD weight: 0.135 (Jamison et al., 2006)

Duration of AIDS: 2 years; YLD weight: 0.505 (Jamison et al., 2006)

Age at infection: 26 years for low, medium, or high risk groups, 25 years for very high risk group, and 24 years for the highest risk group

Life expectancy: 81.25 years (PSI default, which equals life expectancy for the Japanese (Jamison et al., 2006))

PSI uses Japanese life expectancy as the ideal standard for years of life a person can live when s/he is free from diseases. It is used in the model estimating the impact of PMTCT on HIV transmission for two reasons: one is related to ethics; the other takes into consideration the effects of country-specific factors.

1. PSI usually measures program impact by estimating DALYs averted across products/services and countries. It would be unfair therefore to use country-specific life expectancy in a model that uses non-country-specific calculation of new infections/deaths averted.

2. The lower life expectancies reported in many developing countries (compared with developed countries like Japan) may actually be associated with a variety of country-specific factors such as 1) disease burden, 2) diet and feeding practices, and 3) socio-economic status. When these variables
(individually) in developing countries are generally the same as those in Japan – assuming that genetics alone does not cause a substantial difference in life expectancy – people in developing countries are likely to live as long as the Japanese.

2.3 Reducing Heterosexual Transmission of HSV-2

2.3.1 Herpes incidence rate by sex and region

Table 4: Herpes incidence rate by sex and region

<table>
<thead>
<tr>
<th>STI infection</th>
<th>Sex</th>
<th>South East Asia</th>
<th>Eastern Europe &amp; Central Asia</th>
<th>East Asia</th>
<th>Latin America &amp; Caribbean</th>
<th>Sub-Saharan Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes</td>
<td>M</td>
<td>0.014313</td>
<td>0.001585</td>
<td>0.001012</td>
<td>0.039279</td>
<td>0.049814</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0.012114</td>
<td>0.001616</td>
<td>0.000859</td>
<td>0.031106</td>
<td>0.039103</td>
</tr>
</tbody>
</table>

South East Asia includes:
Afghanistan, Cambodia, India, Lao, Myanmar, Nepal, Pakistan, Philippines, Thailand, and Vietnam.

Eastern Europe & Central Asia include:
Armenia, Azerbaijan, Belarus, Bosnia, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Poland, Republic of Moldova, Romania, Russia, Slovakia, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan.

East Asia includes:
China, Papua New Guinea, and other East Asian countries.

Latin America & Caribbean include:
Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Netherlands, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Suriname, Trinidad and Tobago, Uruguay, and Venezuela.

Sub-Saharan Africa includes:

Source:
Calculated by multiplying syphilis incidence rate by the ratio of herpes prevalence to syphilis prevalence. Syphilis incidence rate was obtained from Global Prevalence and Incidence of Selected Curable Sexually Transmitted Infections-Overview and Estimates, WHO 2001. The ratio of herpes prevalence to syphilis prevalence was obtained from Establishing STI Surveillance – Basic Data Needs, Methodology and Indicators. Surveillance, Research, Monitoring & Evaluation, Department of HIV/AIDS, WHO.

2.3.2 Disease-related information

Duration of initial genital herpes episodes: 4 weeks (online resources: http://www.cdc.gov/STD/Herpes/; http://www.herpesguide.ca/facts/hsv_2_infections.html; http://www.ihmf.org/general/resources03.asp);

Disability weight of initial genital herpes episodes: 0.1 (The number is not available in Jamison et al., 2006. I assume that the weight may be higher than that for primary syphilis and chancroid because it may have generalized symptoms (such as fever, aches and pains, swollen lymph nodes) in addition to genital symptoms. http://www.fpnotebook.com/ID/STD/GntlHrps.htm)
Case fatality rate: 0 (herpes does not cause death).

2.4 Reducing Heterosexual Transmission of HR-HPV

2.4.1 Anogenital cancer incidence rates

Table 5: Age-standardized incidence rate for cervical cancer, cumulative risk of cancer, and cumulative risk of death, five countries in sub-Saharan Africa

<table>
<thead>
<tr>
<th>Country</th>
<th>Age-standardized incidence rate (/100,000)</th>
<th>Cumulative risk [0-74] of cancer (%)</th>
<th>Cumulative risk [0-74] of death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesotho</td>
<td>35.0</td>
<td>3.61</td>
<td>2.48</td>
</tr>
<tr>
<td>South Africa</td>
<td>26.6</td>
<td>2.93</td>
<td>1.7</td>
</tr>
<tr>
<td>Swaziland</td>
<td>50.0</td>
<td>5.01</td>
<td>3.3</td>
</tr>
<tr>
<td>Zambia</td>
<td>52.8</td>
<td>6.14</td>
<td>4.93</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>47.4</td>
<td>5.26</td>
<td>3.94</td>
</tr>
</tbody>
</table>

Source: GLOBOCAN 2008 (Ferlay et al., 2010).

Table 6: Cancer incidence rates (per 100,000) in Zimbabwe, other anogenital cancers

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Rate (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulva, vagina</td>
<td>3.4</td>
</tr>
<tr>
<td>Penis</td>
<td>0.9</td>
</tr>
<tr>
<td>Rectum and anus (m)</td>
<td>3.6</td>
</tr>
<tr>
<td>Rectum and anus (f)</td>
<td>3.1</td>
</tr>
</tbody>
</table>


The incidence rates for these cancers are within reported global incidence rates (Table 1, Giuliano et al., 2008). We used the Zimbabwe data for the other countries because incidence rates for anogenital cancers other than cervical cancer were lacking in these countries.

2.4.2 Case fatality rate

Case fatality rate of cervical cancer is calculated by dividing cumulative risk of death by cumulative risk of cancer. For other anogenital cancers, due to lack of data on cumulative risk of cancer and death, we assume they have the same case fatality rate as cervical cancer. The justification for this assumption is that they share the similar risk profile and histology as cervical cancer.
2.4.3 Other cancer-related data

Table 7: Attributable fraction of cancers due to high-risk human papillomavirus (HR-HPV) infection (Parkin, 2002; Giuliano et al., 2008)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Attributable fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>cervix</td>
<td>100%</td>
</tr>
<tr>
<td>vulva, vagina</td>
<td>40%</td>
</tr>
<tr>
<td>penis</td>
<td>40%</td>
</tr>
<tr>
<td>anus</td>
<td>90%</td>
</tr>
</tbody>
</table>

Percentage of anorectal malignancies that are anal cancers: 3.5% (Wietfeldt et al., 2009)

Table 8: Duration and disability weight for the four stages of cervical cancer

| Cancer stage                          | Progression rate to next stage\(|a|\) | Duration (years)\(|b|\) | Disability weight |
|---------------------------------------|----------------------------------------|-------------------------|-------------------|
| Stage I (T1, N0, M0)                  | 0.9/4 yrs                              | 1.737                   | 0.08              |
| Stage II (T2, N0, M0)                 | 0.9/3 yrs                              | 1.303                   | 0.08              |
| Stage III (T3, N0, M0 or T1-3, N1, M0)| 0.9/2 yrs                              | 0.869                   | 0.75              |
| Stage IV (T4, N0, M0 or any T, any N, M1) | -                                    | 2.091                   | 0.81              |

Source: \(a\)Myers et al., 2000; \(^{b}\)Calculated by assuming the occurrence of cervical cancer follows Poisson distribution; \(^{c}\)Jamison et al., 2006

Duration of cervical cancer to death (years): 6 (Goldie et al., 2008)

Age at death of cervical cancer: 55 (calculated based on age-specific death data reported by GLOBALCAN 2008 (Ferlay et al., 2010)

Duration of penile cancer to death (years): 2 (Pow-Sang et al., 2010)

Disability weight of penile cancer: 0.75 (which equals the disability weight of regional cancer (i.e., cancer cells have spread to nearby or regional lymph nodes) used in Jamison et al., 2006. The justification for using the disability weight of regional cancer stage is based on the fact that patients with penile cancer usually die within two years of diagnosis because of complications due to uncontrollable local/regional growth or distant metastasis, and that metastatic spread to distant sites (e.g., lungs, liver, bone, and brain) is uncommon (1%-10% in most large series) and usually occurs late in the disease course (Pow-Sang et al., 2010)).

Cancers of the vulva, vagina, and anus are rare and no data were found on the duration of these cancers. However, vulva/vagina cancer associated with HR-HPV follows a similar risk profile and histology as cervical cancer (Forcier and Musacchio, 2010). Anal cancer associated with HR-HPV follows a similar risk profile and epidemiology as cervical cancer (Giuliano et al., 2008). We assume that these cancers have the same duration and disability weight as cervical cancer. The overall disability weight is calculated by weighting the disability weight of each stage of cervical cancer by the duration of cervical cancer.
Table 9: Age at diagnosis (based on cancer registry data from Harare, Zimbabwe, 1998-2002):

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Age at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>vulva, vagina</td>
<td>43.4</td>
</tr>
<tr>
<td>penis</td>
<td>47.0</td>
</tr>
<tr>
<td>rectum and anus (m)</td>
<td>53.2</td>
</tr>
<tr>
<td>rectum and anus (f)</td>
<td>48.5</td>
</tr>
</tbody>
</table>

References


