PSI Health Impact Estimation Model: Use of Highly Active Antiretroviral Therapy to Treat People Living with HIV/AIDS

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Research & Metrics
Population Services International

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PSI shares its models with all interested individuals or organizations. Please note that the models are updated periodically based on the latest available epidemiological, demographic, intervention effectiveness, and utilization data. As a result, numbers used in this document should be considered illustrative only. They show how the model works, but they may have changed since the time of writing.

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

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Health Impact Estimation Model for Use of Highly Active Antiretroviral Therapy (HAART) to Treat People Living with HIV/AIDS

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 providing highly active antiretroviral therapy (HAART) to people living with HIV/AIDS (PLWHA). 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 products/services and behavior change communications (BCC) interventions. The DALY model presented here is the HAART model for treatment of people living with HIV/AIDS. The goals of HAART treatment are prolonged life for PLWHA and reduced heterosexual transmission of HIV.

Highly active antiretroviral therapy (HAART) is a treatment regimen that uses a combination of (three or four) antiretroviral drugs to treat HIV infection. Since the introduction of HAART in 1996, treatment regimens have become increasingly effective, are better tolerated by patients, and have simpler dosing procedures. The current WHO antiretroviral therapy (ART) guidelines (WHO, 2010) recommend that initial HAART should contain the following:

- **A non-nucleoside reverse transcriptase inhibitor (NNRTI)** — either nevirapine (NVP) or efavirenz (EFV), and
- **Two nucleoside reverse transcriptase inhibitors (NRTIs)** — one of which should be lamivudine (3TC) or emtricitabine (FTC) and the other zidovudine (AZT) or tenofovir disoproxil fumarate (TDF).

Because AZT and TDF are more expensive, require more laboratory monitoring and have higher initial discontinuation rates, stavudine (d4T), an alternative nucleoside reverse transcriptase inhibitor, continues to be widely used in resource-limited settings, including Myanmar (WHO, 2010).

HAART acts by suppressing HIV replication to such an extent that plasma HIV-1-RNA levels (the viral load) typically become undetectable. This allows the person’s immune system to recover, leading to long-term remission of the disease and avoidance of its otherwise fatal course (Braitstein et al., 2006; Hogg et al., 1997). In the new “era of HAART,” HIV infection has become a chronic disease requiring lifelong adherence to antiretroviral therapy, but it is no longer a death sentence.

Studies in both developed and developing countries indicate that lifelong adherence to HAART by people with HIV reduces mortality rates and increases life expectancy (Braitstein et al., 2006; Jahn et al., 2008; Mocroft et al., 1998) (see Table 1). For example, the studies show that at age 20, the average number of years of life remaining for a person with HIV being treated with HAART is two-thirds that of the general population

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\(^1\) 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 83.1 years (male: 79.6, female: 86.5) 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)).

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PSI | 4
(Antiretroviral Therapy Cohort Collaboration 2008; Mills et al., 2011; Lohse et al., 2007; van Sighem et al., 2010).

HAART plays an important role in the prevention of HIV transmission by reducing vertical transmission of HIV (from mother to child) and horizontal transmission of HIV (between sero-discordant sexual partners). With the addition of maternal HAART during pregnancy and labor, and neonatal antiretroviral prophylaxis for 6 weeks, the risk of mother-to-child transmission has been reduced from 35% to less than 5% in breastfeeding populations (WHO, 2010). Recent studies of the impact of HAART on HIV transmission in heterosexual sero-discordant couples indicate that HAART reduces HIV transmission in this context (Cohen et al., 2011; Schwartländer et al., 2011). Early initiation of ART among HIV-infected patients with CD4 counts between 350 and 550 cells per cubic millimeter reduces rate of sexual transmission of HIV by 96% (95% CI: 73%- 99%) (Cohen et al., 2011). Reductions in HIV transmission rates in excess of 90% were also reported in several cohort studies of heterosexual sero-discordant couples, when the index member of the couple was treated with HAART (Attia et al., 2009). A recent prospective cohort analysis indicates that combination antiretroviral therapy (cART) reduces the per-sexual-act transmission rate by 92% for those on cART (Donnell et al., 2010).

**PSI HAART program in Myanmar**

Currently, PSI has a HAART program only in Myanmar. It is expected that more PSI platforms will initiate HAART programs in the future. According to the Myanmar national antiretroviral therapy guidelines (Srikantiah et al., 2010), PLWHA with a CD4<200 cells/mm³ should receive cART and those with a CD4 between 200 and 350/mm³ can be considered for treatment. In 2009, approximately 18% (16%-22%) of those eligible for HAART according to WHO 2010 guidelines (i.e., CD4<350 cells/ mm³) received cART (WHO 2011) in Myanmar.

PSI/Myanmar launched its first HAART program in October 2008. Two first-line fixed-dose combinations (FDCs) were provided free of charge to PLWHA who were eligible for treatment (CD4<350). The two FDCs were d4T (i.e., stavudine) 30mg/3TC 150mg/ NVP 200mg and AZT 300mg/3TC 150 mg/ EFV 600mg or NVP 200mg. In the next three years, the free HAART program enrolled a total of 61 clients, of which 50 clients are ongoing (nine died, and two transferred out). PSI/Myanmar implemented the HAART program through the Sun Quality Health (SQH) network, which manages more than 1000 general practitioner clinics in Myanmar.

The HAART program in Myanmar targets the SQH doctors who provide TB and STI treatment. Eligible doctors are trained to provide the first-line HAART treatment supported financially by PSI/Myanmar (the two FDCs). They are also trained in how to support patient adherence to the HAART program, when and how to switch to alternative first-line and second-line regimens, how to use laboratory support, and how to manage opportunistic infections (OIs). Since July 2010, PSI/Myanmar has been providing a first-line generic FDC of 3TC/d4T/NVP at cost to trained SQH doctors. In the past year, 50 clients have been enrolled in the at-cost HAART program. The selling price to doctors is 7,500 Kyats (8.3 USD) for a one-month supply of drugs (a bottle of Triomune 30, Cipla), with the end-user price varying from 7,500 Kyats (8.3 USD) to 10,000 Kyats (11 USD), depending on the provider.
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Study period</th>
<th>Study population</th>
<th>Sample characteristics</th>
<th>HAART</th>
<th>Median survival on HAART</th>
<th>General pop. survival</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark national HIV cohort</td>
<td>1995-2005</td>
<td>All HIV-positive adults (&gt;16 years) treated in Danish HIV clinics since 1 Jan 1995.</td>
<td>n=3990, 77% men, median observation time=5.8 years (2.2-9.9 yrs), mode of infection: 47% homo-, 35% hetero- and 12% injecting drug use, 17% HCV infected. Lost to follow-up: 3% (mostly due to emigration). No report on adherence rate and failure rate.</td>
<td>A combination of ≥3 drugs, including ≥1 protease inhibitor, 1 NNRTI, or abacavir; or the 2-drug combination of efavirenz and ritonavir-boosted lopinavir. HAART introduced in 1996, ≥75% coverage in 2002 to 2004, &lt;5% of patients were interrupting treatment at any given time (no taking drugs for ≥2 weeks after initiation of HAART).</td>
<td>During the late HAART period (2000-2005), median survival after age 25 (95% CI): total: 32.5 yrs (29.4-34.7); men: 32.1 yrs (28.5-34.9); women: 32.3 yrs (24.5-36.1)</td>
<td>Median: 51.1 yrs from age 25 (50.8 yrs for men and 54.8 yrs for women)</td>
<td>Lohse et al., 2007</td>
</tr>
<tr>
<td>14 HIV cohorts in Europe and North America</td>
<td>1996-2005</td>
<td>Antiretroviral-naive patients age 16 years or older who initiated combination therapy with ≥3 drugs and did not receive fusion inhibitors in initial regimen.</td>
<td>n=43355, about 70% men, &gt;20% had clinical CDC stage C when initiation treatment, mode of infection: injecting drug use decrease from 18.8% in 1996-1999 to 8.4% in 2003-2005. CD4 count: about 50% ≥200 cells/μL and 25% &lt;100. Death: 4.7%. No report on adherence rate and failure rate.</td>
<td>First-line combination therapy containing either non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (Pis). In 2003-2005, 50% patients on PI-based regimen, 39% on NNRTI-based and 9% on three NRTIs.</td>
<td>During 1996-2005, median survival at age 20: 43.1 (SE 0.33) for all, 42.8 (SE 0.45) for men, 44.2 (SE 0.55) for women, 32.6 (SE 1.06) for IDUs and 44.7 (SE 0.34) for non-IDUs. Median survival at age 35: all 31.7 (SE 0.21), m 31.7 (SE 0.24), w 32.5 (SE 0.44), IDUs 23.4 (SE 0.6), and non-IDUs 33 (SE 0.22). Survival by three study periods available.</td>
<td>HIV-positive person on HAART can expect to live about 43 years at age 20, about 2/3 as long as the general population in these countries.</td>
<td>The antiretroviral therapy cohort collaboration, 2008</td>
</tr>
<tr>
<td>ATHENA national observational HIV cohort in Netherlands</td>
<td>1998-1 Jun 2008</td>
<td>HIV-1 infected individuals who were diagnosed with HIV in 1998-2007, age 16 or older at the time of diagnosis, had ≥24 weeks of follow-up, and ART-naive as of 24 weeks after diagnosis.</td>
<td>n=4612, 80% men, mode of transmission: 60% hetero, 32% hetero and 2% injecting drug use. HCV &amp; HBV co-infection: 8.9% &amp; 6.4% (additionally, 9.2% &amp; 5.1% unknown, respectively). At 24 weeks after diagnosis: 4% had AIDS &amp; median CD4 count 480 (IQR 360-650) cells/μL. Median follow-up after 24 weeks: 3.3 yrs (IQR): 1.6-5.8 yrs. 58% ever started cART after 24 weeks. Death during follow-up: 2.6%.</td>
<td>Survival analysis: n=4174 (excluding those with AIDS at 24 weeks and had a history of drug use). 8.4% lost to follow-up. Median survival from age 25 was 52.7 (IQR 44.2-59.3) for men and 57.8 (49.2-63.7) for women.</td>
<td>Median survival from age 25: 53.1 (IQR 44.9-59.5) for men and 58.1 (50.1-63.9) for women.</td>
<td>Median survival from age 25: 53.1 (IQR 44.9-59.5) for men and 58.1 (50.1-63.9) for women.</td>
<td>van Sighem et al., 2010</td>
</tr>
<tr>
<td>Uganda national HIV cohort</td>
<td>2000-1 Jan 2010</td>
<td>HIV infected patients age 14 years or older who initiated antiretroviral therapy at AIDS Support Organization clinics in Uganda from 1 Jan 2000 to 31 Dec 2009.</td>
<td>n=22315, 30% men, median age: 37 years, CD4 count at initiation: 16% ≥250, 31% 150-249, 18% 100-149, 16% 50-99 and 19% &lt;50 cells/μL. Death: 6.7% and lost to follow-up: 6.4%.</td>
<td>A NNRTI with first-line treatment with fixed-dose combinations comprising nevirapine or efavirenz plus lamivudine and stavudine; second-line therapy consists of boosted lopinavir, didanosine, and zidovudine.</td>
<td>Age 14-19: all 26.2, men 22.2, women 27.9; age 20-24: all 26.7, m 19.1, w 30.6; age 25-29: all 28.1, m 21.3, w 32.3; age 30-34: all 28.2, m 21.8, w 32.8; age 35-39: all 27.9, m 22, w 32.5; age 40-44: all 26.9, m 21.9, w 31.3; age 45-49: all 25.4, m 20.9, w 29.6; age 50-54: all 24, m 20.2, w 27.8.</td>
<td>Age 14-19: 45.9; age 20-24: 41.6, age 25-29: 37.4, age 30-34: 33.5; age 35-39: 30.1; age 40-44: 27.1; age 45-49: 24.3; age 50-54: 21.3.</td>
<td>Mills et al., 2011</td>
</tr>
</tbody>
</table>
Criteria for selection of HIV cases for HAART in the Myanmar at-cost HAART program

Confirmed adult and adolescent cases of HIV are selected for treatment if their CD4 ≤ 350 cells/mm3 (irrespective of clinical symptoms) OR if they have progressed to WHO clinical stage III or IV (irrespective of CD4 count) OR if they have active TB disease (irrespective of CD4 count). Pregnant women, children, and HBV/HCV co-infected cases are excluded.

The role of HAART providers

Providers in the at-cost program focus on the delivery of generic first-line HAART; however, they are also expected to know appropriate local referral sites for management of side effects, toxicity, ART failure, severe OIs, and sites for common lab tests. The initial HAART counseling session is particularly important because providers are required to inform patients and caregivers of the following:

HAART is life-long treatment for HIV;

There are inherent costs associated with HAART;

HAART has short-term and long-term side effects;

Adherence to the HAART medication regimen is extremely important; and

Patients should be cognizant of any new symptoms.

In both the free and at-cost HAART programs, after the patient has been stabilized on ART medication, the provider gives the patient 60 tablets (a one-month supply) of FDC (d4T/3TC/NVP) at each visit (sometimes 120 to 180 tablets if requested by the patient). Providers are required to keep a supply of at least one month of HAART medication available per registered patient. Initial follow-ups are every two weeks for the first three months, and then every month for up to a year. After that, follow-up is done every one to three months, depending on the patient’s situation. At each visit, providers measure body weight and check for drug side effects and the occurrence of OIs. Providers also count the pills at each visit and record the number as “adherence rate” in the PSI record book. The number of FDC tablets distributed to PLWHA each month is reported to PSI headquarter for health impact estimation.

The HAART Health Impact Estimation Model

The HAART health impact estimation model developed by PSI provides an estimate of the DALY coefficient – DALYs averted per tablet of FDC. This report 1) describes the principles and structure of a simple deterministic model (in Excel) that estimates the health impact of the HAART program in DALYs averted per tablet of FDC, and 2) identifies the parameters and assumptions used in the model.
Section 1: Principles and Structure of the Model

Unlike other PSI DALY models, the HAART DALY model does not estimate burden of disease (BOD). This is because 1) the BOD for HIV has already been estimated by other PSI DALY models, and 2) the study population, *people living with HIV/AIDS (PLWHA)*, is a sub-population, not the general population. Instead, the DALY model just estimates the health impact of the PSI HAART program.

The PSI HAART program records and reports on the number of FDC tablets distributed to PLWHA for treatment. The impact of the distribution is measured by the number of new infections averted, deaths averted, and DALYs averted per tablet of FDC distributed. HAART has been observed to prolong life and to reduce both vertical and horizontal transmission of HIV. Because pregnant women are excluded from the Myanmar program, the role of HAART in vertical transmission of HIV (MTCT) is not considered. Instead, the model focuses on the impact of HAART on 1) increasing the life span of people living with HIV/AIDS (PLWHA), and 2) reducing heterosexual transmission of HIV (horizontal transmission).

**1.1 Part One of HAART Model: Living Longer with HIV**

Part one of the HAART model examines the increased life span of HIV-positive persons who have been treated with HAART. It estimates the *averted disability-adjusted life years (DALYs) of people living with HIV/AIDS (PLWHA)* due to prolonged survival.

Before the advent of HAART an infected person was expected to live 10 years with HIV and another two years with AIDS before death. Today, a person on lifelong HAART is observed to live much longer in both developed and developing countries. A longer survival translates into a smaller number of DALYs. Table 1 summarizes studies on expected survival of patients with HIV who are on HAART. The studies were all conducted in real community settings rather than randomly controlled trial settings. Persons with predictors of lower survival were included, such as poor response to therapy, AIDS diagnosis, low CD4 count, high viral load, and poor adherence to treatment. All of these studies reported that HIV-infected person who is on HAART can live about two-thirds the life expectancy of those who are HIV-negative in the general population in his/her country (Antiretroviral Therapy Cohort Collaboration, 2008; Mills et al., 2011; Lohse et al., 2007; van Sighem et al., 2010). We therefore assume that other well-organized and well-operated community-level treatment programs should be likely to achieve this ratio.

While it is clear that HAART prolongs the life of people living with HIV/AIDS, studies have shown that there is considerable variation in life expectancy by background variables such as age and gender. For example, a collaborative analysis of 14 antiretroviral therapy cohorts in Europe and North America reported higher life expectancies among women than men (The antiretroviral therapy cohort collaboration, 2008). The authors explained the difference as the result of earlier diagnosis of women (in antenatal settings) and higher median baseline CD4 cell count. Similarly, a study of 22,315 HIV-positive patients in Uganda found that women had a longer life expectancy than men (Mills et al., 2011). Interestingly, adolescent patients (14-19 years) in the Uganda study had a shorter life expectancy than older patients (20-49 years) (Mills et al., 2011). Poor adherence to the treatment regimen by adolescents is thought to explain some of the difference. There may be some other explanations. Variation in response to ART by age has been observed (COHERE, 2008). For example, Nachega et al (2009) found that adolescents were less likely to achieve persisted virological suppression despite adjustment for potential confounders (including adherence, although adjustment for
adherence did weaken the measured association) and more likely to have viral rebound after successful suppression in both unadjusted and adjusted models.

To capture the variation in life expectancy in the PSI HAART model, we created four categories of HAART patients by age and gender:

- Men 15-19
- Men 20 and above (20+)
- Women 15-19, and
- Women 20 and above (20+).

Next, the health impact of HAART on survival was estimated separately for each of the four categories. This was done by computing the remaining years of life to be lived for each category. We used data from the Uganda cohort study which reported detailed life expectancies for the four categories. With this information, the life-expectancy ratio of PLWHA on HAART to the general population in Uganda was calculated for each category. Then, the life expectancies of PLWHA on HAART in Myanmar were calculated for each category by assuming the Uganda ratios apply to the Myanmar population.

HAART requires a lifelong commitment to treatment and not all patients are able to maintain the treatment regimen. Studies in developing countries report a lost-to-follow-up rate of 20% at six months after initiation of HAART treatment (Brinkhof et al., 2008; Nachega et al., 2010; Rosen et al., 2007) and 24% to 77% (with a plausible midpoint scenario of 50%) at 24 months after initiation (Rosen et al., 2007). Similarly, in rural Zambezia (Mozambique), the lost-to-follow-up rate among HIV-positive patients was about 50% in 2008 (Groh et al., 2011). In developed countries, adherence to medication for chronic diseases in general is estimated to be 50% (Sabate, 2003). Based on these rates, the PSI HAART model assumes that 50% of patients will be lost to follow-up at some point during lifelong treatment.

Regarding median length of adherence to HAART prior to patients being lost to follow-up, no information was available; however, in the PSI model we assume one year (12 months) adherence to HAART. This assumption is based on the results of a review by Rosen et al. (2007) which reported that 25% of HAART patients were lost to follow-up at 12 months after initiating treatment. If 50% of the patients are assumed lost to follow-up during lifelong treatment, we assume (for purposes of the model) that among all the patients lost to follow-up, half (50%) dropped out before 12 months and half (50%) dropped out after 12 months.

For HAART to be effective, patients must maintain an approved level of adherence to their treatment regimen. Adherence is defined as the extent to which patients take the prescribed medical regimens. It has a positive correlation with virologic and immunologic responses (Lima et al., 2008). Poor adherence can lead to the emergence of drug resistance and, eventually, loss of immune function, resulting in disease progression (Hogg et al., 2002). For non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART, recent studies indicate that a moderate adherence rate (70% to 90%) can achieve and maintain adequate viral load suppression (Nachega et al., 2010). For example, the treatment failure rate reported for first-line NNRTI-based HAART was 5.9% in patients with adherence of 80% to 89%, and 1.4% in patients with adherence ≥90% (Martin et al., 2008).

By counting pills at each follow-up visit, the Myanmar HAART program reported that all patients on HAART took at least 95% of the prescribed FDC of drugs from 2008 to July 2011. If treatment failure occurred,
patients were referred to appropriate sites for alternative first-line treatment or for second-line treatment. The PSI model assumes therefore that patients who maintain lifelong adherence to HAART are able to achieve adequate viral load suppression and live a lifespan of about two-thirds that of the HIV-negative general population in Myanmar.

The PSI model goes through a number of steps to estimate the impact of HAART on survival of HIV-infected people. The first step is to calculate the number of lifelong DALYs averted per person by category. Because the program reports only the number of tablets distributed (with no breakdown by category), a weighted coefficient (i.e., DALYs averted per tablet) is used in the model. The coefficient is calculated by dividing the weighted number of lifelong DALYs averted per person by the weighted number of tablets needed per person for lifelong treatment. “Weight” here refers to the proportions of the four categories (i.e., adolescent men, adult men, adolescent women and adult women). The proportion in each category is obtained from the program and needs to be updated each year.

\[
\text{Weighted DALY coefficient} = \sum_{i=1}^{4} \left( \text{lifelong DALYs averted per person in category } i \right) \times \text{proportion of HAART patients in category } i \\
/ \sum_{i=1}^{4} \left( \text{number of tablets needed for lifelong treatment per person in category } i \right) \times \text{proportion of HAART patients in category } i
\]

1.2 Part Two of HAART Model: Reducing Heterosexual Transmission of HIV

According to Bernoulli probability theory (Gray et al., 2001; Mastro et al., 1994; Satten et al., 1994), the probability of HIV transmission within a discordant partnership, \( \lambda \), is equal to \( 1 - (1 - \gamma)^n \), where \( \gamma \) refers to per-act infectivity of HIV during unprotected vaginal intercourse and \( n \) represents the number of sexual contacts with each partner. This assumes that the probability of HIV transmission during each sexual contact is independent. If partner choice is random, a person who is HIV positive has \( (1 - p) \) chance of having sexual intercourse with a partner who is HIV negative, where \( p \) represents the prevalence of HIV in the general adult population. Additionally, a person who is HIV positive is assumed to have, on average, \( m \) sexual partners in a year. Therefore, the average number of people infected through heterosexual contact with an HIV-positive person during the study period (one year) is modeled as \( P = (1 - p) \times \lambda \times m \). Substituting for \( \lambda \) in the above expression results in the equation,

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

which shows that the probability of transmission through heterosexual contact is associated with both 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. (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:

\[ P = \sum_{i=regular, casual, commercial} (1 - p_i) \cdot (1 - (1 - \gamma)^n) \cdot m_i \]

A number of factors may influence the per-act infectivity of HIV transmission including STD infection status within the partnership, baseline 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 person who is HIV positive may encounter while having sexual intercourse with his/her sexual partners who are HIV negative. Although infection stage of the HIV-positive partner also affects the per-act infectivity, we assume all our patients are not in acute stage while they are on HAART because of the fact that the treatment starts when their CD4 counts are less than 350 cells/mm³.

Part two of the HAART model is designed to estimate the reduction in risk of HIV transmission that occurs as a result of implementation of the PSI HAART program. The program is expected to reduce the per-act infectivity of HIV during heterosexual intercourse, while other factors (the epidemic and sexual behaviors) remain the same. Studies indicate that after initiation of treatment it takes anywhere from 6 to 24 weeks for the viral load to fall below 50 copies (Gross et al., 2001; Hull et al., 2009; Meech, 2011) and achieve a reduced per-act transmission rate. The model assumes an average of four months on HAART is needed to achieve an appropriate level of viral suppression and reduced per-act infectivity. The proportion of patients on HAART for less than 4 months is obtained from the program.

For each treated patient, the model runs a scenario in which the patient has \( x \) partners, \( y \) sexual contacts with each type of partner, and \( z \) sexual contacts protected by a condom. The likelihood of HIV transmission when the patient is on HAART is subtracted from the likelihood of HIV transmission when the patient is not on HAART to obtain an estimate of reduced risk of HIV transmission per person per year. Deaths averted per person per year are estimated by assuming all the new infections will die of AIDS-related diseases.

The estimated number of new infections averted and deaths averted per person per year is translated into an equivalent figure measured in DALYs averted per person per year. In this step, the model assumes that sexual partners of PLWHA contract HIV at age 26. On average, an infected partner who is not on HAART lives 10 years with HIV and another two years with AIDS before death. If the infected partner is covered by HAART, he/she is expected to live a much longer life, as explained in part one above (section 1.1) on the results for infected index cases on HAART. In the model, the likelihood of an infected partner being covered by HAART equals the coverage rate of HAART in the country. Because the program reports only number of tablets distributed without reporting detailed information about the breakdown by category, coefficients are calculated by dividing the weighted impact per person per year by the weighted number of tablets needed per person per year. The proportion of patients in each category serves as the weight.
Section 2: Parameters and Data Sources

This section presents information on the deterministic data points for the parameters used in the HAART DALY model and their sources.

2.1 Parameters for Part One: Living Longer with HIV

2.1.1 Life expectancies (LE)

<table>
<thead>
<tr>
<th>Group</th>
<th>Both</th>
<th>Male</th>
<th>Female</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE ratio Ugandan HAART patients to general pop., age 15-19</td>
<td>57.6%</td>
<td>53.1%</td>
<td>56.1%</td>
<td>Calculated based on data from Mills et al., 2011 &amp; WHO, 2011</td>
</tr>
<tr>
<td>LE ratio Ugandan HAART patients to general pop., age 20+</td>
<td>65.1%</td>
<td>50.9%</td>
<td>67.8%</td>
<td>Calculated based on data from Mills et al., 2011 &amp; WHO, 2011</td>
</tr>
<tr>
<td>LE general Myanmarese, age 15-19</td>
<td>54.4%</td>
<td>52.2%</td>
<td>56.6%</td>
<td>WHO, 2011</td>
</tr>
<tr>
<td>LE general Myanmarese, age 20+</td>
<td>49.7%</td>
<td>47.6%</td>
<td>51.9%</td>
<td>WHO, 2011</td>
</tr>
<tr>
<td>LE Myanmarese HAART patients, age 15-19</td>
<td>31.3%</td>
<td>27.7%</td>
<td>31.8%</td>
<td>Calculated</td>
</tr>
<tr>
<td>LE Myanmarese HAART patients, age 20+</td>
<td>32.4%</td>
<td>24.2%</td>
<td>35.2%</td>
<td>Calculated</td>
</tr>
</tbody>
</table>

2.1.2 Program-related data (source: Myanmar HAART program, 2008 to July 2011)

Age at infection of HAART patients (Myanmar):

- Male, age 15-19: n/a
- Female, age 15-19: n/a
- Male, age 20+: 37.72
- Female, age 20+: 36.76

Age at initiation of HAART (Myanmar):

- Male, age 15-19: n/a
- Female, age 15-19: n/a
- Male, age 20+: 37.72
- Female, age 20+: 36.76

Proportion of each category of patients, obtained based on PSI/Myanmar HAART program:

- Male, age 15-19: no patients are with this age group
- Female, age 15-19: no patients are with this age group
- Male, age 20+: 75% of HAART patients are males and aged 20 and above
- Female, age 20+: 25% of HAART patients are females and aged 20 and above.

Adherence rate (2008 to July 2011; Myanmar): 100% of patients taking at least 95% of prescribed FDC of drugs. This is obtained based on Myanmar program data.
2.1.3 Lifelong treatment retention

Lost-to-follow-up rate among patients on lifelong HAART: 50% (Rosen et al., 2007; Sabate, 2003).

Median duration on HAART before patient lost to follow-up: 1 year (assumed based on the results of a review by Rosen et al., 2007)

2.2 Parameters for Part Two: Reducing Heterosexual Transmission of HIV

2.2.1 Sexual activity data

Sexual behavior data shown in the table below include the number of sexual partners in the past year, by type, the number of sexual contacts with each partner, and condom use with each type of partner. The data are based on sexual behaviors among 2470 clients of female sex workers obtained from a representative sample of clients of female sex workers in Myanmar².

Among sexually active clients of female sex workers in Myanmar, the number of partners per year, the number of sexual contacts per partner per year, and the percentage who used a condom with partner, by type of partner (regular, casual, or commercial)

<table>
<thead>
<tr>
<th>Type of partner</th>
<th>Mean number of partners/year</th>
<th>Mean number of sexual contacts/partner/year</th>
<th>Used condom with partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>1.05</td>
<td>86.9</td>
<td>13%</td>
</tr>
<tr>
<td>Casual</td>
<td>1.00</td>
<td>5.5</td>
<td>70%</td>
</tr>
<tr>
<td>Commercial</td>
<td>9.12</td>
<td>4.9</td>
<td>92%</td>
</tr>
</tbody>
</table>

2.2.2 Epidemic data

HIV prevalence among regular partner(s): 0.6% (equals HIV prevalence among general adults; source: UNAIDS, 2010)

HIV prevalence among casual partner(s): 0.6% (equals HIV prevalence among general adults; source: UNAIDS, 2010)

HIV prevalence among commercial partner(s): 18.1% (UNAIDS, 2010)

STD prevalence among regular partner(s): 3.355% (equals STD prevalence among general adults, which is calculated; see below in this section for detail)

STD prevalence among casual partner(s): 3.355% (equals STD prevalence among general adults, which is calculated; see below in this section for detail)

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² We use CFSWs’ sexual behavior data as a proxy of the sexual behavior among adults living with HIV/AIDS in Myanmar due to lack of such data among adults living with HIV/AIDS. Such data is not available among general adults in Myanmar either. Justification for using CFSW’s data as a proxy is stated below. The major modes of HIV transmission are hetero-sexual (account for approximately 60% of all infections in Myanmar) and injecting drug use. Because patients with HBV and HCV are excluded from the Myanmar ART program, we therefore assume that majority of our patients was infected through heterosexual but not infected through injecting drug use. FSWs serve as a bridge population in the transmission of HIV in many Asian countries (connecting drug users and general adults). It is therefore reasonable to assume that many of our patients may have had sex with FSWs (i.e., getting infected through having commercial sex).
STD prevalence among commercial partner(s): 80% (a fixed number for all platforms)

Male circumcision rate in Myanmar: 20% (WHO/UNAIDS, 2007).

HAART coverage rate: 18% (16%-22%) (WHO, 2011)

HIV prevalence among commercial partners and the prevalence of STDs in both the adult population and the commercial sex partners were obtained based on adjusted functions of adult HIV prevalence when such data are not readily available from published data sources.

Functional relationships between these populations and HIV prevalence in the adult population, for use in the DALY model, were developed based on existing data. The data used for developing the function for HIV prevalence among commercial sex partners came from the WHO/UNAIDS Epidemiological Fact Sheets on HIV/AIDS and STIs (2008). Ratios of general adult to sex worker HIV prevalence rates were calculated for all countries that had data available. Then the ratios were used to simulate different functions according to WHO regions. The function with the best fit was chosen for each region. The function for the sub-Saharan region fit well the data reported in the article by Buve et al. (2001).

The function for HIV prevalence among commercial sex partners is shown below by region, where $R_g$ is HIV prevalence in the adult population and $R_c$ is HIV prevalence among female sex workers (FSWs):

- Sub-Saharan countries, $R_c = R_g \times (0.625 + \frac{35.987}{R_g \times 100})$;
- Asian countries, $R_c = R_g \times 17$;
- Latin America/Caribbean countries, $R_c = R_g \times (2.198 + 2.715 \times R_g \times 100)$

The data used to develop the function for STD prevalence in the general adult population include HIV prevalence in the general population by region (UNAIDS/WHO, 2006) and the STD prevalence rate for the general population by region (WHO, 2001). Ratios of STD to HIV were calculated for all regions. The ratios were then used to simulate different functions. The function with the best fit was chosen and is shown below, where $R_g$ is HIV prevalence in the adult population and $S_g$ is STD prevalence in the adult population:

$$S_g = R_g \times 4.6 \times (100 \times R_g)^{-0.382}$$

STD prevalence among commercial sex partners is set at 80% for PSI platforms lacking available data.

### 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 & 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 was assumed to be 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 (World Bank/WHO, 2006)

Duration of AIDS: 2 years; YLD weight: 0.505 (World Bank/WHO, 2006)

Age at infection of HIV negative partners: 26 years old (assumed)

Life expectancy at birth (years): the life expectancy at birth for Japanese: 83.1 (all), 79.6 (male) and 86.5 (female) (WHO, 2011). PSI uses Japanese life expectancy as the standard ideal years of life a person can live when s/he is free from diseases. We use it for our impact estimate for two reasons. One is related to ethics. PSI usually compares the DALYs averted across products/services and across countries. It is unfair to use country-specific life expectancy when the same number of new infections/deaths has been averted. The other reason is that the smaller life expectancies observed in many developing countries may actually be a result of a plethora of disease burden, genetics, diet, socio-economic status, and so on. When all the factors in developing countries are the same as those in Japan (except for genetics, but it is reasonable to assume that genetics alone doesn’t make a big difference in human being’s life expectancy), people in the developing world are most likely to live as long as the Japanese do.

2.2.5 Efficacy of product/services

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

Protective efficacy of male circumcision: 60% (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007)

Protective efficacy of HAART on per-act infectivity: 92% (Attia et al., 2009; Cohen et al., 2011; Donnell et al., 2010; Schwartländer et al, 2011).

Average months needed on HAART to suppress viral load to an undetectable level: 4 months (Gross et al., 2001; Hull et al., 2009; Meech, 2011)

2.2.6 Project-related data (source: Myanmar HAART program, year 2008 to July 2011):

Proportion of patients on HAART for ≥ 4 months after initiation: 88%.
References


