Returns on investments of HIV prevention in Vietnam

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Executive summary

This study aimed to estimate the cost-effectiveness and returns on investments of HIV prevention programs implemented during 2006-2010 and to identify the optimal allocation of resources across combinations of programs for an effective HIV prevention response to inform the prioritization of funding and health resources in Vietnam. This study aims to establish evidence of the cost-effectiveness and identify optimal allocations of limited resources for greatest epidemiological impacts. Costs of programs were ascertained through a comprehensive review of published national reports on HIV costing and collection of primary costing data from the original sources. Relationships between program spending over time and program-targeted risk factors or other relevant end points were assessed and incorporated into a mathematical epidemiological HIV model calibrated to reflect the epidemic trends in Vietnam. The spending-outcome relationships and an epidemiological model were used to compare observed conditions with counterfactual scenarios of reduced or no programs to calculate the cost-effectiveness and estimate healthcare costs saved and thus the return on investment. Model simulations of epidemic projections over many combinations of possible resource allocations were used to identify optimal allocations for reducing new infections over the next HIV budget period.

Key results

- The HIV/AIDS response in Vietnam has rapidly scaled up from US ~$50 million to US $139 million during 2006-2010. Among a total of US $480 million spent in this period, domestic spending only accounts for a low proportion of funds (14.2%). Of the total HIV budget, around one-third (32.4%) was allocated to HIV prevention programs, whereas HIV care and treatment and indirect costs (including supporting enabling factors) accounted for 27.5% and 40.1% of the budget, respectively.

- The investment in the HIV/AIDS response in Vietnam over the period 2006-2010:
  - Averted an estimated **54,133** (95% uncertainty bound [95% UB]: 36,398–72,014) new HIV infections, corresponding to a **29.8%** (20.0%–39.6%) reduction in population incidence. That is, it is estimated to have cost around **US $8,867** ($6,666–13,188) for infection averted overall or **US $1,841** ($1,384–2,739) in direct funding on HIV prevention and antiretroviral therapy (ART) per infection averted. The vast majority of the benefits in Vietnam have occurred among female sex workers (FSWs) and their clients and among injecting drug users (IDUs) with respect to the number of HIV infection averted and an observable decline in HIV incidence.
  - Led to the scale-up of life-sustaining ART, with a total of **46,824** adult PLHIV on ART by 2010. The model estimates that **149,020** (95% UB: 132,280-197,040) PLHIV were eligible to receive ART in 2010 (according to threshold CD4<350 cells/mm^3), indicating an ART coverage level of **31.4%** (23.8%-35.4%).
  - These programs averted an estimated total of **37,170** (31,537–47,333) HIV/AIDS-related deaths.

- Approximately one-quarter (26.6%) of spending for prevention was allocated to the most at-risk populations (MARPs): IDUs; FSWs and their clients; and men who have sex with men (MSM). IDUs received the greatest investment of total HIV/AIDS spending (15.9%) but relatively little was spent on programs for MSM (2.5%), with 8.2% spent on programs for FSWs.

- The cost-effectiveness of the HIV prevention programs were assessed by calculating the direct costs of HIV prevention programs per disability-adjusted life year averted estimated by the model evaluation, over the period 2006-2010.
    - HIV prevention programs for FSWs/clients were deemed to have had moderate population-level impacts, reducing HIV prevalence among Vietnamese FSWs by 0.45%-1.15% and 0.25% among their clients. A total of 9,850 (7,056–16,132) HIV infections were estimated to have been averted (or ~5% of all new infections in Vietnam) by these programs alone. At a cost of US $12,761,189, these programs have already been cost-saving compared to the expected additional healthcare expenditure had these prevention programs not been in place. It is projected that they will have a future total return on investment of $4.61 for every $1 invested, in addition to the investment costs.
        - These programs appear to have been effective due to the reported decreases in risk behavior and increases in condom usage among FSWs. There is epidemiological evidence to support the decline in HIV prevalence, and thus HIV incidence has declined, among clients of sex workers and stable or decreasing trends among different groups of sex workers.
    - HIV prevention programs for IDUs also had low population-level impacts; however, the program costs were substantially greater than the costs for FSW programs. The majority of the IDU-targeted money was spent on needle-syringe programs (NSPs) which were determined to be considerably more cost-effective than methadone maintenance therapy (MMT). This is largely due to the substantially higher unit costs of MMT, related to start-up costs but also ongoing unit costs, and retention-related individual-level efficacy.
        - MMT was not considered to be cost-effective with respect to outcomes already observed, as the program was estimated to cost US $1,362,637 per DALY averted (associated with HIV infection alone). It is expected that this cost-effectiveness ratio will decrease substantially in the future.
        - NSPs were estimated to cost US $1,699 in direct program costs per DALY averted already. NSPs are estimated to have a total future return on investment of $0.36 for every $1 spent in addition to the investment.
        - Prevalence among IDUs has decreased substantially in recent years, strongly supporting the large preventative impact of NSPs in reducing HIV incidence.
    - Investment in HIV prevention among MSM has been very modest, at only 2.5% of the prevention budget. This is despite MSM making up the largest MARP group with an estimated population of 285,000 individuals, as compared with an estimated 217,000 IDUs and 65,000 FSWs in Vietnam and experiencing the greatest increase in HIV prevalence.
        - There is inconclusive evidence about the population-impact of programs targeting MSM. HIV prevalence has increased over time. Based on serial cross-sectional surveys that may not be completely comparable, there is some evidence that condom use may not have increased over the time of condom promotion. However, uptake of HIV testing has improved and the prevalence of other STIs has decreased. It is possible that programs targeting

MSM have mitigated what could have been a greater rise in HIV incidence. But the available data are not sufficient to adequately assess their impact.

- Provision of ART for eligible PLHIV has required substantial investment, of US $36 million in antiretroviral drug costs and US $96 million in total costs for other care and treatment (such as opportunistic infection treatment and home-based HIV case), but in addition to sustaining life for over 50,000 people and averting over 37,000 deaths. It has also likely substantially reduced new HIV infections. An estimated 11,187 (8,366–16,260) HIV infections were averted due to ART programs in Vietnam, which have mainly targeted among MARPs.
    - The program cost per DALY averted is just US $23-171 for ART, depending on the time horizon considered, which is highly cost-effective according to any willingness to pay threshold. However, due to the very large costs of implementing ART, it is unlikely that the costs would be recovered in healthcare costs saved.

- It is important to maximize allocative efficiency by distributing resources across programs in ways that minimize the expected number of new HIV infections.
    - There is a misalignment between current allocations of prevention funding and the distribution of new HIV infections. For example, only 2.5% of funding is provided for the ~44% of HIV infections currently occurring among MSM; and the amount of funding provided to FSWs and their clients is only one-half of the funding allocated to NSPs for IDUs despite greater numbers of new HIV infections among FSWs/clients than among IDUs.
    - An analysis of allocative efficiency suggests that if the same amount of resources were to be optimally allocated over the period 2013-2020, the expected number of new HIV infections could be reduced by ~16% compared to current allocations.
        - Optimal resource allocations would shift funding away from the general population at lower risk and towards the MARPs, specifically, substantial scale-up of VCT and condom distribution among FSWs and MSM. It is unlikely that funding provided to the general lower risk population will be as effective at reducing new infections as targeted prevention to groups at higher risk.
    - Optimal resource allocations were calculated for different amounts of funding availabilities. The analyses suggest that if funding is very scarce then the most important prevention programs over the period 2013-2020 are condom promotion targeted to MSM and STI programs. As more funding becomes available, each of these programs should be scaled-up with priority to FSW-targeted condom promotion. Then, at ~40% of the current budget, NSPs for IDUs should be commenced and considerably scaled-up with increased funding availability. NSPs were rightly prioritized in the past which had substantial impact among IDUs and shifted the course of the national epidemic to change future prioritization. VCT should also be available to support programs. At twice the current funding availability it becomes optimal to scale-up MMT programs with respect to HIV outcomes and also prevention among the general population.

- With the need to do more with less funding, there is large need for
    - Applying optimal allocative efficiency;
    - Greater technical efficiency and reduction of overhead costs.

- It is important to implement programs that have proven efficacy and feasibility, that are most cost-effective.

- Although non-MARP targeted programs should be reduced with limited resources, sexual partners of MARPs and other discordant couples should be covered as a priority.
    - With regards to the objective of minimizing new HIV infections, minimizing deaths and health burden (i.e. DALYs), using antiretroviral treatment for prevention (i.e., initiating therapy for people with CD4 counts greater than 350 cells/mm^3) should not be a large priority with currently available resources because greater benefits could be gained through harm reduction programs such as condom programs among MSM and FSW and their clients and NSPs among IDUs.
    - However, scaling up ART to considerably greater levels for the large number of people who are treatment-eligible is essential for addressing the objective of reducing overall morbidity and mortality among people living with HIV and improving population health.
        - Treatment will have large secondary benefits for prevention, as suggested by the simulations in this study. Currently, an estimated one-third of those who are eligible for ART (CD4 cell count <350 cells/mm^3) are on treatment.

- Since the HIV epidemic in Vietnam remains concentrated among MARPs, the most strategic allocation of resources minimizes the number of new infections among MARPs and their partners and has the best potential to prevent the epidemic from also spreading further into the lower-risk populations. In particular, prevention programs among MSM should attract the largest proportion of funding, as a timely response to the rapidly emerging epidemic among MSM. Social stigma against homosexuality is common in Vietnam and therefore structural interventions need to be implemented as critical enablers to support primary prevention among MSM.

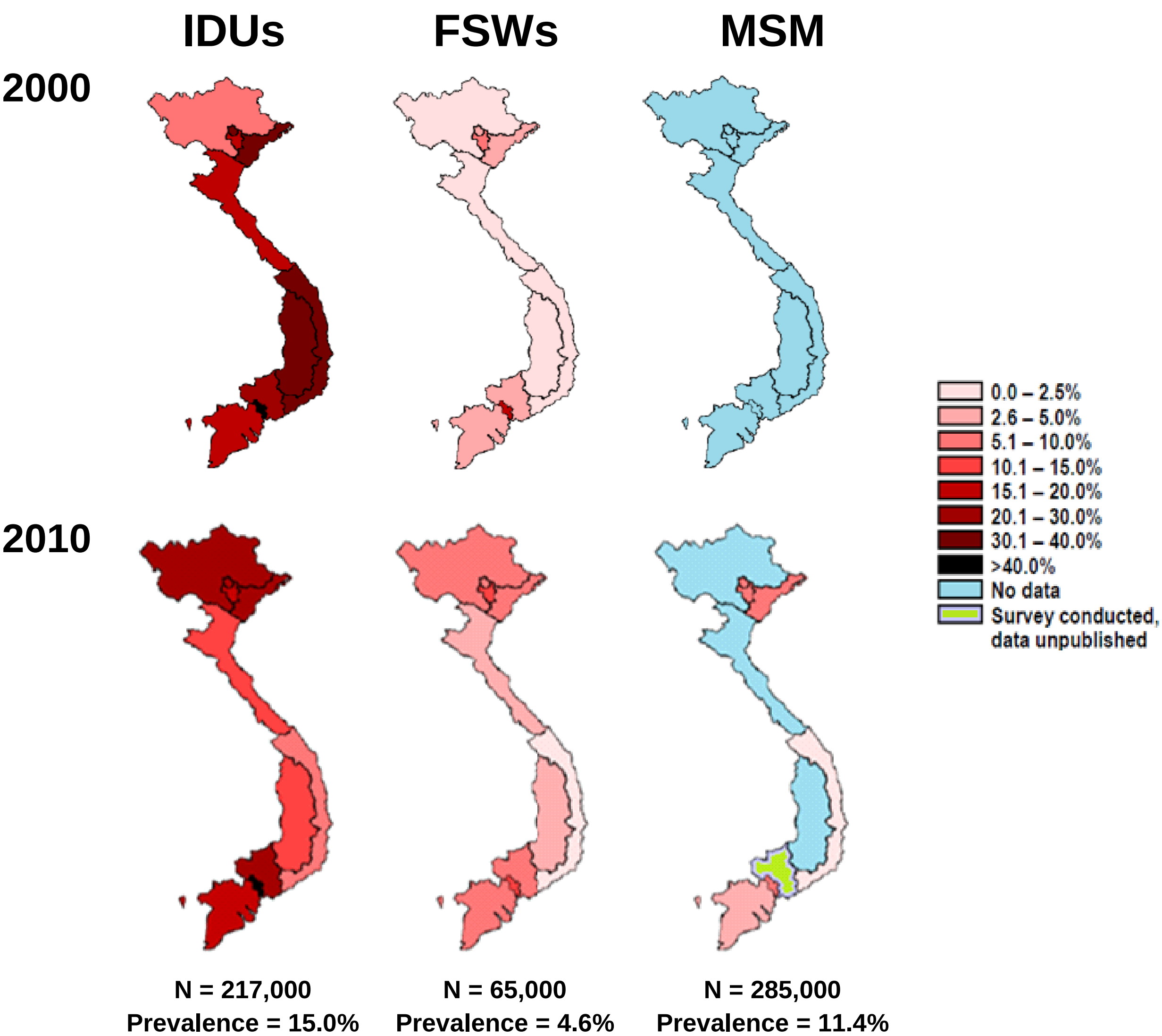
- Vietnam's current HIV response is highly dependent on foreign aid. With the gradual withdraw of foreign investment, domestic support from the Vietnamese government is increasingly important. This also implies that sustaining the current level of response or increasing the response may be unlikely in the near future. The Vietnamese government needs to make best use of the available resources to maximize the potential benefits.

- Financial data are presented at the national level only. However, with budget decreases, the government will need to re-focus the programs by spatial location and prioritize selected provinces where greatest impact is likely based on current epidemiology as well as infrastructure and ability for community mobilization.

Background

The HIV epidemic in Vietnam remains concentrated among populations at higher risk since the first case was reported in late 1990. The overall HIV prevalence was estimated to be 0.44% among all people aged between 15-49 years in 2010 [1]. However, the HIV epidemic in Vietnam is concentrated among specific priority populations. Meta-analyses of published literatures and government reports indicate high HIV prevalence levels among injecting drug users (IDUs, 15.0% in 2010), female sex workers (FSWs, 4.6% in 2010). Importantly, the latest data indicate a substantial increase in HIV prevalence among men who have sex with men (MSM, to 11.4% in 2010). The estimated population of people living with HIV (PLHIV) doubled during the past decade, reaching approximately 254,000 in 2010 [1, 2]. A total of 57,663 PLHIV are currently on antiretroviral treatment (ART). The geographical and typological shift in HIV spread is shown in Figure 1.

Figure 1: Prevalence of HIV in Vietnam by population groups and year



Note: The trend in HIV prevalence presented in the figure was obtained via meta-analysis of available published sources of HIV prevalence in Vietnam.

Harm reduction and other HIV prevention programs have been implemented largely in high HIV prevalence provinces nationwide targeting these most-at-risk populations (MARPs). These interventions have mostly been rolled out since 2004 and include harm reduction programs aiming to reduce sharing of injecting equipment and reduce the extent of unprotected sexual acts among discordant and unknown concordant status, scale-up of antiretroviral treatment, voluntary counseling and testing (VCT), methadone maintenance therapy (MMT) and various health education programs. Domestic and international spending on HIV prevention to mitigate the epidemics have grown considerably in recent years, from around US $5 million in 2000 to over US $103 million in 2009. However, with international donors reducing their financial commitment in Vietnam, Vietnam is required to finance a larger share of the national AIDS response from domestic resources. This requires the Vietnamese government to develop a comprehensive intervention framework to guide the allocation of available limited resources effectively in order to maximize population health benefits.

The majority of financial resources to support the HIV/AIDS response in Vietnam have been donated by the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM), the United States President's Emergency Plan for AIDS Relief (PEPFAR), the World Bank, and the United Kingdom Aid from the Department for International Development (DFID). International funding accounts for approximately 73% of the total investment on HIV/AIDS program in Vietnam. However, funding from DFID and the World Bank (WB) ended in 2012, PEPFAR funding is planned to end in 2015, and the Global Fund in 2016. The Vietnamese government will need to fill the funding gaps, as much as possible, to sustain effective HIV programs.

HIV/AIDS effectiveness evaluation and cost-effectiveness analyses are important tools for understanding what HIV investments have bought, whether the interventions averted new infections and AIDS deaths, and at what cost. They can support decision-making and policy development by informing the HIV/AIDS response with its overall goals of minimizing the burden of disease and maximizing health outcomes.

The goal of this study is to estimate the cost-effectiveness and return on investment of HIV programs implemented over the period 2006-2010 and to contribute to the improvement of the effectiveness and efficiency of HIV prevention responses in Vietnam, specifically to inform the prioritization of resources for the 2013-2020 national HIV budget in the context of reductions in international donor funding. This study aims to establish evidence of cost-effectiveness and optimal allocations of limited resources for greatest epidemiological impact. It does this through:

1. Review of current resource investments from current major HIV prevention programs/projects in Vietnam;
2. Collating available epidemiological data, behavioral data for the MARPs, clinical and program data from available unpublished and published sources;
3. Assessing relationships in data between funding for programs, risk behaviors and the resulting HIV epidemics in Vietnam;
4. Estimating the cost-effectiveness of past HIV prevention and treatment programs in Vietnam, with the use of data-driven modeling to estimate the number of HIV

infections, DALYs and deaths averted due to HIV programs in comparison to the costs of the programs;

5. Projecting the estimated return-on-investment, including savings to government, of investment in HIV prevention. This analysis will inform Vietnam of the savings to government and the wider society, for every dollar invested in HIV prevention.
6. Projecting the expected impact of reductions in the 2013-2020 HIV budget on the HIV epidemic;
7. Identifying the optimal combination of intervention services for a given amount of resources. This study also estimates the optimal balance of funding between prevention programs and treatment, considering the use of ART among treatment-eligible people for the purposes of both HIV prevention and improvement of survival and health of PLHIV.

Methods

Construction of a mathematical epidemic model

A mathematical epidemic model (*Prevtool*) was developed to investigate the impact of HIV prevention programs at a national level in Vietnam. This model is specifically designed to simulate the dynamic HIV epidemic in Vietnam using best-practice HIV epidemic modeling techniques and incorporating realistic biological transmission processes, detailed infection progression, and sexual mixing patterns and drug injection behaviors. Informed by available HIV surveillance data, the model includes seven distinct population groups: males and females at lower-risk, direct and indirect FSWs, male clients of FSWs, MSM, and male IDUs. This model employs a similar approach to the Asian Epidemic Model (AEM). However, the current model is constructed in a way that is flexible to adapt Vietnamese-specific characteristics and data and is amenable to analyses directly relevant to the current research questions including full health economic analyses, production of uncertainty bounds, and resource optimization. Further details of *Prevtool* are available in Appendix 2. According to the latest estimates of the Vietnam Authority of HIV/AIDS Control (VAAC), approximately 217,000 IDUs, 285,000 MSM and 65,000 FSWs are currently in Vietnam – which is most likely a highly conservative estimate. Around 10% of IDUs are female [3], yet epidemiological and behavioral data among female IDUs are almost absent. Thus, HIV transmission among female IDUs was not modeled directly in this mathematical exercise. However, we did include FSWs who injects since 53-78% of female IDUs engaged in commercial sex work [3]. Furthermore, 25% of MSM, 7.3% of street-based FSWs (assumed as direct FSWs [DFSWs]) and 2.4% of entertainment-based FSWs (assumed as indirect FSWs [IFSWs]) report injecting drug use [4]. Of note, 22-40% of MSM reported having had sex with females and 28-54% of FSWs reported having had sex with regular male partners in the past 12 months [4, 5]. Given such overlapping behavioural patterns, HIV may transmit from one at-risk population to another.

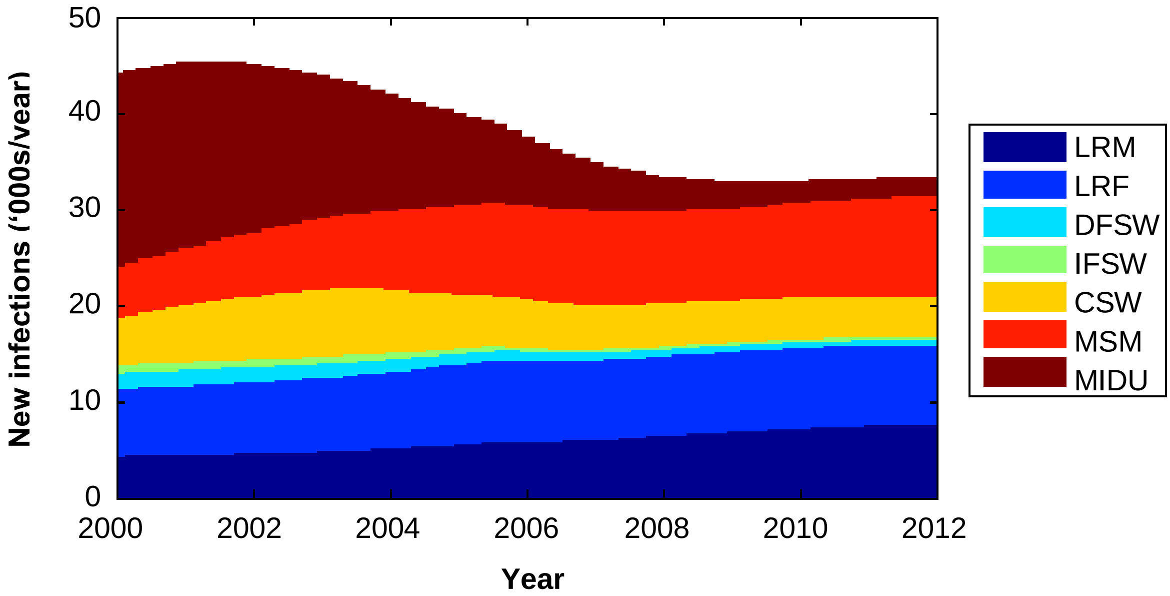
Table 1: Model population groups and health states

Population groups	Health states
1. Low-risk males (LRM)	1. Susceptible (uninfected)
2. Low-risk females (LRF)	2. Infected, undiagnosed, CD4>500
3. Male clients of female sex workers	3. Infected, undiagnosed, 500>CD4>350
4. Direct female sex workers	4. Infected, undiagnosed, 350>CD4>200
5. Indirect female sex workers	5. Infected, undiagnosed, CD4<200
6. Men who have sex with men	6. Infected, diagnosed, CD4>500
7. Male injecting drug users	7. Infected, diagnosed, 500>CD4>350
	8. Infected, diagnosed, 350>CD4>200
	9. Infected, diagnosed, CD4<200
	10. Infected, on 1st-line treatment
	11. Infected, treatment failure
	12. Infected, on 2nd-line treatment

Model calibration

Most model inputs associated with sexual and injecting risk behaviors were taken from national surveillance reports and the Integrated Biological and Behavioral Survey (IBBS) data (year 2006 and 2009) from previous studies in Vietnam, endorsed by the Viet Nam Authority of HIV/AIDS Control of Ministry of Health. The model-estimated annual HIV incidence across Vietnam, by population group and year from 2000-2012, is presented in Figure 2. It is estimated that national HIV incidence remained stable throughout the whole period but there have been shifts in the distribution of modes of transmission. Since 2005, homosexual transmission of HIV has increased among MSM. However, there have been decreases in population incidence among sexual partners of MARPs and the general population at lower risk. This reveals that there has potentially been a shift in dominant mode of transmission from injection-related to sexual (in particular, homosexual). Notably, the prevalence of HIV among MSM increased from 4.6% in 2000 to 10.1% in 2012 and over this period the estimated total number of MSM living with HIV increased from ~15,000 to ~32,000. The estimated annual incidence of HIV infections among IDUs remained at a constant level during 2000-2012 (Figure 2).

Figure 2: Number of new infections by populations in Vietnam, 2000-2012



(See Appendix 3 for further description and results on the calibration of the model)

Data collation

Estimation of population sizes of at-risk populations

a. Population size data were based on the latest estimates from the HIV/AIDS epidemic database in Vietnam (2010–2015), which is a collaborative activity between the Vietnam Authority of HIV/AIDS Control, UNAIDS, Family Health International (FHI), WHO, Hanoi School of Public Health (HSPH) and other partners.

b. The number of HIV diagnoses over time was obtained from the latest HIV/AIDS epidemic database in Vietnam (2010–2015). The report source is the Monitoring & Evaluation Department of VAAC.

c. The number of patients on first-line and second-line ART was obtained from the Care and Treatment Department of VAAC. These include the total number of adults and children receiving ART and pregnant women that have received prevention mother-to-children child transmission of HIV (PMTCT).

d. The total healthcare cost for PLHIV by category of CD4 cell counts (<200, 200-350, 350-500, and >500 cells/mm^3) was calculated based on unit cost of services provided by in-country collaborators (personal communication). Unit costs for ART were obtained from VAAC (unpublished data) and published literature [6]. We used median costs of HIV counseling and testing per client from a recent cost-analysis study conducted by FHI 360 in Vietnam (unpublished data).

Collation of costing and program data from 2006 – 2010

Available data on HIV spending in Vietnam in 2006-2010 were used. We obtained relevant data from an available report of the National AIDS Spending Assessment (NASA) for the period of 2008-2010, whereas spending prior to this period was collected by the HSPH team. Following a formal letter from the VAAC to HIV/AIDS projects, the HSPH team contacted the coordinator at each central project management unit of core projects supported by five key international donors (including PEPFAR, World Bank, DFID, Global Fund, and Asian Development Bank) to collect all available annual financial reports and activity reports for any projects implemented in 2006-2010. For programs initiated by the Vietnamese government, we obtained data directly from VAAC.

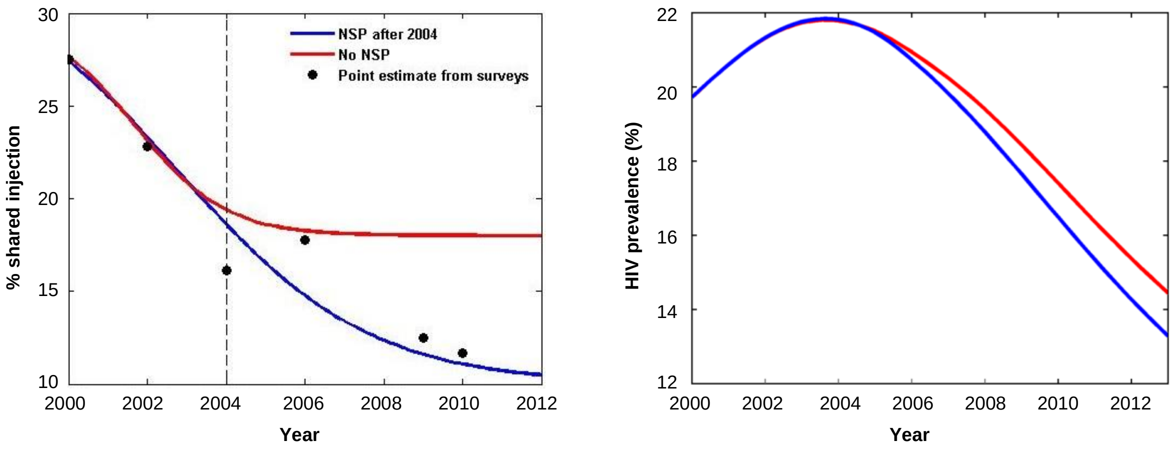
As for program data, especially the number of commodities distributed (such as needle-syringes and condoms), data were collected from the M&E department of each project. However, different projects have different formats and may not have identical indicators. In this case, data may be partially incomplete.

Economic analysis methods

The effectiveness of past HIV programs was estimated by comparing the expected number of new infections and HIV/AIDS related deaths according to actual conditions with the estimated numbers under counterfactual scenarios in the absence of funding for specific programs. Data were used to formulate evidence-based assumptions on the relationship between funding and risk factors, particularly for hypothetical intermediate funding levels.

An example of counterfactual scenarios of needle-syringe exchange programs (NSPs) and the resulting projected change in the HIV epidemic is shown in Figure 3. We assumed that no funding for this harm reduction approach leads to baseline risk factors remaining constant over time. Further details of all counterfactual assumptions and the cost-effectiveness calculations are provided in Appendix 5. Epidemic trajectories were projected according to the counterfactual scenarios (red curve); comparing these trajectories with the calibrated epidemic trajectory according to actual conditions (blue curve) resulted in an estimation of the effectiveness of the programs in the context of fixed effects of other interventions (such as condom promotions for FSWs/CSWs and MSM, STI program, ART, etc) on the HIV epidemic.

Figure 3: Example of assumed counterfactuals (red) compared with actual conditions (blue) for evaluating the effectiveness of HIV prevention programs for IDU in Vietnam. The solid red curve represents no funding with baseline risk factors remaining constant over time.



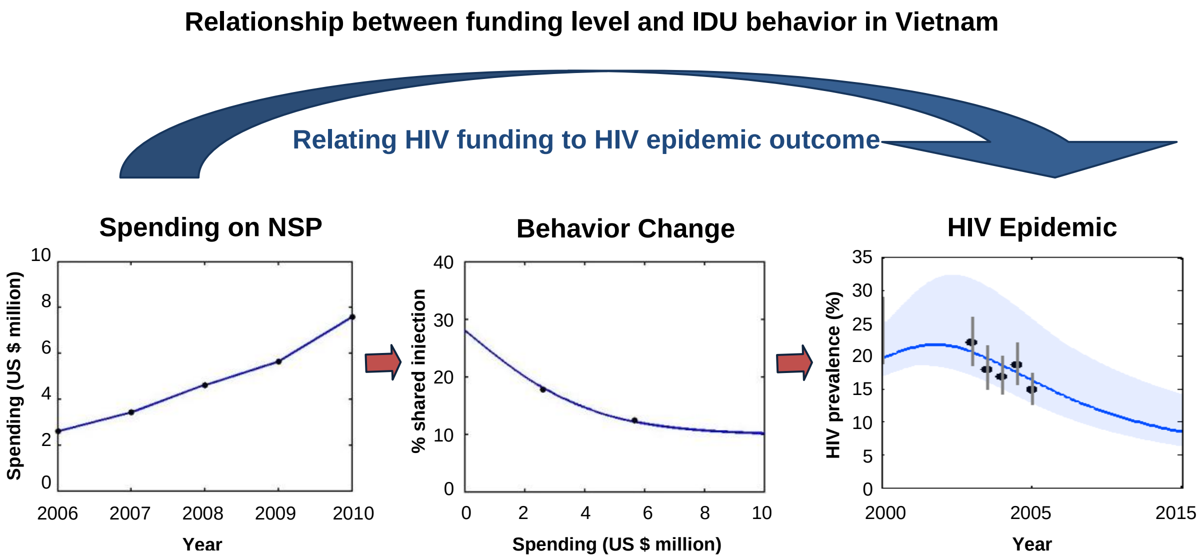
The cost-effectiveness of each program was then assessed by comparing the spending of each program, as well as estimated annual healthcare costs incurred/saved, with the estimated effectiveness of the programs. An estimate of the incremental cost-effectiveness ratio (ICER) of each program was calculated based on the counterfactual scenarios. Two time horizons were used: 2000-2010 and 2000-lifetime. Epidemic data, programme and costing data were obtained over the first time period, namely the past. Evaluation of the impacts of HIV prevention programmes was conducted and the healthcare costs already saved was estimated. However, the infections averted over this period will lead to savings in future healthcare costs that will not need to be spent. Forecasting future health outcomes and expected healthcare expenditure with and without the programmes in the future, to 2100 were explored to compare the total future cost savings attributable to programme implementation during 2000-2010. Further details are in Appendix 5. This economic analysis was conducted using detailed data on costs. Discounting and consumer price indices (CPI) were used to assess the value of money at different time periods. Healthcare CPIs were based on year-to-year data from Global Rates CPI, which sources its data from Bureau of Statistics Vietnam. Disability-adjusted life-years (DALYs) were calculated with the model for all scenarios and were also discounted.

The timeline from 2000-2011 was investigated to estimate the number of HIV infections averted due to implementation of the prevention programs in the past. Assuming a continuation of the status quo in terms of programme funding and sexual and injecting behaviors, the model was then used to project long-term health outcomes and healthcare costs incurred in the future (with discounting) in order to estimate the future benefits of the past programs. The cost-effectiveness of the HIV prevention programs were assessed by calculating the cost per DALY averted, over the period 2000-2011. A return on investment analysis considered the future healthcare costs saved that are attributable to the past financial investment in HIV/AIDS programs.

Optimal allocation of funding for reduced HIV prevention budget

In order to calculate an optimal allocation of funding across HIV programs, it was necessary to make assumptions about the relationship between a given program funding amount and targeted risk behaviors of the program. Details of program spending and targeted risk behaviors are depicted in Appendix 4. The model projects the future epidemics based on different scenarios of allocations of funding investments.The approach taken in this study is illustrated in Figure 4 through an example – of IDUs in Vietnam.

Figure 4: Example of the relationship between spending on IDU programs and the HIV epidemic



In summary, the analysis was done by the following procedure:

1. Identify HIV risk factors targeted by each prevention program (e.g. needle-syringe programs aim to alter rates of needle sharing among IDUs; rate of unprotected sex among FSWs and MSM).
2. Assess trends over time in spending on each program and the identified risk factors – link these variables together in a data association between risk factor and level of program spending.
3. Fit sigmoid/logistic curves to the data associations between risk factor and program spending. These sigmoid relationships describe predicted values for indicators under different potential spending levels.
4. Calibrate the mathematical epidemiological model to HIV prevalence data in Vietnam, while also reflecting the change in risk behaviors and other factors. Uncertainty was estimated using a Markov chain Monte Carlo algorithm, in which a large number of randomized simulations (“priors”) are re-sampled in accordance with their goodness-of-fit to both behavioral and epidemiological data (“posteriors”).

5. For a given total budget available, sample a very large number of possible combinations of funding breakdowns across programs and use the sigmoid relationships to assume a given program response on the targeted risk factors. Then simulate the epidemic trajectories according to these conditions and estimate the expected number of new HIV infections.

<u>Identifying optimal funding allocations</u>

The mathematical model calibrated to the Vietnam HIV epidemic, *Prevtool*, was used to project the number of HIV infections and HIV/AIDS related deaths over 2010-2019 according to different funding allocations to HIV/AIDS prevention, treatment and supporting programs. The software adapts a novel stochastic linear gradient-descent optimization method to find the optimal allocation of funding, using total infections as the quantity to be minimized. Funding levels are kept similar from 2010 to 2012 according to allocation data from 2010. The expected change in funding (decrease), of which government is expected to invest for HIV programs ~ 20 million per year, is assumed to occur in 2013, hence different allocation of funding from 2013 to 2020 is analyzed. For a given total budget available, 4,000 distributions of funding breakdowns across all programs were determined through computational sampling across the range of all possible distributions. Two sets of simulations were run: (1) maintain current rates of ART; (2) increased ART programs, to allow the effects of treatment as prevention to be factored into shifts to ART if deemed optimal for spending on prevention.

The expected behavioral and clinical outcomes associated with each funding scenario were identified (through the pre-determined, data-driven sigmoid/logistic relationships) for each funding allocation and *Prevtool* was used to simulate the expected epidemic trajectory according to these conditions. The funding allocation to each program that resulted in the minimum cumulative number of new HIV infections was identified as the optimal allocation of available funding for HIV prevention programs. The optimal allocation methodology is presented in more detail in Appendix 6. Using this methodology, the optimal allocation of increased domestic funding and reductions in inefficiencies was also identified. The optimal allocation of resources for preventing new infections was investigated with core prevention methods (harm reduction), along with introducing programs based on using antiretroviral treatment as prevention in combination with other programs.

Key assumptions and data gaps

Below is a list of key assumptions made in carrying out the analyses. These assumptions need to be taken into consideration when interpreting the study findings.

Costing and spending breakdown

- Collected data on costs/spending of the HIV/AIDS programs in Vietnam between 2006 and 2007 that were only available in Vietnam Dong were converted into US dollars based on the annual average currency exchange rate provided by the Joint Stock Commercial Bank for Foreign Trade of Vietnam. Data for 2008-2010 are available in U.S. dollars in NASA report. Present value of data were calculated using consumer price indices.
- According to the 2008-2010 NASA report, HIV spending was contributed by the Vietnamese government (14.3%), the private sector (15.1%) and the international sources (70.6%). Among international sources, 88.9% of the total spending was contributed by the five major donors: including PEPFAR, the World Bank, DFID, GFATM, and Asian Development Bank. In this evaluation, we were only able to obtain the total spending of the five key international donors and Vietnamese government in 2006-2007. Thus, we used the aforementioned percentages to estimate the investment from small international donors and the private sector. This provides estimates of the total spending in 2006 ($50,686,443) and 2007 (US $66,499,122), which are comparable to official reported figures (at least US $50,000,000 in 2006 [7] and US $66,280,815 in 2007 [8])
- Itemized breakdowns of total budgets to program areas and supporting costs were only available for years 2008-2010 in the latest NASA report. The spending breakdown in this period was used to calculate proportional allocations to be applied to prior years.
- Costs of harm reduction programs for IDUs were assumed to contain costs for NSPs and MMT only. We split NSP spending by subtracting the total spending of harm reduction programs for IDUs by the spending of MMT, the data of which were collected though the MMT programs funded by PEPAR, the World Bank and DFID, GFATM, and Vietnamese government during 2008-2010

Relationship between spending and risk behavior – sigmoid/logistic curve fits to data

- A four-parameter sigmoid/logistic relationship between spending on a program and changes in behavior was assumed, fitted by empirical data of relevant indicators.
- Based on available data and international evidence, it was assumed that a maximum (or minimum depending on parameter) saturation value for each behavioral parameter existed with increasing spending.
- When there is no funding for a prevention program, the parameter values were assumed to be identical to the year 2000 value.
- It was assumed that NSP affects the percentage of shared injections and the average number of injections per year in IDUs.
- It was assumed that MMT affects the number of IDUs taking methadone.
- 100% condom use programs were assumed to affect percentage of condom use with non-commercial and commercial partner of FSWs and of MSM.
- STI programs were assumed to affect the prevalence of STI among FSWs and MSM.

- It was assumed that VCT programs affect the rate of HIV testing among IDUs, FSWs, and MSM and general population.

Model

- Once categorized, it was assumed that over the studied period, individuals do not move between population groups.
- Diagnosed individuals are assumed to have the same characteristics as those undiagnosed except they can begin ART.
- Individuals who fail first-line ART are expected to be switched to second-line therapy, whereas persons who fail second-line treatment are assumed to no longer be on ART.

Counterfactual scenarios and cost-effectiveness calculations

- The change in parameter values over time is obtained from the calibrated model, informed by the data-driven relationships between spending and the relevant indicator associated with the parameter.
- Counterfactual scenarios represent what is assumed to have occurred in the absence of HIV/AIDS programs. It was assumed that removing spending for a particular program meant that the model parameters affected by that program remained fixed at their value at the initial year of program implementation.
- Programmatic costs are assumed to include all consumables and services for target groups.

Optimal allocation of spending analysis

- A constant amount was allocated to essential funding, consisting of ART and associated indirect costs consisting of critical enablers, synergies with the development sector, M&E, administration and other support costs.
- It was assumed that no programs had an effect on the population size of MARPs.
- Program spending was assumed to be directly related to program coverage and intensity among MARPs.
- Only direct costs were used in program budget assessments. We assume indirect costs are proportionally associated with direct costs.
- The assumed budget in 2011-2014 is equal to the budget allocation in 2010. Decreases in budget were assumed to occur in 2015 and remains at the same annual level during 2015-2020.

Treatment as prevention scenarios

- Treatment as prevention scenarios were investigated by determining the number of people that can begin ART for a fixed amount of funding. The testing and treatment initiation rates were then adjusted in the model to match this number.

Data gaps

- The HPTN 052 trial reported a 96% reduction in HIV transmission among heterosexual discordant couples who initiated early ART compared to couples who deferred ART initiation. Impacts of ART on homosexual transmission of HIV and transmission through sharing of injecting equipment remains unknown. In this model, we assume these impacts are similar to that of heterosexual transmission. The same relative reduction in infectiousness was assumed for these other modes of transmission.
- The prevalence of HIV/STI and behaviors among at-risk populations were collected with different sampling method during 2000-2010, thus caution should be taken in generalizing the temporal trend of these parameter presented in this report. This is the most critical limitation of the entire study and of the surveillance/monitoring system in Vietnam. It is crucial, for monitoring and evaluation purposes, that future surveillance (including IBBS and sentinel surveillance) is carried out consistently over time and with representativeness of the target population.
- Pilot MMT programs for drug users were implemented in 2008 and their coverage remains low (1.8% in 2010). Based on the available data during 2008-2010, our analysis may not capture the actual benefits of MMT because the current unit cost is high due to new infrastructure set-ups (such as clinics, equipment, training healthcare workers and supporters, and other administrative works) as well as difficulties in enrolling patients in the initial phase. However, similar to NSPs for IDUs [9], the unit cost of MMT is expected to drop remarkably in the near future when its coverage increases (>5%). We have also only included the HIV-related benefits of MMT whereas MMT has other primary objectives.
- Spending data were not stratified to the regional level so the cost-effectiveness of programs in individual Vietnamese regions was not assessed.
- There are incomplete costing data in 2000-2005, which limited investigation of the relationship between AIDS spending with key behavioral indicators.
- Unpublished data from numerous small projects supported by international donors and private sections were not conducted comprehensively in the data synthesis.
- Case reporting is not stratified by populations or likely exposure routes resulting in transmission. Adding this data field would substantially improve national surveillance in the future.

Results

HIV program spending in Vietnam during 2006-2010

A total of US $480 million was spent on the HIV/AIDS programs in Vietnam between 2006 and 2010 with an annual spending nearly tripling from ~US $50.6 million in 2006 to ~US $139.2 million in 2010 (Figure 5 and Table 2). Unsurprisingly, the domestic contribution to the total HIV/AIDS spending in the entire country remained at a low level and most funding was from international donors (72.7%), of which PEPFAR spending acts as the largest source of support for HIV/AIDS programs in Vietnam and followed by WB/DFID.

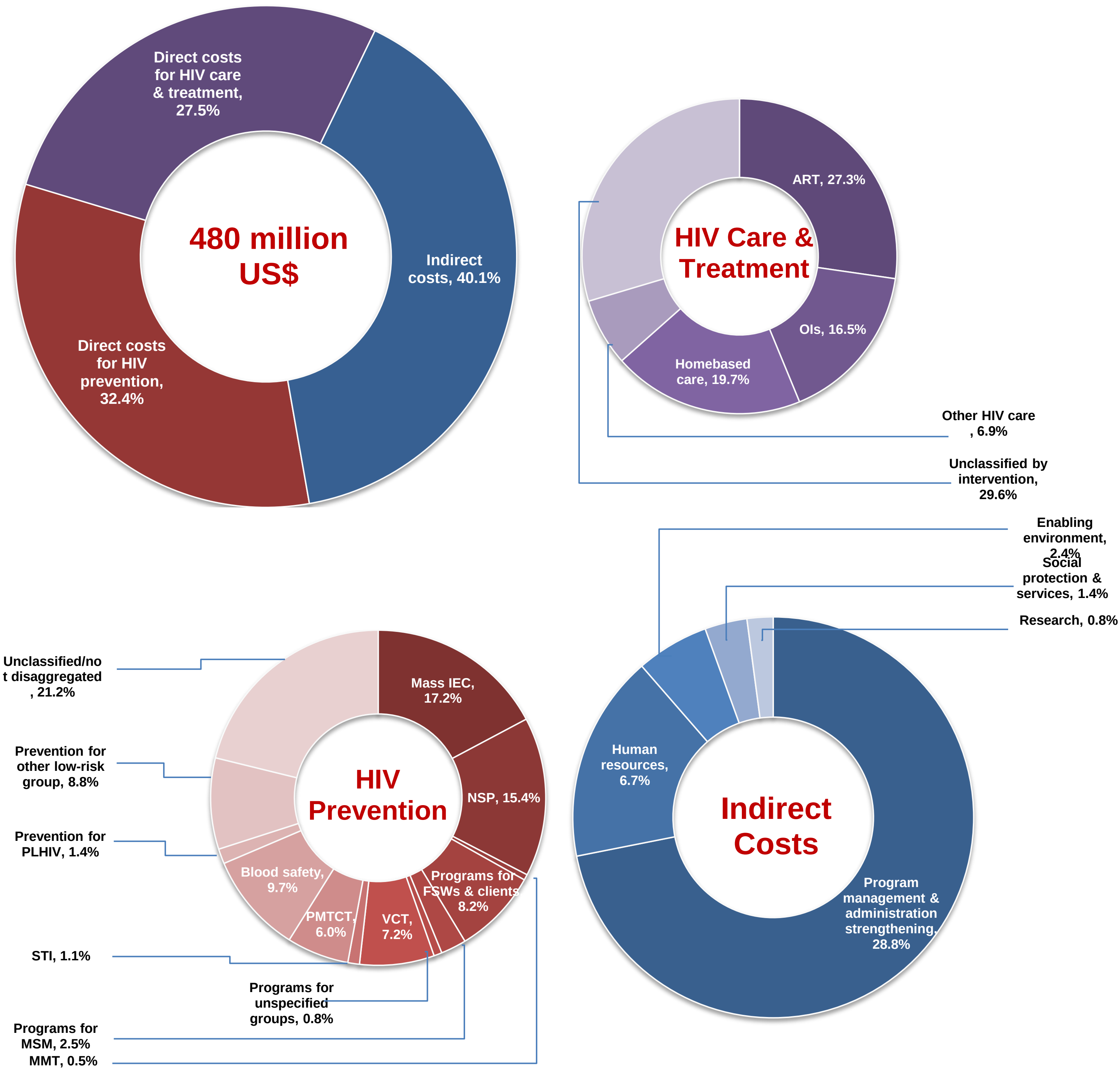
From 2006 to 2010, approximately 60% of the overall HIV/AIDS budget was allocated directly for HIV prevention (32.4%) and HIV care and treatment (27.5%), while a high percentage of 40.1% was spent on essential indirect costs which included costs of program management and administration strengthening, human resources, enabling environment, social protection and services, and research (Figure 6). Of the total prevention costs, only one-quarter of the costs were allocated directly to MARPs, including IDUs (15.9%), FSWs and clients (8.2%) and MSM (2.5%). The total annual costs for prevention scaled-up rapidly from US $16.4 million in 2006 to US $31.9 in 2008 and then decreased to US $40.8 million in 2009 and US $44.9 million in 2010 (Figure 5 and Table 2). The total direct cost for prevention was around US $155.7 million during this period. This total direct costs were split into many sub-programs, including mass information education communication (IEC, 17.2%), NSP (15.4%), the ‘100% condom use’ promotion (targeting FSW and clients, 8.2%; MSM, 2.5%; and unspecified populations, 0.8%); and blood safety (9.7%), prevention for youth and people in work force (8.8%), VCT (7.2%), preventing mother-to-child transmission of HIV (6.0%), preventions for people living with HIV (1.4%), STI treatment and management (1.1%), and MMT (0.5%). Approximately 21.2% of spending in HIV prevention was unclassified. Expenditures for HIV care and treatment totaled US $132 million, with US $36 million (27.3%) spent on ART, US $21.8 million (16.5%) spent for the prophylaxis and treatment of opportunistic infections, and US $25.9 million (19.7%) spent for home-based HIV care. A detailed summary of the annual HIV/AIDS spending in 2006-2010 in Vietnam is listed in Table 2.

Table 2: Estimated HIV spending in Vietnam, 2006-2010

Funding allocations	Cost (US $) 2006	2007	2008	2009	2010
Total	**50,686,443**	**66,499,122**	**96,208,777**	**127,374,483**	**139,253,245**
Programmatic spending					
Direct costs for prevention	16,438,820	21,567,248	31,913,529	40,811,053	44,951,932
Direct costs for care and treatment	13,943,701	18,293,726	24,274,597	33,378,767	42,161,961
Indirect costs	20,303,922	26,638,148	40,020,651	53,184,663	52,139,352
HIV prevention costs					
Mass information, education and communication	2,833,007	3,716,822	6,861,283	7,423,982	5,994,680
Needle and syringes program for IDUs	2,615,871	3,431,946	4,624,843	5,655,741	7,591,711
Methadone maintenance therapy program for IDUs			77,538	118,828	656,930
Programs for FSWs and clients	1,347,478	1,767,852	3,021,373	3,917,357	2,707,129
Programs for MSM	405,109	531,492	835,613	1,007,369	1,056,975
HIV voluntary counselling and testing	1,183,172	1,552,287	1,308,824	2,483,879	4,676,980
Sexually transmitted infection program (including microbicides)	184,224	241,695	253,540	287,499	777,716
Preventing mother-to-child transmission of HIV	985,708	1,293,220	1,673,181	2,402,482	2,980,480
Blood safety	1,593,317	2,090,385	4,316,317	3,965,649	3,123,716
Prevention for people living with HIV	237,393	311,452	234,779	548,978	915,607
Prevention for youth/people in work force/vulnerable and accessible populations/healthcare workers	1,445,606	1,896,592	3,467,647	2,714,047	4,166,602
Programs for unspecified groups	128,391	168,445	49,126	204,681	665,276
Unclassified/not disaggregated	3,479,544	4,565,060	5,189,465	10,080,561	9,638,130
HIV care and treatment costs					
Antiretroviral therapy	3,804,310	4,991,143	6,172,042	8,118,648	12,942,285
Opportunistic infection prophylaxis and treatment	2,299,671	3,017,101	4,617,644	5,061,769	6,782,672
Home-based HIV care	2,742,733	3,598,383	6,013,968	7,033,055	6,586,691
Other inpatient/outpatient HIV care	968,980	1,271,274	1,243,154	1,706,885	3,986,365
Unclassified/not disaggregated	4,128,007	5,415,825	6,227,789	11,458,410	11,863,948
Indirect costs					
Program management and administration strengthening	14,597,950	19,152,081	28,980,635	38,745,169	36,772,929
Human resources	3,393,942	4,452,752	6,600,136	7,999,570	9,695,665
Enabling environment	1,192,919	1,565,074	2,574,831	3,444,920	2,519,703
Social protection and services (including services for OVC)	692,324	908,309	1,158,137	1,786,977	2,010,858
Research	426,787	559,932	706,912	1,208,027	1,140,197

IDUs stands for injecting drug users; FSWs, female sex workers; MSM, men who have sex with men; OVC, orphan vulnerable children.

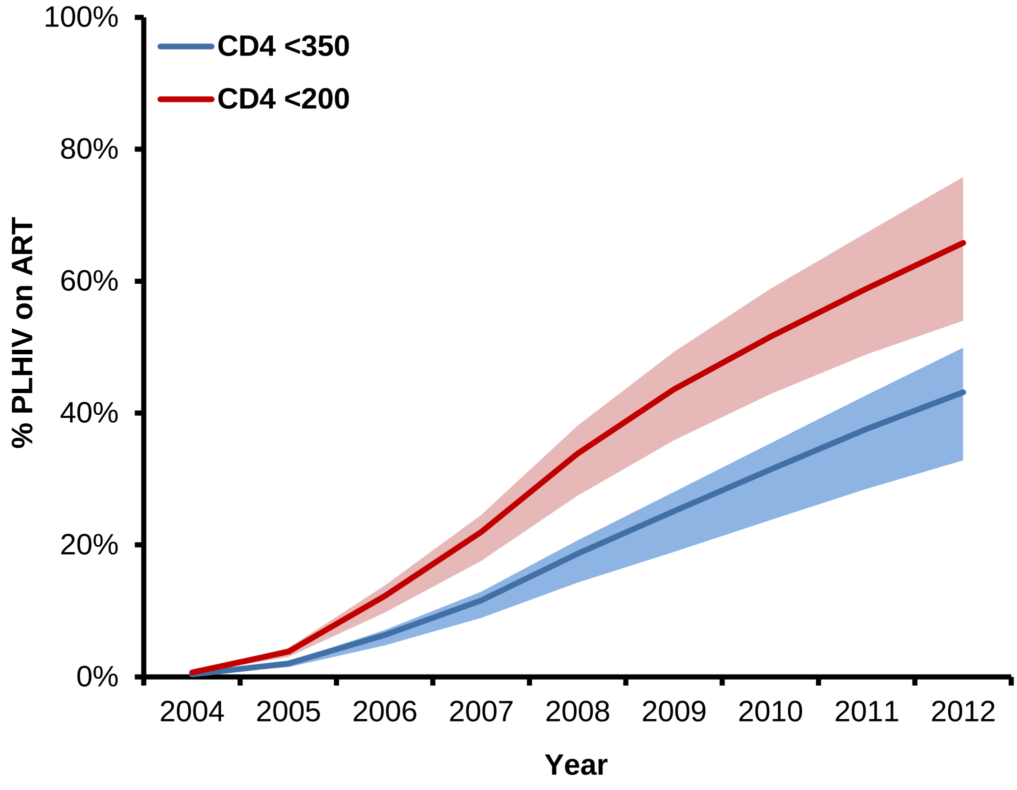
Figure 5: Budget allocation in Vietnam, 2006-2010



Impacts of HIV prevention programs in Vietnam

ART was initiated in Vietnam in 2005 and subsequently rapidly expanded as a national program. and the number of people on ART increased to 46,824 by 2010. PLHIV were eligible for ART if their CD4 cell count is below 200 cells/mm^3 during 2006-2009, while a higher CD4 cell count threshold of <350 cells/mm^3 was implemented since early 2010, aligned with World Health Organization guidelines. Treatment coverage for those who require ART is poorly documented in Vietnam. Here, we estimate ART coverage in 2006 to be ~12.3% for those with CD4<200 cells/mm^3 and 6.3% for those with CD4<350 cells/mm^3. These percentages substantially increased to 51.6% and 31.4% in 2010, respectively (Figure 7). Notably, provision of ART for eligible PLHIV (CD4<350 cells/mm^3) substantially reduces both new HIV infections (by an estimated 11,187 (8,366–16,260)) and HIV/AIDS-related deaths (by an estimated 34,144 (29,122–44,052)). Following ART, the next most effective intervention in reducing new HIV infections is condom promotion for FSWs and their clients. During 2006-2010, an estimated 9,850 (95% UB: 7,056–16,132) new HIV infections were averted by this program. Condom promotion for MSM was estimated to have potentially averted 7,963 cases (2,363–10,247); STI programs averted 6,268 (2,424–7,801), and NSPs for IDUs averted 4,459 (2,371–6,441) HIV infections. In total, HIV prevention programs and ART in Vietnam have potentially averted an estimated 54,133 (36,398–72,014) new HIV infections and 37,170 (31,537–47,333) deaths during 2006-2010 (Table 3).

Figure 6: Estimated ART coverage (with 95% confidence bound bands) for PLHIV in Vietnam, based on treatment threshold of CD4<200 and CD4<350.



At a total cost of US $480 million, each HIV infection averted has cost an estimated US $8,867 ($6,666–13,188) in the HIV response. When considering only the direct costs associated with HIV programs, NSPs have cost approximately US $5,364 ($3,714–10,089) per infection averted, condom distribution cost US $1,296 ($791–1,809) per infection averted among FSWs and US $482 ($374–1,624) per infection averted among MSM. ART was largely cost-effective when considering the preventative benefits alone at US $3,849 ($2,790–5,422) per infection averted.

The entire HIV investment was estimated to yield approximately US $1,047 ($861–1,385) per DALY averted and US $627 ($516–830)) per DALY averted when considering just direct HIV prevention and ART program costs. The cost-effectiveness ratios vary by program, ranging from US $97 ($81–250) per DALY averted for STI programs to $1,699 ($1,142–3,223) for NSPs programs among IDUs (Table 3). The willingness to pay threshold for these interventions in Vietnam is not well-known. According to the WHO-CHOICE criteria, a program is regarded as very cost-effective when the incremental cost-effectiveness ratio is less than one GDP per-capita and cost-effective when it is less than three GDP per-capita . The GDP per-capita in Vietnam is $1,113 in 2010. As such, it could be considered that all programs are cost-effective when considering the short-term benefits but all programs except MMT are cost-effective or cost-saving when future benefits of infections already averted are considered.

Not only does the investment in HIV prevention avert new infections and prolong or save lives, but it also represents good values for money. The return on investment of HIV prevention programs provides a metric for assessing the relative net monetary benefit for an investment. It is calculated as the gains from the investment in savings in the healthcare budget minus the investment costs, divided by the investment costs. It was found that condom promotion programs among FSWs, possibly MSM, and STI programs had likely averted sufficient numbers of infections such that the healthcare costs saved due to these averted infections surpass the investment costs. As such, these programs are already cost-saving and it is anticipated that there will be many-fold returns on the investments in these programs (Table 3). Needle-syringe programs are estimated to have already returned an estimated $0.35 ($0.18–0.51) in healthcare savings for every $1 invested in the programs but the future healthcare cost savings are projected to result in a return of the original investment plus an additional $0.36 for every $1 invested in the programs. The costs of HIV testing programs, which are often bundled with other HIV prevention programs in Vietnam, and treatment programs far surpass the direct health cost savings associated with the infections averted due to their implementation; the primary objectives of these programs are to support other programs and other objectives (keep people alive).

Table 3: Estimated epidemiological impact and cost-effectiveness of past HIV/AIDS programs in Vietnam

Indicators measured at 2010	Baseline	No NSP	No methadone	No FSW condom program	No MSM condom program**	No STI programs	Lower testing	No treatment	No interventions
Prevalence in 15-49 year old population									
Overall	0.61% (0.53%, 0.98%)	0.62% (0.54%, 0.99%)	0.61% (0.53%, 0.98%)	0.64% (0.55%, 1.01%)	0.63% (0.54%, 1%)	0.62% (0.54%, 1%)	0.63% (0.54%, 1.01%)	0.58% (0.5%, 0.95%)	0.66% (0.56%, 1.06%)
Low risk male	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.21% (0.17%, 0.48%)	0.19% (0.15%, 0.47%)	0.2% (0.16%, 0.48%)
Low risk female	0.28% (0.27%, 0.54%)	0.28% (0.27%, 0.54%)	0.28% (0.27%, 0.54%)	0.29% (0.27%, 0.55%)	0.28% (0.27%, 0.54%)	0.28% (0.27%, 0.54%)	0.29% (0.27%, 0.55%)	0.27% (0.25%, 0.53%)	0.28% (0.27%, 0.55%)
Direct FSWs	6.92% (6.19%, 9.5%)	6.97% (6.22%, 9.56%)	6.92% (6.19%, 9.5%)	8.07% (7.12%, 11.07%)	6.94% (6.2%, 9.52%)	7.42% (6.59%, 10.11%)	7.03% (6.26%, 9.63%)	6.6% (5.87%, 9.14%)	8.93% (7.74%, 12.27%)
Indirect FSWs	2.41% (2.13%, 3.63%)	2.43% (2.14%, 3.65%)	2.41% (2.13%, 3.63%)	2.86% (2.47%, 4.3%)	2.42% (2.13%, 3.64%)	2.48% (2.17%, 3.71%)	2.42% (2.13%, 3.64%)	2.26% (1.97%, 3.47%)	2.93% (2.47%, 4.46%)
Clients of FSWs	1.3% (1.14%, 2.19%)	1.31% (1.14%, 2.2%)	1.3% (1.14%, 2.19%)	1.55% (1.32%, 2.56%)	1.3% (1.14%, 2.19%)	1.31% (1.14%, 2.2%)	1.34% (1.17%, 2.25%)	1.2% (1.04%, 2.08%)	1.55% (1.3%, 2.61%)
MSM	12.14% (5.2%, 15.34%)	12.15% (5.21%, 15.36%)	12.14% (5.2%, 15.34%)	12.17% (5.22%, 15.37%)	13.38% (5.57%, 16.9%)	12.82% (5.4%, 16.16%)	12.98% (5.49%, 16.39%)	12.09% (5.05%, 15.33%)	15.33% (6.11%, 19.34%)
IDUs	15.1% (11.83%, 23.95%)	15.87% (12.24%, 25.16%)	15.1% (11.83%, 23.95%)	15.2% (11.94%, 24.03%)	15.1% (11.83%, 23.95%)	15.11% (11.84%, 23.96%)	15.32% (11.91%, 24.31%)	13.51% (10.3%, 21.84%)	14.87% (11.14%, 23.91%)
New infections	127,600 (102,155, 220,736)	132,059 (105,652, 225,663)	127,600 (102,155, 220,736)	137,450 (109,423, 235,412)	135,563 (106,635, 229,750)	133,868 (105,763, 227,738)	136,058 (107,919, 231,219)	138,787 (110,672, 236,995)	181,732 (139,042, 289,701)
Deaths	102,944 (92,069, 133,468)	103,139 (92,229, 133,665)	102,944 (92,069, 133,468)	103,609 (92,687, 134,237)	103,404 (92,321, 133,836)	103,021 (92,121, 133,535)	105,705 (94,295, 136,542)	137,088 (121,231, 176,245)	140,114 (123,606, 179,334)
Cumulative no. people starting 1st line ART	52,432 (43,073, 67,203)	52,501 (43,126, 67,310)	52,432 (430,73, 67,203)	52,643 (43,259, 67,454)	52,638 (43,180, 67,357)	52,457 (43,090, 67,226)	50,231 (41,500, 64,497)	0 (0, 0)	0 (0, 0)
Cumulative no. people starting 2nd line ART	768 (549, 1,039)	768 (549, 1,039)	768 (549, 1,039)	769 (550, 1,040)	770 (550, 1,040)	768 (549, 1,039)	732 (524, 990)	0 (0, 0)	0 (0, 0)
Infections averted	0 (0, 0)	4,459 (2,371, 6,441)	0 (0, 0)	9,850 (7,056, 16,132)	7,963 (2363, 10,247)	6,268 (2,424, 7,801)	8,458 (5,055, 10,946)	11,187 (8,366, 16,260)	54,133 (36,398, 72,014)
Deaths averted	0 (0, 0)	195 (92, 299)	0 (0, 0)	665 (478, 930)	460 (175, 548)	77 (47, 91)	2,761 (2,207, 3,344)	34,144 (29,162, 44,052)	37,170 (31,537, 47,333)
Program costs	$0	$23,920,112	$853,296	$12,761,189	$3,836,558	$1,744,674	$11,205,142	$45,363,499	$99,684,470
Healthcare cost (2006-10)	$558,174,406 ($466,374,144, $893,342,217)	$566,580,065 ($472,843,635, $902,808,395)	$558,174,448 ($466,374,176, $893,342,265)	$578,210,690 ($481,086,624, $923,394,511)	$575,427,109 ($476003994, $913116360)	$570,771,778 ($473,372,587, $907,199,546)	$569,728,886 ($474,002,769, $911,330,520)	$409,936,364 ($340,335,371, $731,167,023)	$493,933,478 ($394,999,769, $837,243,658)
Healthcare cost (2006-10, 3% discounted)	$594,546,433 ($496,887,384, $950,795,578)	$603,491,139 ($503,772,436, $960,855,803)	$594,546,478 ($496,887,418, $950,795,629)	$615,872,631 ($512,550,528, $982,739,007)	$612,889,325 ($507,128,294, $971,799,024)	$607,930,730 ($504,324,838, $965,504,550)	$606,915,509 ($505,051,212, $969,952,034)	$438,451,504 ($364,093,776, $780,224,346)	$527,937,223 ($422,353,253, $893,057,217)
Cost lifetime	$4,798,788,890 ($3,892,596,304, $7,736,282,596)	$4,860,459,472 ($3,938,788,532, $7,813,316,884)	$4,798,789,188 ($3,892,596,526, $7,736,282,979)	$4,928,610,418 ($3,985,482,237, $7,945,302,775)	$4,926,713,475 ($3,962,225,593, $7,902,860,266)	$4,887,064,450 ($3,940,176,366, $7,847,698,924)	$4,843,848,225 ($3,952,835,656, $7,999,475,666)	$1,359,765,371 ($1,158,711,946, $2,427,770,288)	$1,570,083,242 ($1,299,055,665, $2,725,696,214)

Cost lifetime (3% discounted)	$2,670,158,499 ($2,213,043,885, $4,181,531,714)	$2,702,821,927 ($2,237,859,706, $4,220,477,579)	$2,670,158,653 ($2,213,044,001, $4,181,531,902)	$2,742,268,973 ($2,265,674,734, $4,293,479,551)	$2,736,549,059 ($2,249,920,894, $4,264,004,696)	$2,715,255,684 ($2,237,809,025, $4,235,909,109)	$2,702,740,792 ($2,24,5610,444, $4,293,750,779)	$1,278,210,394 ($1,091,876,481, $2,194,328,985)	$1,461,706,652 ($1,213,039,886, $2,445,507,597)
DALY (2006-10)	252,223,252 (251,509,900, 252,480,475)	252,208,969 (251,500,457, 252,469,125)	252,223,252 (251,509,900, 252,480,475)	252,187,353 (251,466,187, 252,450,520)	252,195,363 (251,486,743, 252,467,894)	252,204,965 (251,495,071, 252,471,629)	252,174,182 (251,465,281, 252,448,653)	251,954,308 (251,208,170, 252,260,172)	251,789,013 (251,042,591, 252,152,323)
DALY (2006-10, 3% discounted)	2,613,123,539 (2,606,665,476, 2,615,255,890)	2,612,991,834 (2,606,525,113, 2,615,1497,79)	2,613,123,538 (2,606,665,475, 2,615,255,889)	2,612,789,439 (2,606,193,561, 2,614,974,595)	2,612,856,956 (2,606,372,859, 2,615,135,213)	2,612,940,861 (2,606,470,083, 2,615,166,981)	2,612,728,198 (2,606,268,650, 2,615,010,592)	2,611,169,975 (2,603,897,376, 2,613,619,583)	2,609,557,565 (2,601,984257, 2,612,570,152)
DALY lifetime	252,223,252 (251,509,900, 252,480,475)	252,208,969 (251,500,457, 252,469,125)	252,223,252 (251,509,900, 252,480,475)	252,187,353 (251,466,187, 252,450,520)	252,195,363 (25,1486,743, 252,467,894)	252,204,965 (251,495,071, 252,471,629)	252,174,182 (251,465,281, 252,448,653)	251,954,308 (251,208,170, 252,260,172)	251,789,013 (251,042,591, 252,152,323)
DALY lifetime (3% discounted)	267,582,993 (266,827,200, 267,855,547)	267,567,903 (266,817,228, 267,843,557)	267,582,992 (266,827,200, 267,855,546)	267,545,077 (266,781,039, 267,823,905)	267,553,555 (266,802,750, 267,842,263)	267,563,724 (266,811,571, 267,846,223)	267,531,078 (266,779,955, 267,821,834)	267,298,761 (266,507,493, 267,622,703)	267,124,409 (266,335,175, 267,508,899)
Cost saved (2006-2010)	$0 ($0, $0)	$8,944,706 ($4,696,725, $13,064,133)	$45 ($24, $66)	$21,326,198 ($15,480,679, $34,518,749)	$18,342,892 ($5,550,665, $23,698,263)	$13,384,297 ($5,076,411, $16,541,746)	$12,369,076 ($7,314,315, $19,156,455)	-$156,094,929 ($-194,887,049, $-131,584,393)	-$66,609,209 ($-125,582,775, $-50,532,177)
Cost saved lifetime	$0 ($0, $0)	$32,663,428 ($16,663,046, $48,383,492)	$153 ($80, $233)	$72,110,474 ($52,057,348, $117,588,166)	$66,390,560 ($20,753,961, $89,339,479)	$45,097,185 ($17,594,698, $59,584,954)	$32,582,293 ($22,602,179, $113,921,617)	-$1,391,948,105 ($-1,987,202,729, $-1,121,167,404)	-$1,208,451,847 ($-1,736,024,117, $-9,981,664,46)
DALY averted until 2010	0 (0, 0)	15,089 (7,966, 22,488)	0 (0, 0)	37,916 (28,482, 56,035)	29,437 (9,042, 35,998)	19,269 (7,467, 23,053)	51,915 (32,269, 59,318)	284,232 (229,155, 357,101)	458,583 (346,648, 557,194)
DALY averted lifetime	0(0, 0)	131,705 (71,196, 193,664)	1 (0, 1)	334,100 (25,0468, 524,479)	266,583 (81,335, 333,636)	182,678 (69,924, 220,607)	395,341 (227,177, 447,994)	1,953,564 (1,563,083, 2,768,099)	3,565,974 (2,655,680, 4,751,071)
Program cost/DALY averted (until 2010)	$0 ($0, $0)	$1,699 ($1,142, $3,223)	$13,799,805 ($9,206,886, $25,617,378)	$361 ($244, $480)	$140 ($114, $457)	$97 ($81, $250)	$232 ($203, $373)	$171 ($136, $212)	$233 ($191, $309)
Program cost/DALY averted (lifetime)	$0 ($0, $0)	$182 ($124, $337)	$1,362,637 ($923,556, $2,460,412)	$38 ($24, $51)	$14 ($12, $47)	$10 ($8, $25)	$28 ($25, $50)	$23 ($16, $29)	$28 ($21, $38)
Return on investment (until 2010)*	0.00 (0, 0)	-0.65 (-0.82, -0.49)	-1.00 (-1, -1)	0.55 (0.12, 1.51)	3.43 (0.34, 4.73)	6.12 (1.70, 7.81)	0.02 (-0.40, 0.58)	-4.22 (-5.02, -3.72)	-1.64 (-2.19, -1.49)
Return on investment (lifetime)*	0.00 (0, 0)	0.36 (-0.31, 1.01)	-1.00 (-1, -1)	4.61 (3.04, 8.16)	16.21 (4.38, 22.17)	24.80 (9.05, 33.09)	1.85 (0.96, 9.10)	-31.66 (-44.78, -25.69)	-13.13 (-18.43, -11.02)

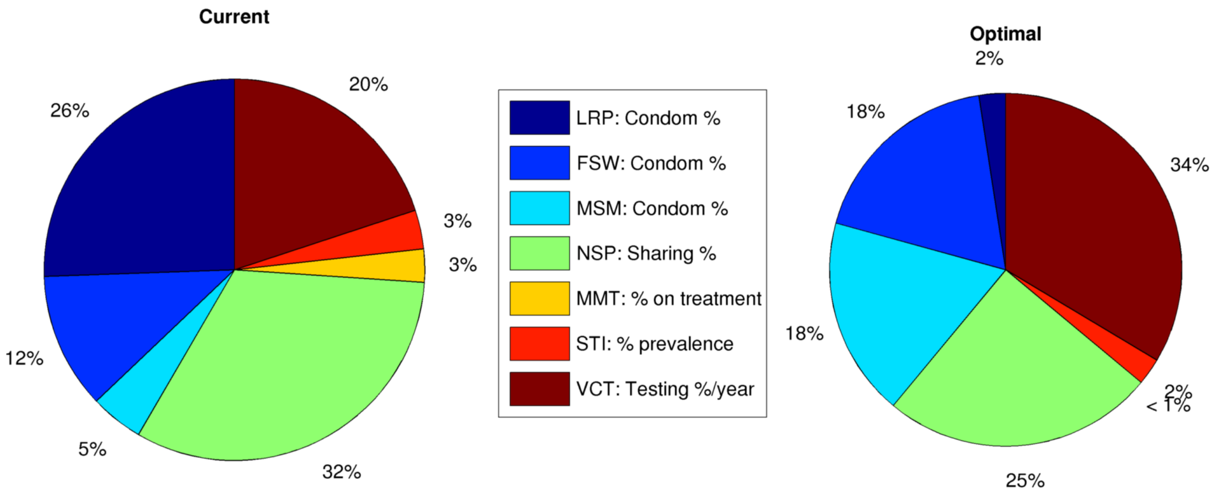
* Return on investment was calculated by (costs saved – program costs) / program costs.

** The evaluation of MSM condom programs must be interpreted very cautiously. Indeed, the available surveillance data do not support evidence for epidemiological impact and the values in this column are related to an assumed relationship which is used for future resource allocations.

Optimal allocation of HIV prevention funding in Vietnam

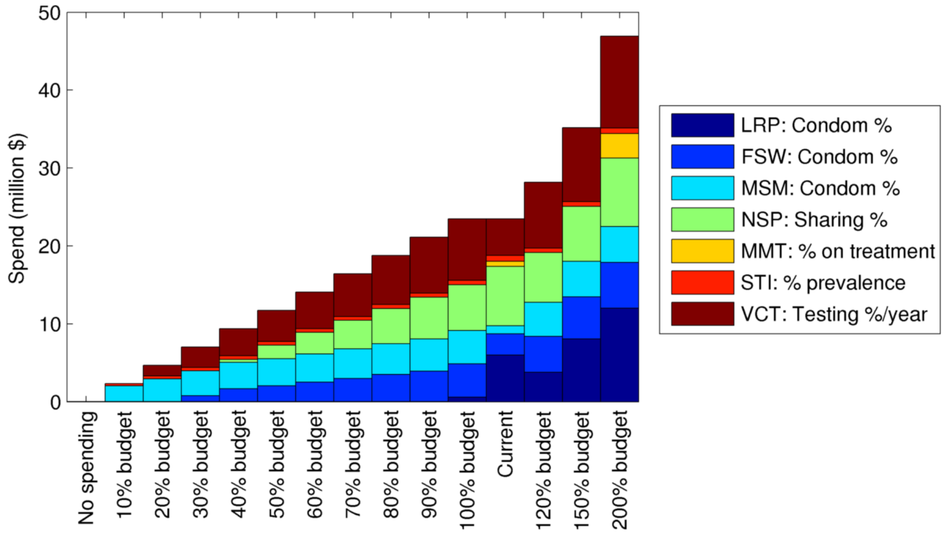
In Figure 7, the distribution of prevention funding in 2006-2010 is compared to the model-produced optimal allocation of the same amount of funding calculated to minimize the total number of new HIV cases. Optimal allocation according to the model calculations suggests that available resources should be concentrated on MARPs rather than low-risk populations. This specifically prioritizes VCT and recommends substantial increases of investment to NSP for IDUs and condom promotion programs among MSM and FSWs.

Figure 7: Current allocation of HIV prevention funding to programs versus the optimal budget allocation to reduce HIV incidence



The optimal allocation of resources was also considered in scenarios with reduction in available resources. Such scenarios are shown in Figure 8. Of note, resources from government sectors contributed to 15.4% of total AIDS spending in Vietnam in 2010. Hypothetically, in extreme situation where all external funds are withdrawn from Vietnam and available resources become extremely scarce, MSM-targeted condom distribution and STI programs are the ones to be first funded. As funding becomes more available (30%-40% of the total spending for in 2010), NSPs among IDUs and condom promotion program among FSWs and clients should be scaled up to consolidate the positive gains in prevention. Across different budgeting scenarios, it is imperative to fund VCT since it is not only essential in identifying undiagnosed individuals and providing counselling to reduce risk behaviours, but also facilitate ART uptake to reduce AIDS-related morbidity and mortality and secondary transmission of HIV. If funding was to become more readily available (1.2-fold the current funding amount), condom programs targeting the low-risk populations should be considered for implementation. Notably, MMT for IDUs should be introduced to cover the reachable target populations when the resource available increases to double the current funding. Our analysis has indicated that the current HIV prevention and ART programs (CD4 threshold of <350 cell/mm^3) would have cumulatively averted 219,854 new HIV infections and 26,524 HIV/AIDS-related deaths in 2013-2020. These programs will also facilitate the commencement of 59,091 and 10,568 eligible PLHIV on first-line and second-line ART in the next 7 years (Table 4). In comparison, doubling the current investment amount would only avert an additional 6,187 new cases and 999 HIV/AIDS-related deaths (Table 4). This could be due to the fact that the greater the investment, the higher the marginal costs required for averting extra infections. This is likely due to the saturation effects in which further expansion of programs result in limited outcomes, such as increasing difficulty in reaching more at-risk individuals and thus inability to increase program coverage and also in changing risk behaviours. Further, the optimizing procedure in our model aims to reduce the total number of new infections. MARPs are hence prioritised for the prevention programs. As resources become more available, more of these resources will be directed to lower-risk population groups. The unit costs of averting a new infection hence become higher.

Figure 8: Optimal allocation of funding to prevention programs for a reduced HIV prevention budget and corresponding incidence in each population group, 2013-2020 (see Table 4 for details)



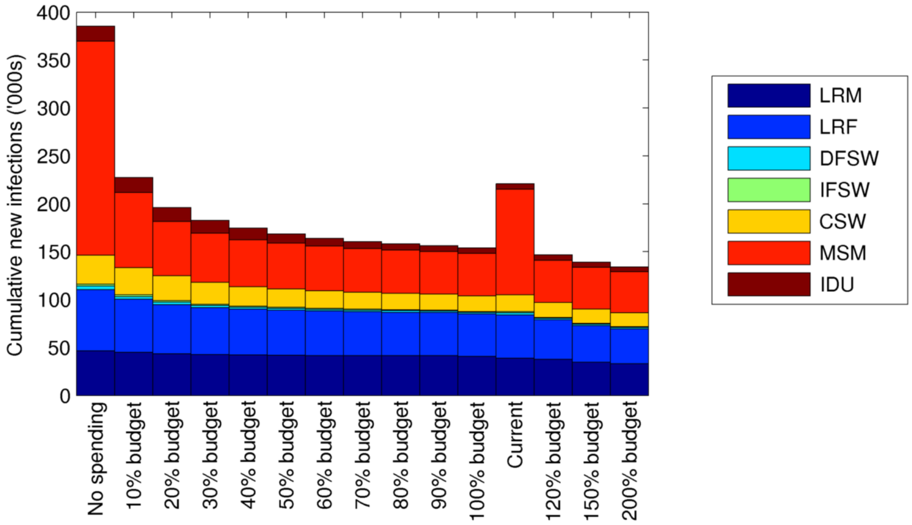


Table 4: HIV outcomes and budget breakdown for reduced 2013-2020 prevention budget

	Current funding		Budget scenarios (% decrease/increase)												
Outcomes 2013-2020	Current status	100%	10%	20%	30%	40%	50%	60%	70%	80%	90%	120%	150%	200%	No interven-tion
Cumulative no. new infections	163,656	137,663	204,139	175,330	163,204	155,750	150,283	146,021	142,843	140,532	138,860	135,683	133,498	131,476	357,517
Cumulative no. people starting 1st-line ART	84,611	82,501	57,169	69,655	76,136	78,484	79,415	80,364	81,214	81,796	82,257	82,677	82,855	83,127	59,091
Cumulative no. people starting 2nd-line ART	11,170	10,829	10,260	10,490	10,632	10,693	10,723	10,753	10,782	10,802	10,819	10,837	10,845	10,858	10,568
Cumulative no. deaths	135,250	133,296	149,736	142,806	139,017	137,250	136,250	135,336	134,560	133,998	133,560	133,000	132,678	132,297	159,820
Condom promotion in low-risk population	$5,130,246	$574,981	$0	$0	$0	$0	$0	$0	$0	$0	$0	$3,771,631	$8,062,889	$11,993,883	$0
Condom promotion in FSWs	$3,216,306	$4,288,754	$0	$0	$785,443	$1,686,420	$2,045,958	$2,498,929	$3,001,896	$3,480,030	$3,904,409	$4,618,269	$5,391,550	$5,889,884	$0
Condom promotion in MSM	$1,537,251	$4,284,178	$2,048,495	$2,937,134	$3,176,637	$3,366,327	$3,485,324	$3,629,155	$3,796,544	$3,961,497	$4,136,975	$4,391,588	$4,563,310	$4,606,806	$0
NSP	$5,299,099	$5,864,782	$0	$0	$0	$365,907	$1,718,161	$2,763,609	$3,651,236	$4,505,032	$5,360,689	$6,366,343	$7,031,827	$8,802,606	$0
MMT	$759,984	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$3,137,971	$0
STI Programs	$663,619	$578,746	$297,717	$395,762	$425,033	$480,840	$461,307	$481,683	$497,850	$515,580	$541,330	$566,030	$613,358	$697,704	$0
VCT	$6,855,617	$7,870,681	$0	$1,359,529	$2,651,524	$3,485,355	$4,020,310	$4,703,897	$5,475,959	$6,307,559	$7,172,506	$8,440,683	$9,530,247	$11,795,388	$0

Impact of optimal allocation on HIV prevalence, 2013-2020

In Figure 9, projected prevalence levels are shown by population group according to three scenarios: (i) continued current conditions with no change in budget levels or allocations; (ii) optimal allocation of current budget levels for maximal allocative efficiency at the national level across all populations; (iii) no budget for HIV prevention programs but sustained ART programs.

The epidemic trajectories reveal that without prevention for IDUs, there is potential for substantial increases in prevalence among IDUs. This is why NSPs are prioritized so much in the optimal resource allocations. Similarly, in the absence of HIV prevention programs, HIV prevalence among Vietnamese FSWs and their clients are likely to markedly increase to high levels. The current resource allocation indicates that the HIV prevention programs will have little impact on the HIV prevalence among MSM. However, with the optimized allocation of the available funding, the rapidly increasing trend of HIV prevalence among Vietnamese MSM can be reversed in the near future and at the same time sustaining comparable levels of HIV prevalence in other populations. Notably MSM are much more important in acting as a bridge for HIV transmission from MARPs to the general population in Vietnam as approximately 40% Vietnamese MSM are bisexual. Therefore, it is important to target MSM to minimize the total number of new infections beyond 2020 with efficient HIV prevention strategies.

Figure 9: National HIV prevalence in 2000-2020

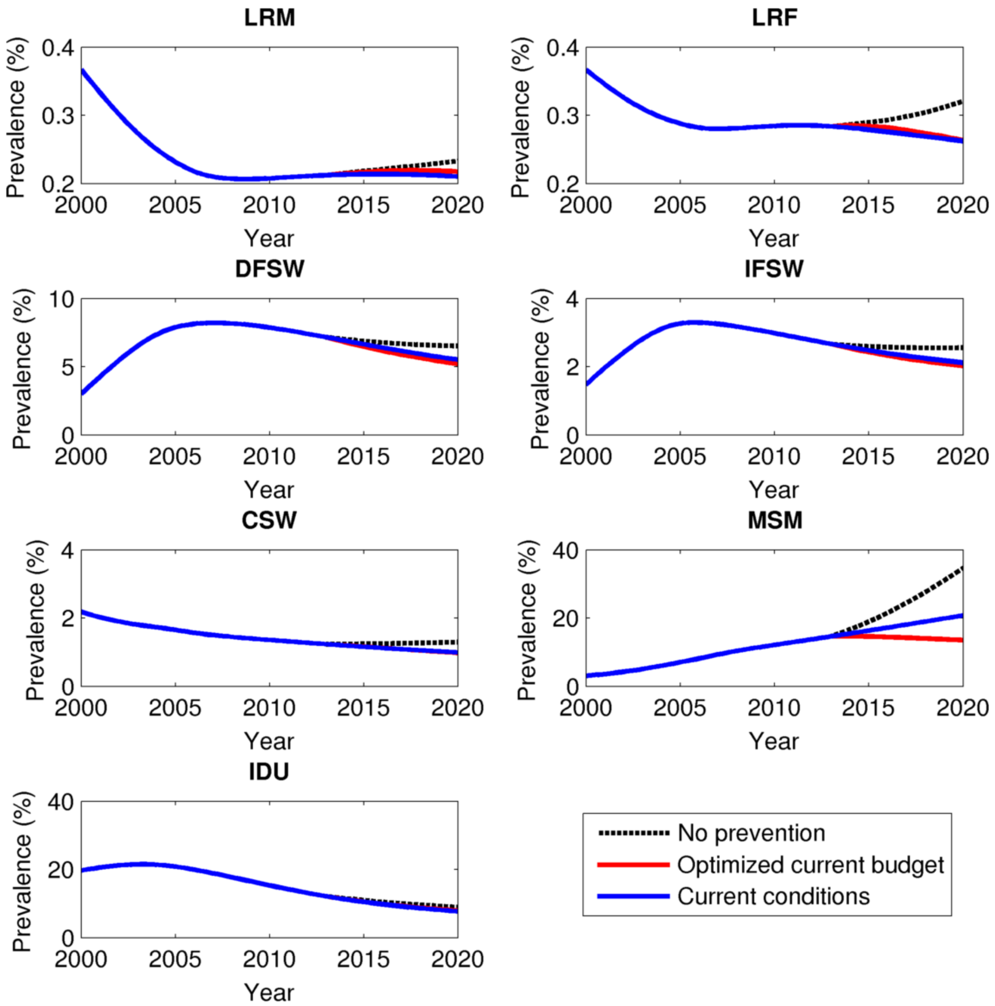
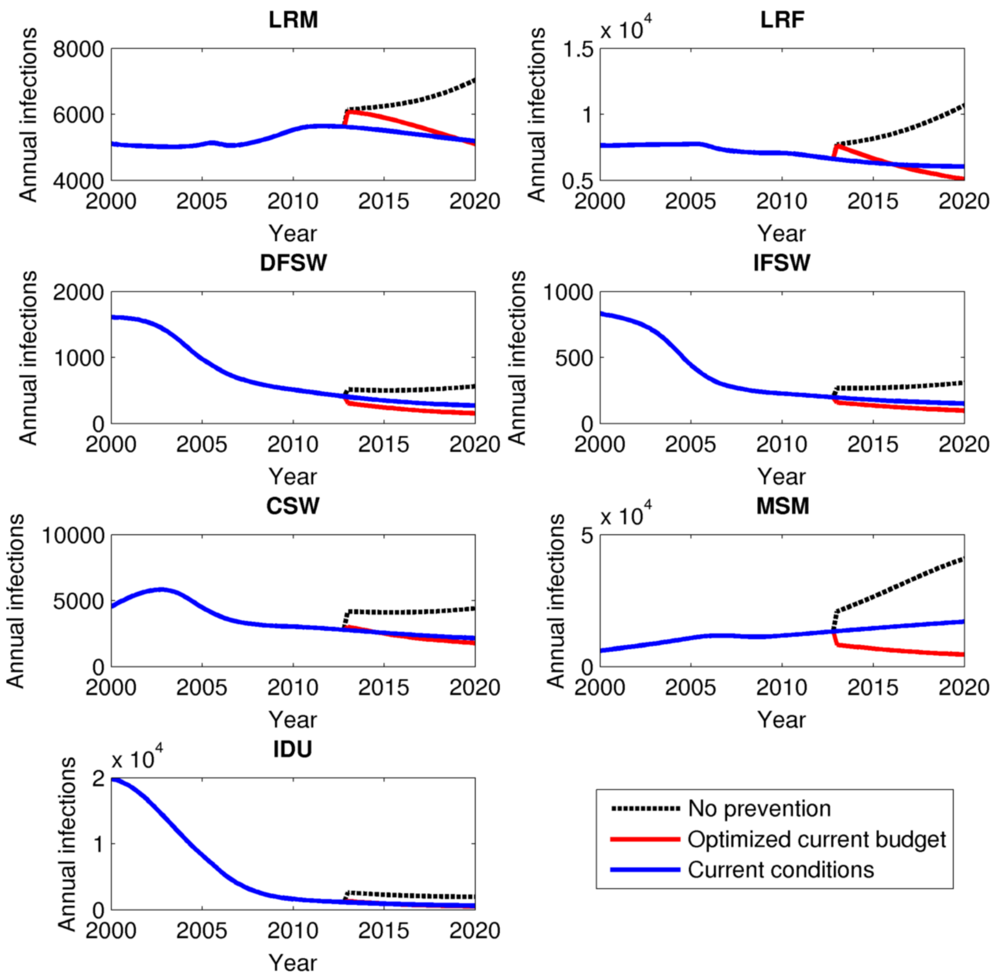


Figure 10: National HIV incidence in 2000-2020



Appendix

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Appendix 1: Collection of epidemiological and behavioral data in Vietnam

In Vietnam, the transmission pattern of HIV epidemics is monitored by the national sentinel surveillance system annually and the periodic integrated biological and behavioral surveillance (IBBS) and behavioral surveillance surveys (BSS). Besides, regional studies with substantially smaller sample sizes are published in international peer-reviewed journals or as internal reports in in-country health organizations. For independent studies outside sentinel surveillance, a systematic review was conducted to collating relevant parameters from published English literatures during 1990-2011. We performed searches in January 2011 for on PubMed according to the following key word search strategies:

Epidemiological and behavioral parameters among drug users

- ['HIV' OR 'human immunodeficiency virus' OR 'STI' OR 'STIs' OR 'STD' OR 'sexually transmitted infection' OR 'sexually transmitted disease'] AND ['IDU' OR 'injecting drug user' OR 'injection drug user' OR 'drug user' OR 'heroin user' OR 'substance user' OR 'opioid use' OR 'methadone' OR 'methadone maintenance therapy' OR 'methadone maintenance treatment' OR 'MMT' OR 'injecting behaviour' OR 'injecting behavior' OR 'sharing behaviour' OR 'sharing behavior' OR 'sharing practice' OR 'injection practice' OR 'injecting practice'] AND ['Vietnam'];

Epidemiological and behavioral parameters among female sex workers

- ['HIV' OR 'human immunodeficiency virus' OR 'STI' OR 'STIs' OR 'STD' OR 'sexually transmitted infection' OR 'sexually transmitted disease'] AND ['FSW' OR 'female sex worker' OR 'sex work' OR 'sex worker' OR 'condom' OR 'condom use' OR 'condom practice' OR 'sexual behaviour' OR 'sexual behavior' OR 'sexual partner' OR 'sexual partnership'] AND ['Vietnam'];

Epidemiological and behavioral parameters among men who have sex with men

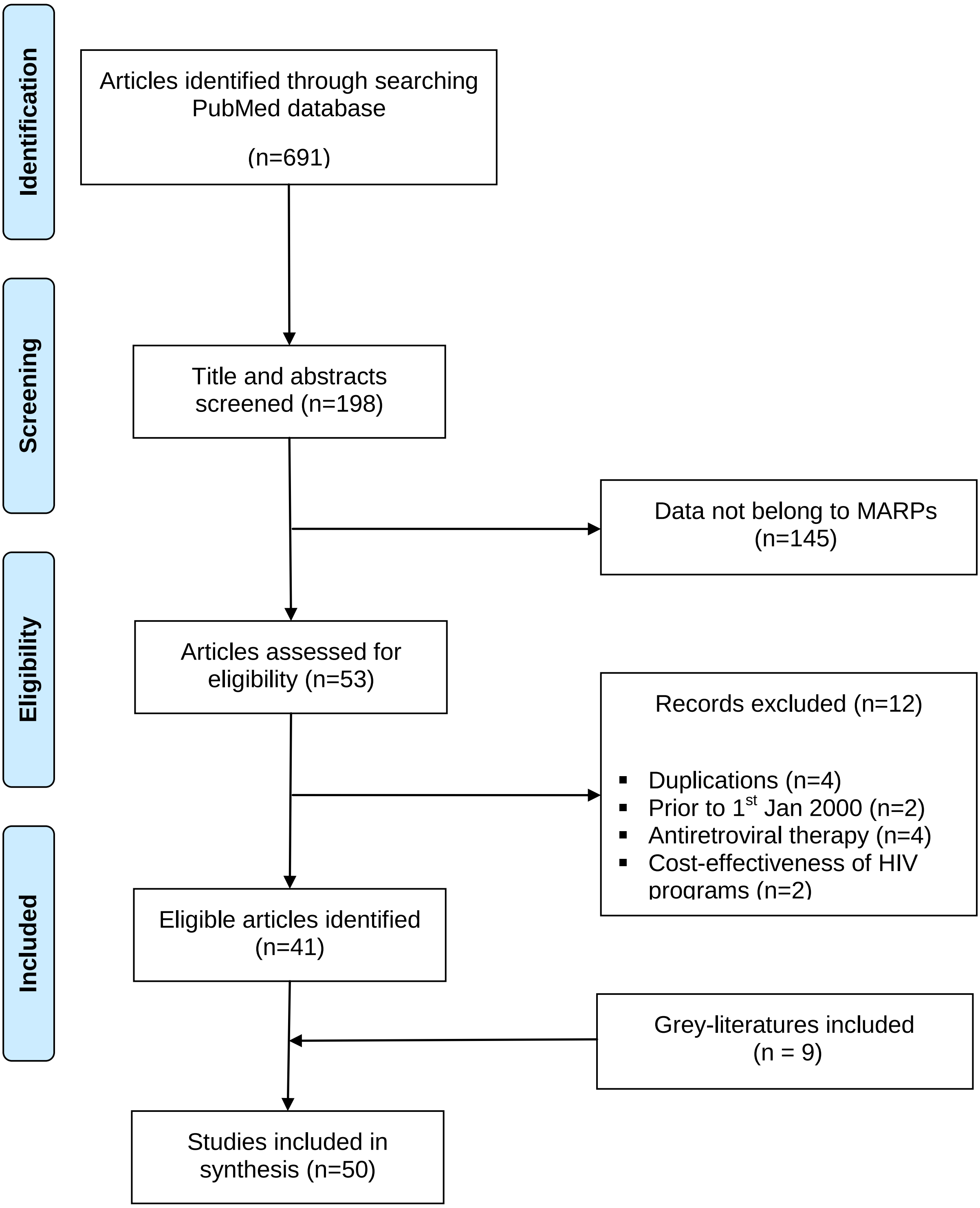
- ['HIV' OR 'human immunodeficiency virus' OR 'STI' OR 'STIs' OR 'STD' OR 'sexually transmitted infection' OR 'sexually transmitted disease'] AND ['MSM' OR 'men who have sex with men' OR 'gay' OR 'bisexual' OR 'homosexual' OR 'same sex' OR 'male sex worker' OR 'MSW' OR 'transgender' OR 'homosexual' OR 'homosexuality'] AND ['Vietnam'];

HIV intervention programs in Vietnam

- ['HIV prevention' OR 'HIV intervention' OR 'HIV program'] AND ['Vietnam'].

In this review, a publication was included if it reported prevalence levels of HIV and/or sexually transmitted infections (STI), sexual and/or drug-using behaviors among most at-risk populations (MARPs including IDUs, FSWs, clients of FSWs, and MSM) in Vietnam. Our review excluded systematic review and qualitative studies, studies prior to 1st January 2000, or sample size less than 30 and publications from the identical data source.

Figure S. 1: Flow chart of article selection



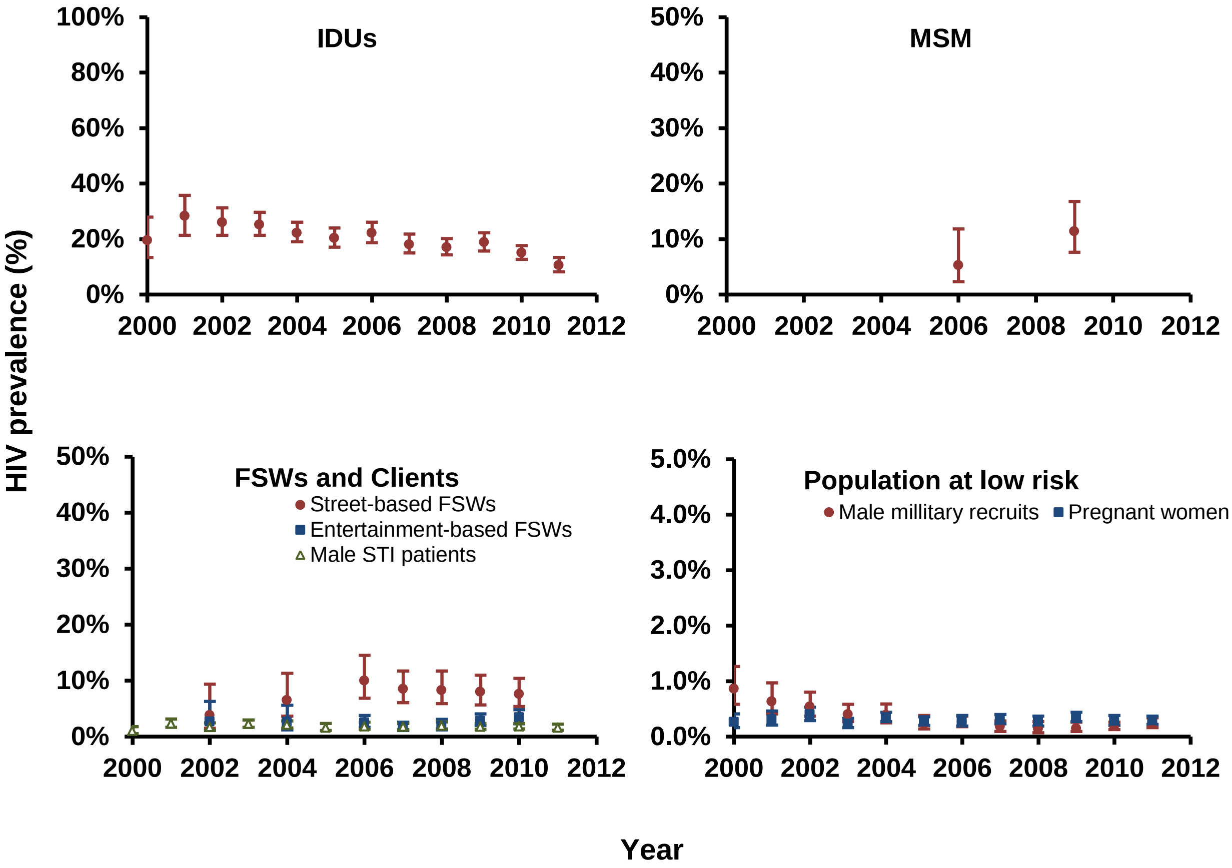
For this study, HIV sentinel data was provided by the Vietnam Authority of HIV/AIDS Control for the period 2000-2010. Additional prevalence data was also collected through a systematic review of published peer-reviewed research articles published after 1st January 2000 by searching the Medline database through PubMed. In brief, a total of 691 articles were identified through our search strategy and were screened but after applying strict exclusion criteria, 41 independent published studies were chosen to provide HIV prevalence data over the period 2000-2010. Additional nine gray-reports were also collected by in-country consultants. A total of 50 literatures were included in this systematic review (Figure S.1). These studies represent a total of 24,213 of IDUs screened in 23 provinces, 22,831 FSWs screened in 17 provinces, and 3,960 MSM screened in 8 provinces, these numbers represent 10.1%, 35.0%, and 1.4% of population size estimates in the entire country, respectively.

Required data were extracted and entered into a database using *Microsoft Access*. Meta-analyses on HIV prevalence data were carried out using the Comprehensive Meta-Analysis software version 2.0 (Biostat, Englewood, New Jersey). We used random effect models to estimate the effect rates of pooled HIV prevalence and its 95% confidence intervals. We used a similar method as a preceding report of evaluation of harm reduction in Vietnam occurring during 2009 and 2010 to estimate the weight average of key behaviors (i.e. sharing rate, estimated number of partner per year, and percentage of condom use with different partnerships) in various groups [10]. In this analysis, we only included surveys which enrolled participants in several provinces (i.e. BSS 2000, Baseline in 2002 and endpoint survey of the project of “Community Action for Preventing HIV/AIDS”, and IBBS 2006 and 2009)

The trend of HIV prevalence between 2000 and 2012 was presented in seven high-risk (including IDUs, MSM, street-based FSWs, entertainment-based FSWs, male STI patients) and low-risk populations (including male military recruits, and pregnant women) (Figure S1.2). The trend of key available behavioral parameters is indicated among four sub-groups, including IDUs, MSM, street-based FSWs, and entertainment-based FSWs (Table S.3 and Figure S.3-S.7).

Program and costing data at the national level was obtained through in-country consultants. These include the number of commodity distributed, number of people diagnosed with HIV, number of IDUs receiving MMT, and number of people receiving ART in Vietnam, by contacting with key central project management units and the Vietnam Authority of HIV/AIDS Control (Figure S8-11). In the process of data collection, we also collated healthcare costs of HIV infected people and health utilities for cost effectiveness calculations (Table S.1 and S.2, respectively).

Figure S. 2: HIV prevalence among various populations in Vietnam, 2000-2011



Note: The presented data integrated data from sentinel surveillance and independent studies data sources.

Figure S. 3: Estimated number of drug injections per year among IDUs, MSM and FSWs in Vietnam, 2000-2009

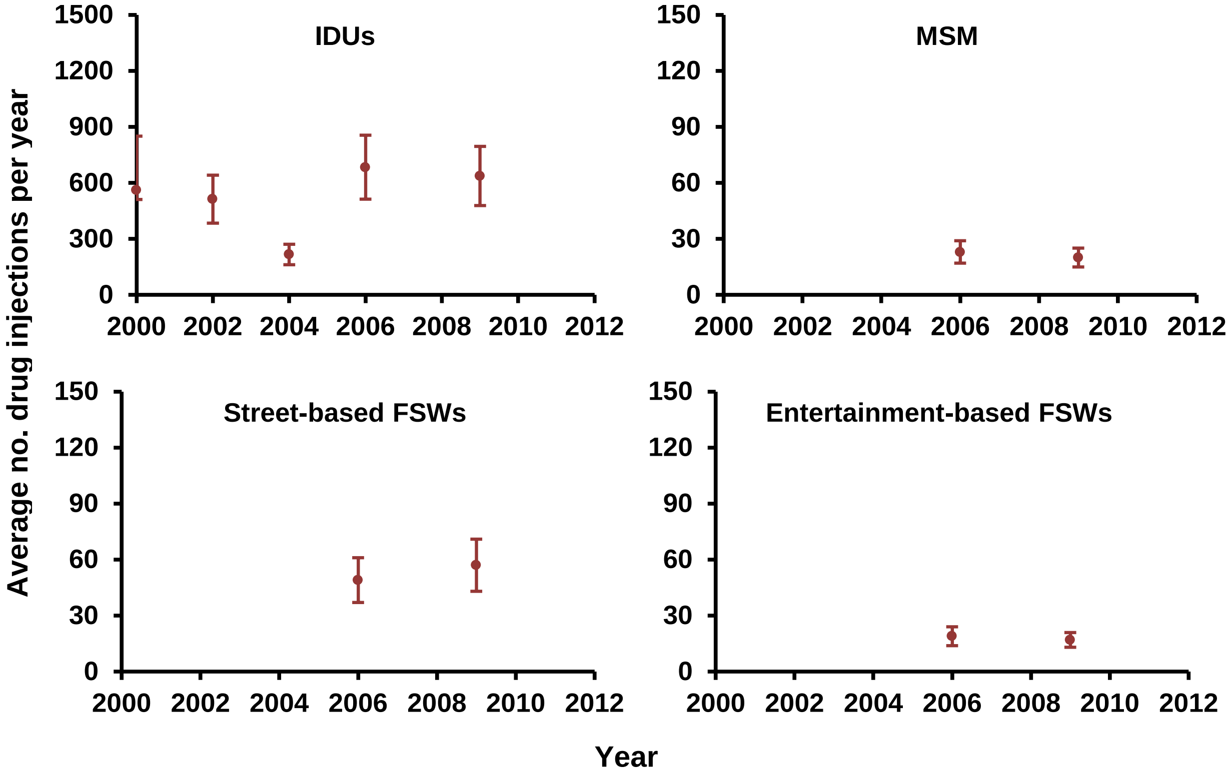


Figure S. 4: Receptive sharing rate in the last month among IDUs, injecting MSM and injecting FSWs in Vietnam, 2000-2009

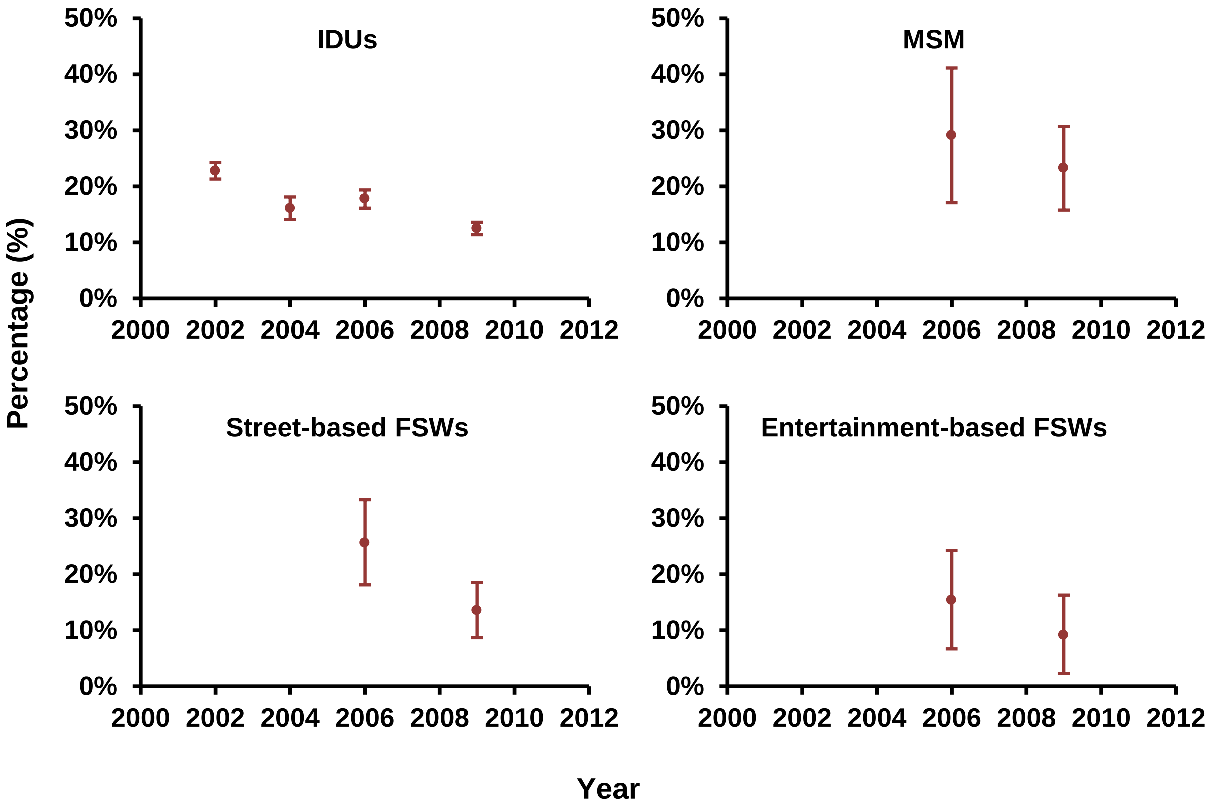


Figure S. 5: Average number of sexual acts with different sexual partners per year among IDUs, MSM and FSWs in Vietnam, 2000-2009

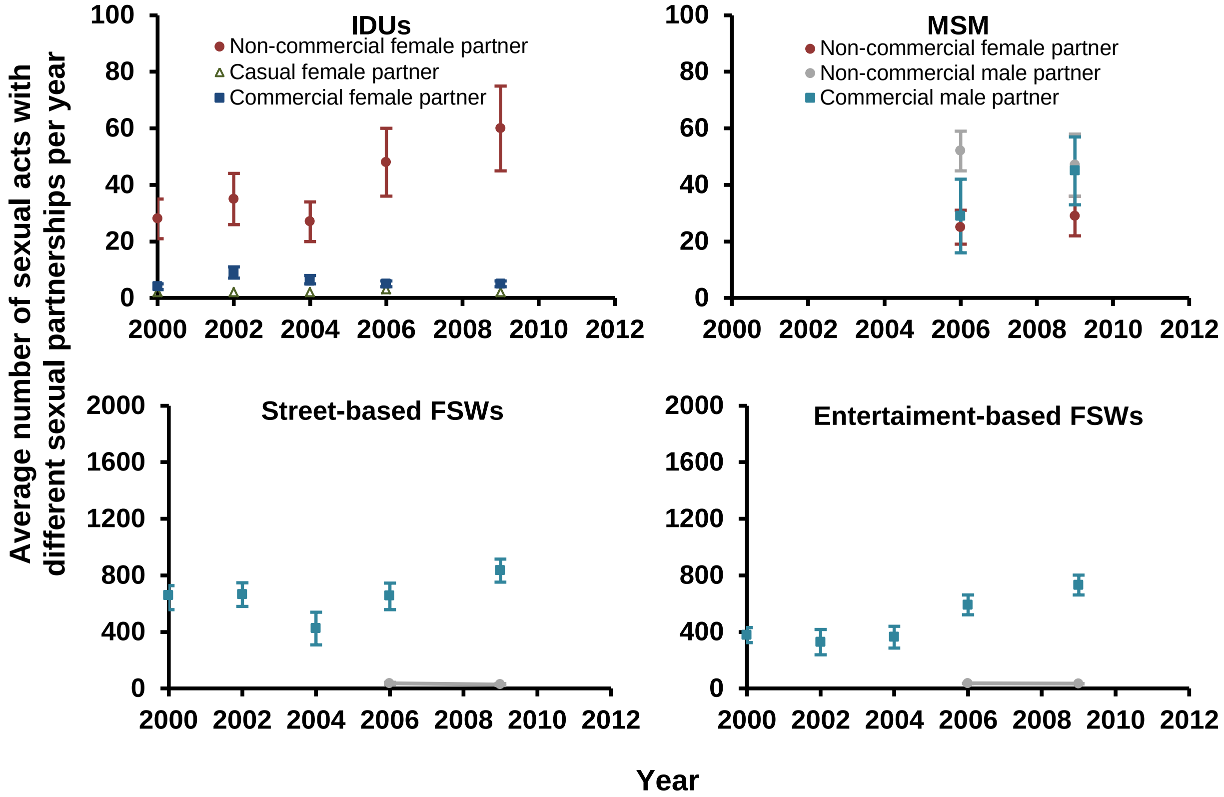


Figure S. 6: Proportion of people who reported using a condom at last sexual act by partner types among IDUs, MSM and FSWs in Vietnam, 2000-2009

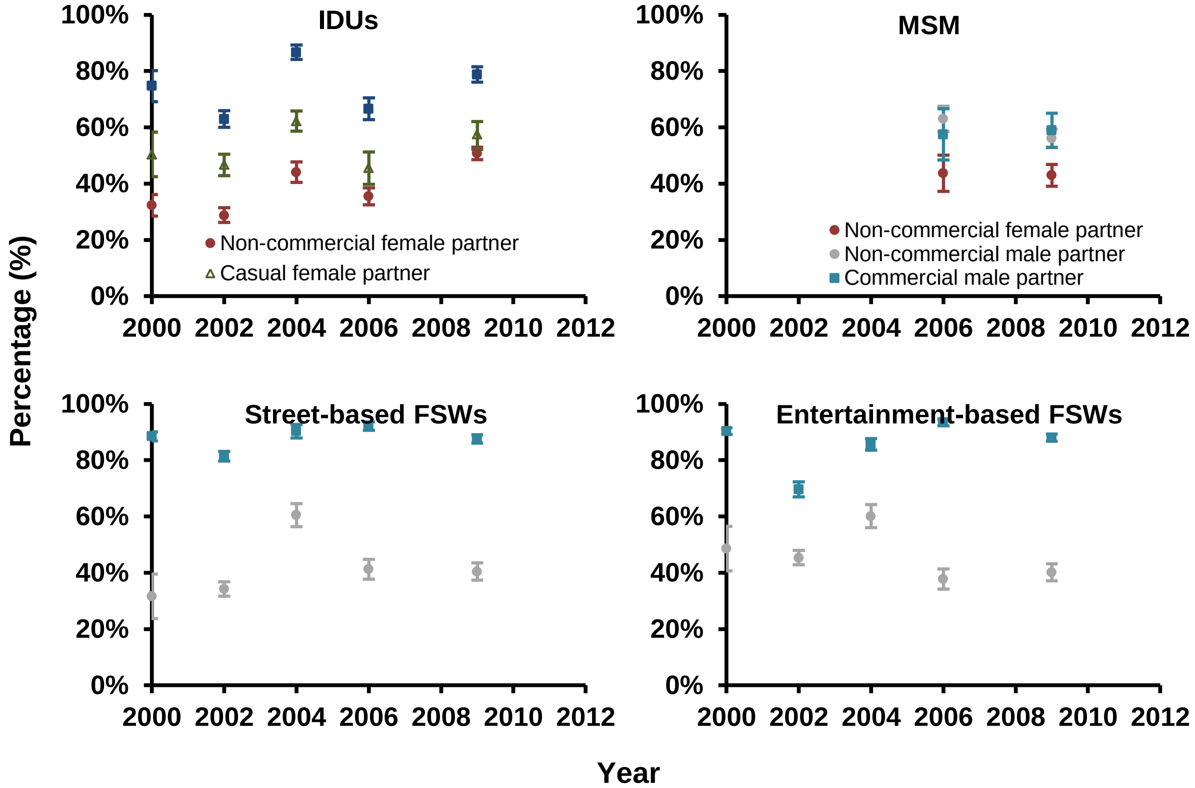


Figure S. 7: Proportion of people who reported having had a HIV test in the last 12 months among IDUs, MSM and FSWs in Vietnam, 2006-2009

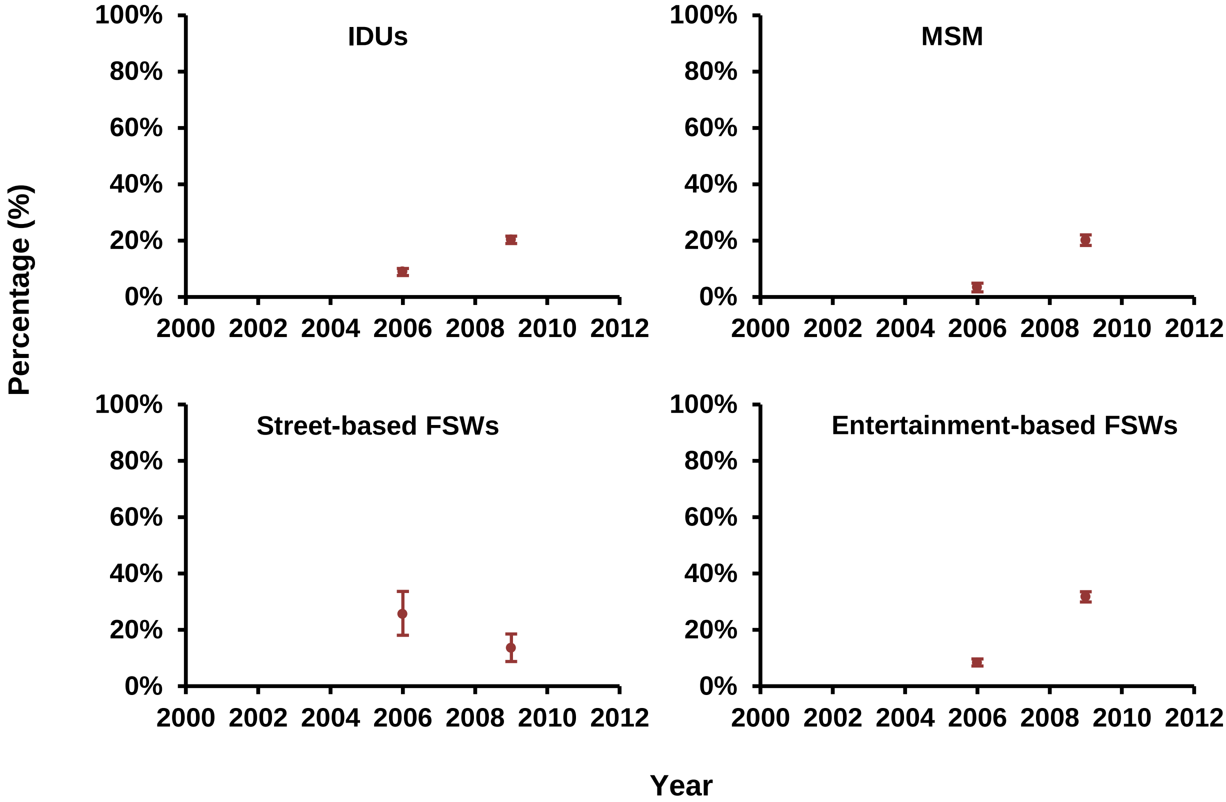


Figure S. 8: Number of reported HIV diagnoses in Vietnam, 2000-2011

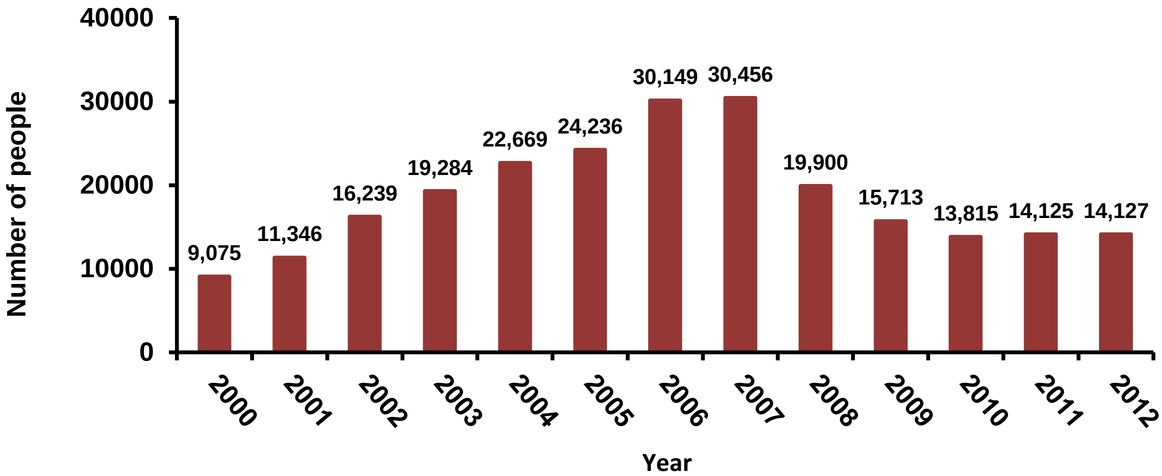


Figure S. 9: Number of commodities distributed in Vietnam, 2006-2010

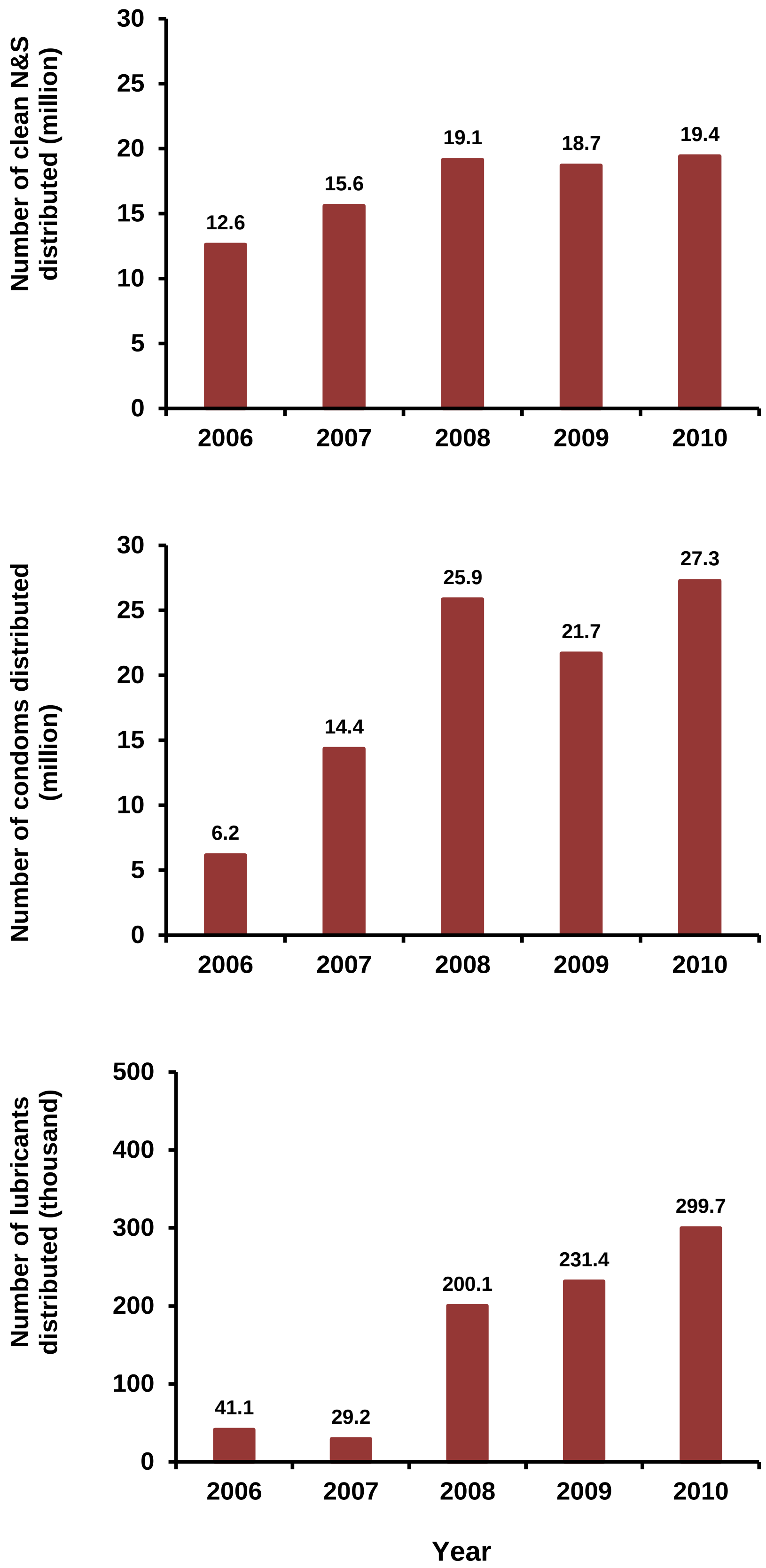


Figure S. 10: Number of IDUs registered methadone maintenance therapy

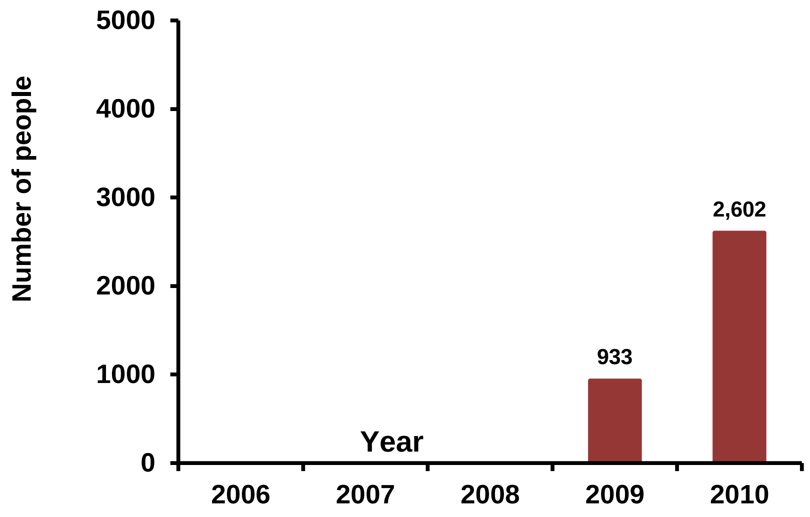


Figure S. 11: Number of people receiving ART in Vietnam, 2006-2010

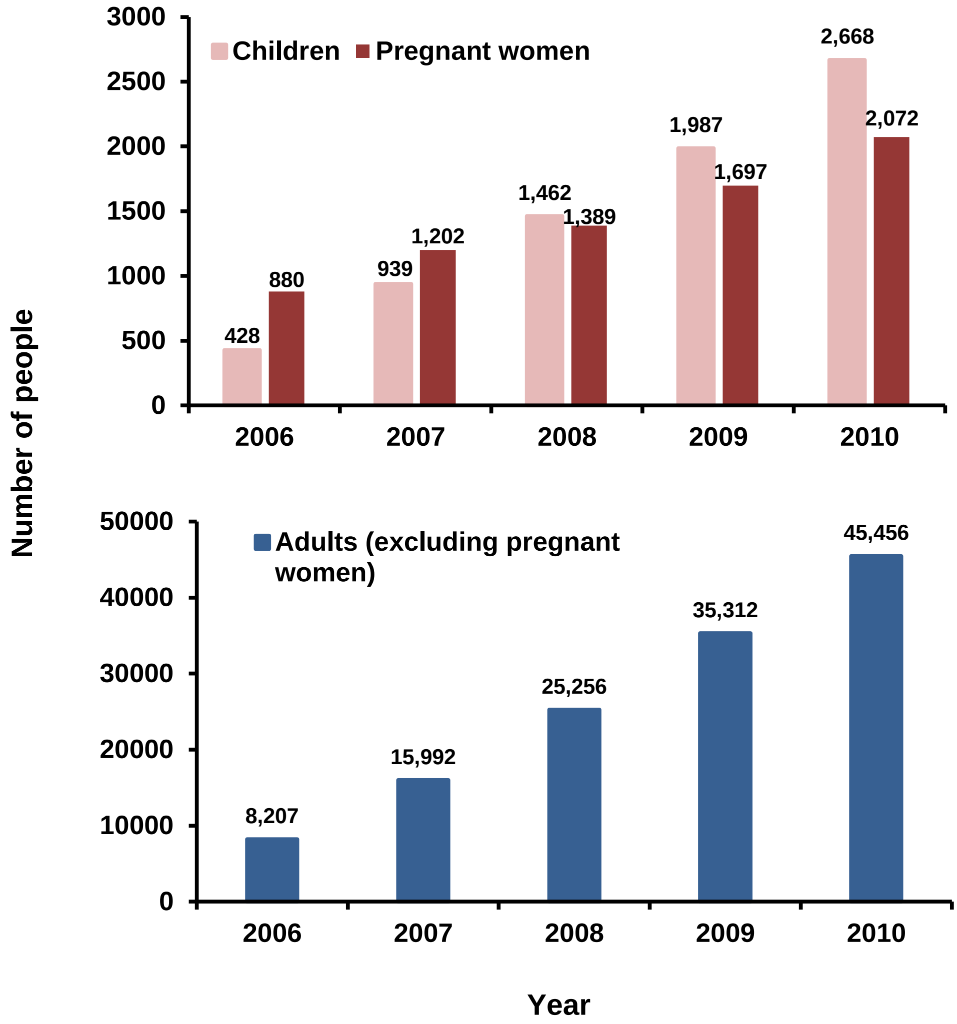


Table S. 1: Healthcare costs of HIV infected people in 2009

Stage of HIV Infection	Annual costs per person
PLHIV who have CD4 count >500 cells/mm^3	US $213.9
PLHIV who have CD4 count 350-500 cells /mm^3	US $348.6
PLHIV who have CD4 count 200-350 cells/mm^3	US $426.5
PLHIV who have CD4 count <200 cells/mm^3	US $566.6
Cost of first-line ART	US $519.0
Cost of second-line ART	US $1176.7
HIV diagnosis	US $7.2

Table S. 2: Health utilities for cost effectiveness calculations

Health utility parameters by populations	Average estimate	Lower estimate	Upper estimate
Uninfected IDU	0.86	0.85	0.87
Untreated population			
PLHIV with CD4 >500 cells/mm^3	0.72	0.70	0.73
PLHIV with CD4 350-500 cells/mm^3	0.57	0.56	0.58
PLHIV with CD4 200-350 cells/mm^3	0.43	0.42	0.43
PLHIV with CD4 <200 cells/mm^3	0.14	0.138	0.142
Treated population			
PLHIV on cART with CD4 >500 cells/mm^3	0.762	0.732	0.792
PLHIV on cART with CD4 350-500 cells/mm^3	0.756	0.735	0.777
PLHIV on cART with CD4 200-350 cells/mm^3	0.716	0.694	0.738
PLHIV on cART with CD4 <200 cells/mm^3	0.645	0.618	0.671

Appendix 2: Modeling HIV transmission in Vietnam

Model structure

We investigated the cost effectiveness of HIV prevention programs in Vietnam and the impact of changes in HIV funding using a detailed mathematical model of HIV transmission. Relating the changes in funding to the appropriate transmission parameters in the model, we calculated the change in HIV incidence, the number of HIV/AIDS deaths and cost-effectiveness of HIV prevention programs. To do this we used the Projection and Evaluation Tool (Prevtool), which was developed from the HIV in Indonesia Model (HIM). Previously, HIM was used to investigate the impact of HIV prevention programs in eight regions of Indonesia. A detailed description of Prevtool is available elsewhere. Here we provide a brief summary.

Informed by available HIV surveillance data the model divides the 15-49 year old into 7 distinct population groups in Vietnam:

- Low-risk males (LRM)and low-risk females (LRF)
- Direct and indirect female sex workers (DFSWs and IFSWs)
- Clients of FSW (CSWs)
- Men who have sex with men (MSM)
- Male injecting drug users (IDUs)

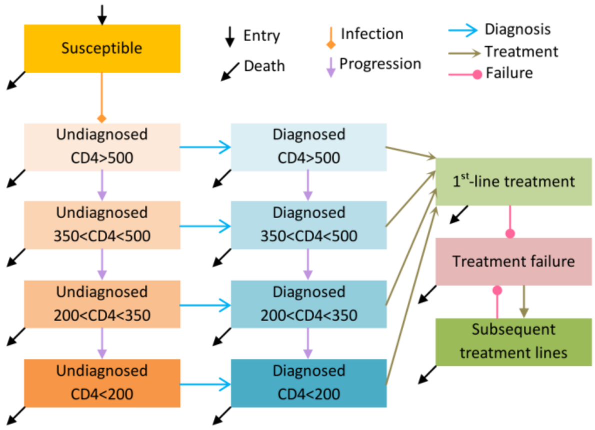
Prevtool was specifically calibrated for Vietnam using best-practice HIV epidemic modeling techniques incorporating realistic biological transmission processes, detailed infection progression, and sexual mixing patterns and drug injection behaviors. Through a set of ordinary differential equations, the model tracks HIV transmission and the number of HIV positive people and their rate of disease progression via CD4 count. Prevtool also records deaths due to HIV/AIDS or other causes. The model distinguishes people who are undiagnosed, diagnosed, and on effective anti-retroviral therapy (ART) as shown in Figure S.12. HIV transmission within the population occurs through the interaction between different population groups. HIV infections occur through regular, casual, or commercial sexual partnerships or through sharing of injecting equipment.

Table S. 3: Population interactions

	LRM	LRF	DFSWs	IFSWs	CSWs	MSM	IDUs
LRM		RC	RC	RC			
LRF							
DFSWs							
IFSWs							
CSWs		RC	RC$	RC$			
MSM		R	R	R		C$	
IDUs		RC	RC$	RC$			I

Notes: R, regular sex; C, casual sex; $, commercial sex; I, injecting. Rows show insertive acts and columns show receptive acts

Figure S. 12: Model schematic for HIV infection progression



Sexual transmission depends on the prevalence of HIV, the number of casual and regular homosexual and heterosexual partnerships per person, the frequency of sexual acts within a partnership, condom usage, male circumcision, and the infection stage of HIV-positive partners. For IDUs intravenous transmission is dependent on number of injecting partners, frequency of injecting, frequency of sharing equipment, cleaning of syringes, and the efficacy of cleaning. These factors are incorporated into risk-equations within the model to determine the annual per-capita risk of a susceptible person becoming infected with HIV. Prevtool describes the impact of HIV prevention programs indirectly through their influence on behavioral, clinical, and injecting parameters. Methadone maintenance programs (MMT) are explicitly incorporated into the model.

Model input parameters were informed by all available behavioral data regarding sexual or injecting risk activities, biological data on disease progression and heterogeneous transmission rates, and clinical data (such as rates of VCT and antiretroviral coverage). Any data available from 2000-2011 were used as inputs; where data were not available, assumptions were made based on consultations with Vietnamese stakeholders.

To calibrate Prevtool to the HIV epidemic, all parameters were first assigned a best estimate with uncertainty bounds. The model was then calibrated using adaptive stochastic linear gradient-descent optimization to identify parameter values that yielded epidemic projections that matched available population-level epidemiological data from 2000-2011 including HIV prevalence in each population group, the number of diagnoses, and the number of people on ART.

Mathematical details

The model uses a coupled system of ordinary differential equations to track the movement of people between health states. The overall population is partitioned in two ways: by group and by health state. Individuals are assigned to a given population based on their dominant risk; however, to capture important cross-modal types of transmission (e.g., FSW becoming infected via injecting drug use), relevant behavioral parameters can be set to small but nonzero values (e.g., male IDUs occasionally engage in commercial sex; CSW occasionally inject drugs).

The rate at which uninfected individuals in each population group become infected is determined by the force-of-infection for that population. This depends on the number of risk events an individual is exposed to in a given period of time and the infection probability of each event. Sexual transmission risk depends on the number of people in each HIV-infected stage (that is, the prevalence of infection in the population of partners), the average number of casual, regular, and commercial homosexual and heterosexual partnerships per person, the average frequency of sexual acts per partnership, the proportion of these acts in which condoms are used, the efficacy of condoms, the extent of male circumcision, and the prevalences of ulcerative STIs (which increase transmission probability) and HIV. The stage of infection (chronic, AIDS-related illness/late stage, or on treatment) for the HIV-positive partner in a serodiscordant couple also influences transmission risk due to different levels of infectiousness in each infection stage. Intravenous transmission risk depends on the number of injecting partners per person per year, frequency of injecting per year, frequency of sharing injecting equipment and percentage of shared syringes that are cleaned before re-use and the efficacy of cleaning.

Mathematically, the force-of-infection is given by:

$$\lambda = 1 - (1 - \beta)^n$$

where λ is the force-of-infection, β is the transmission probability of each event, and *n* is the effective number of at-risk events (thus *n* gives the average number interaction events with infected people where HIV transmission may occur). The value of the transmission probability β is inversely related to CD4 count, differs for different modes of transmission (intravenous drug injection, heterosexual intercourse, and homosexual intercourse), and may be modified by behavioral interventions (for example, condom use or circumcision). The number of events *n* not only incorporates the total number of events, but also other factors that moderate the possibility that these events are capable of transmitting infection, such as condom use or circumcision. There is one force-of-infection term for each type of interaction (for example, casual sexual relationships between low-risk males and indirect female sex workers), and the force-of-infection for a given population will be the sum of overall interaction types.

In addition to the force-of-infection rate, in which individuals move from uninfected to infected states, there are seven other means by which individuals may move between health states. First, individuals may die, either due to the background death rate (which affects all populations equally), due to injecting behavior, or due to HIV/AIDS (which depends on CD4 count). Second, in the absence of intervention, individuals progress from higher to lower CD4 counts. Third, individuals can move from undiagnosed to diagnosed states based on their HIV testing rate, which is a function of CD4 count (for example, people with AIDS symptoms have a higher testing rate) and population type (for example, IDUs usually get tested more frequently than low-risk males). Fourth, diagnosed individuals may move onto treatment, at a rate which is dependent on CD4 count. Fifth, individuals may move from treatment to treatment failure, and sixth, from treatment failure onto second-line treatment. Finally, while on successful first- or second-line treatment, individuals may progress from lower to higher CD4 count.

In total, the model can accommodate up to 294 compartments (14 populations each with 21 health states), and the change in the number of people in each compartment is determined by the sum over the relevant rates described above multiplied by the compartments on which they act. For example, the number of individuals in the compartment corresponding to undiagnosed female sex workers with a CD4 count between 200 and 350 cells/□L changes according to the following equation:

$$\frac{dU_{FSW200-350}}{dt} = U_{FSW_{350-500}}\tau_{350-500} - U_{FSW_{200-350}}(\mu_{200-350} + \tau_{200-350} + \eta_{FSW_{350-500}})$$

where $U_{FSW_{350-500}}$ is the current population size of people with undiagnosed HIV and with a CD4 count between 350 and 500 cells/μL, $U_{FSW_{200-350}}$ is the population size of the compartment with lower CD4 count (200-350 cells/μL), τ is the disease progression rate for the given CD4 count, μ is the death rate, and η is the HIV testing rate. (Note: this example does not consider movement between populations, such as female sex workers returning to the low-risk female population and vice versa.) Each compartment (Fig. S.12, boxes) corresponds to a single differential equation in the model, and each rate (Fig. S.12, arrows) corresponds to a single term in that equation.

Model parameters

Table S. 4 shows the best-fit model parameters for 2012, along with the median empirical data value over the range 2000-2012, with the associated uncertainty interval.

Table S. 4: Model and data parameters.

Parameter name		Model value (2012)	Data value (2000-2012)
Populationsize:			
	LRM:	27000000	29000000 (28000000, 30000000)
	LRF:	26000000	33000000 (33000000, 33000000)
	DFSW:	110000	44000 (20000, 68000)
	IFSW:	130000	54000 (24000, 84000)
	CSW:	3300000	2400000 (1600000, 3200000)
	MSM:	740000	290000 (180000, 390000)
	IDU:	690000	220000 (98000, 340000)
stiprevalence:			
	LRM:	1.00%	0% (0%, 0%)
	LRF:	1.00%	0% (0%, 0%)
	DFSW:	20%	12% (10%, 15%)
	IFSW:	20%	9.4% (7.4%, 11%)
	CSW:	1.00%	1.4% (0.53%, 3.5%)
	MSM:	12%	18% (16%, 20%)
	IDU:	20%	1.3% (0.95%, 1.9%)
testingrate:			
	LRM:	0.01	0.026 (0.022, 0.030)
	LRF:	0.01	0.021 (0.018, 0.025)
	DFSW:	0.05	0.17 (0.15, 0.18)
	IFSW:	0.05	0.20 (0.19, 0.22)
	CSW:	0.01	0.19 (0.14, 0.23)
	MSM:	0.05	0.13 (0.12, 0.15)
	IDU:	0.05	0.15 (0.13, 0.16)
testingrateaids:		0.4	0.80 (0.60, 0.90)

treatment1rate:			
	>500:	0	0.00020 (0.00010, 0.00030)
	350-350:	0	0.00020 (0.00010, 0.00030)
	200-350:	0.2	0.38 (0.28, 0.47)
	<200:	0.5	0.35 (0.26, 0.44)
treatment2rate:		0.15	0.050 (0.025, 0.075)
numdiagnoses:		0	16000 (15000, 18000)
numactsregular:			
	LRM:	45	50 (38, 63)
	LRF:	45	52 (36, 65)
	DFSW:	26	33 (26, 39)
	IFSW:	26	35 (29, 41)
	CSW:	75	98 (73, 120)
	MSM:	20	27 (21, 34)
	IDU:	34	35 (26, 44)
numactscasual:			
	LRM:	2.7	2.0 (1.0, 3.0)
	LRF:	2.7	2.0 (1.0, 3.0)
	DFSW:	2.7	2.0 (1.0, 3.0)
	IFSW:	2.7	2.0 (1.0, 3.0)
	CSW:	2.7	2.0 (1.0, 3.0)
	MSM:	50	50 (37, 62)
	IDU:	2.7	2.0 (1.0, 3.0)
numactsother:			
	LRM:	0.0011	0 (0, 0)
	LRF:	0.0011	0 (0, 0)
	DFSW:	600	660 (560, 750)
	IFSW:	66	380 (330, 440)
	CSW:	1200	34 (26, 43)
	MSM:	25	37 (28, 46)
	IDU:	4.3	5.0 (4.0, 6.0)
condomprobregular:			
	LRM:	20%	19% (17%, 22%)
	LRF:	20%	14% (13%, 16%)
	DFSW:	45%	40% (37%, 44%)
	IFSW:	45%	45% (38%, 48%)
	CSW:	31%	29% (23%, 37%)
	MSM:	44%	43% (38%, 48%)
	IDU:	39%	36% (33%, 39%)
condomprobcasual:			
	LRM:	30%	76% (65%, 79%)
	LRF:	30%	7.1% (0.80%, 23%)
	DFSW:	40%	0% (0%, 0%)

IFSW:	40%	0% (0%, 0%)
CSW:	29%	0% (0%, 0%)
MSM:	58%	60% (56%, 63%)
IDU:	50%	50% (43%, 58%)
condomprobother:		
LRM:	0%	0% (0%, 0%)
LRF:	0%	0% (0%, 0%)
DFSW:	95%	89% (87%, 90%)
IFSW:	95%	88% (87%, 89%)
CSW:	95%	95% (91%, 97%)
MSM:	70%	58% (51%, 66%)
IDU:	70%	75% (69%, 80%)
circumcisionprob:		
LRM:	5.00%	5.0% (2.0%, 6.0%)
LRF:	0%	0% (0%, 0%)
DFSW:	0%	0% (0%, 0%)
IFSW:	0%	0% (0%, 0%)
CSW:	5.00%	5.0% (2.0%, 6.0%)
MSM:	10%	10% (8.0%, 12%)
IDU:	10%	10% (8.0%, 12%)
numinjections:		
LRM:	0	0.0020 (0.0010, 0.0030)
LRF:	0	0.0020 (0.0010, 0.0030)
DFSW:	31	53 (40, 66)
IFSW:	31	18 (14, 23)
CSW:	25	28 (21, 35)
MSM:	20	22 (21, 23)
IDU:	390	560 (480, 800)
syringesharingprob:	10%	17% (15%, 19%)
methadoneprob:	0.00%	0.85% (0.55%, 1.9%)
syringecleaningprob:	74%	8.3% (4.9%, 14%)
initialhivprevalence:		
LRM:	0.37%	0.40% (0.30%, 0.60%)
LRF:	0.37%	0.26% (0.16%, 0.41%)
DFSW:	3.00%	3.0% (2.0%, 4.0%)
IFSW:	1.50%	2.5% (2.0%, 3.0%)
CSW:	2.20%	1.0% (0.55%, 1.8%)
MSM:	3.00%	3.0% (2.0%, 5.0%)
IDU:	20%	23% (19%, 29%)
transheteroinsertive:	0.0015	0.00040 (0.00010, 0.0010)
transheteroreceptive:	0.00067	0.0010 (0.00060, 0.0060)
transhomoinsertive:	0.00067	0.00060 (0.00020, 0.0020)
transhomoreceptive:	0.0024	0.0050 (0.0020, 0.020)

transinjecting:		0.00041	0.0030 (0.0010, 0.010)
transbycd4:			
	>500:	1.6	1.6 (1.2, 1.8)
	350-350:	1	1.0 (0.80, 1.2)
	200-350:	1	1.0 (0.80, 1.2)
	<200:	3.8	3.8 (3.6, 4.0)
transontreatment:		0.0004	0.00040 (0.00020, 0.0010)
progressionrate:			
	>500:	0.25	0.25 (0.23, 0.26)
	350-350:	0.51	0.51 (0.47, 0.55)
	200-350:	0.51	0.51 (0.47, 0.55)
recoveryrate:			
	>500:	0.45	0.45 (0.14, 0.93)
	350-350:	0.7	0.70 (0.29, 1.1)
	200-350:	0.36	0.36 (0.28, 0.43)
deathbackground:		0.014	0.014 (0.0094, 0.020)
deathinjecting:		0.01	0.010 (0.0075, 0.013)
deathhiv:			
	>500:	0.00051	0.00052 (0.00035, 0.00068)
	350-350:	0.0013	0.0013 (0.00092, 0.0016)
	200-350:	0.011	0.011 (0.0020, 0.020)
	<200:	0.5	0.50 (0.40, 0.66)
deathtreatment:		0.040	0.040 (0.010, 0.10)
treatment1failurerate:		0.045	0.045 (0.030, 0.060)
treatment2failurerate:		0.045	0.045 (0.030, 0.060)
condomefficacy:		95%	95% (85%, 99%)
circumcisionefficacy:		60%	60% (50%, 65%)
stitransincrease:		2	2.0 (1.0, 4.0)
syringecleaningefficacy:		75%	75% (70%, 80%)
methadoneefficacy:		95%	95% (90%, 99%)

Model inputs

The below table indicates model inputs at national level. Main data sources include:

1. 2000 HIV/AIDS Behavioral Surveillance Survey (BSS 2000).
2. 2002 and 2004 Baseline and Endpoint Survey Report of ADB Project.
3. 2005-2006 HIV/STI Integrated Biological and Behavioral Surveillance.
4. 2009 HIV/STI Integrated Biological and Behavioral Surveillance (IBBS 2009).
5. Estimated size of at-risk population by the Vietnam Authority of HIV/AIDS Control.
6. General Statistics Office of Vietnam.

Table S. 5: Mathematical modeling inputs at national level

Parameters	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	Ref
Low risk males (excluding men who do not inject drugs, clients of female sex workers, and men who have sex with men)												
Estimated population size (in thousand [min-max]										28,803 (27,759–29,782		[11, 12]
Average number of regular sexual acts per year						50 (38–63)						[13]
Average number of casual sexual acts per year						1 (1–1)						[13]
Condom use percentage for last sex act with regular partner						19.2% (17.1–21.5%)			22.6% (20.9–24.2%)			[14, 15]
Condom use percentage for last sex act with casual partner						75.5% (62.5–79.1%)						[14, 15]
Circumcision probability	5.0% (2.0–6.0%)											[*]
HIV testing rate per year						2.6% (2.2–3.0%)						[13]
Male clients of female sex workers												
Estimated population size (in thousand [min-max]										2,372 (1,582–3,163)		[11]
Average number of regular sexual acts per year								98 (73–122)				[16]
Average number of casual sexual acts per year								34 (26–43)				[16]
Condom use percentage for last sex act with regular partner								29.4% (22.9–36.9%)				[16]
Condom use percentage for last sex act with casual partner								94.5% (91.3–96.6%)				[16]
Circumcision probability	5.0% (2.0–6.0%)											[*]
Average number of injections per year								28 (21–35)				[16]
HIV testing rate per year								18.5% (14.5–23.3%)				[16]
Prevalence of syphilis								1.37% (0.53–3.46%)				[16]
Injecting drug users												
Estimated population size (in thousand [min-max]										217 (98–335)		[11]

Average number of regular sexual acts per year	28 (21–35)		35 (26–44)		27 (20–35)		48 (36–60)			60 (45–75)		[4, 5, 17-19]
Average number of casual sexual acts per year	2 (2–3)		2 (2–3)		2 (2–3)		3 (2–4)			2 (2–3)		[4, 5, 17-19]
Average number of commercial sexual acts per year	4 (3–5)		9 (7–11)		6 (5–8)		5 (4–6)			5 (4–6)		[4, 5, 17-19]
Condom use percentage for last sex act with regular partner	32.3% (28.5–36.1%)		28.7% (26.2–31.4%)		44.0% (40.4–47.7%)		35.5% (32.5–38.5%)			50.7% (48.5–52.9%)		[4, 5, 17-19]
Condom use percentage for last sex act with casual partner	50.4% (42.5–58.3%)		46.8% (42.8–50.5%)		62.2% (58.6–65.8%)		45.6% (39.8–51.3%)			57.6% (52.1–62.1%)		[4, 5, 17-19]
Condom use percentage for last sex act with commercial partner	74.7% (69.1–80.1%)		62.9% (60.0–65.9%)		86.6% (84.1–89.2%)		66.6% (62.7–70.5%)			78.7% (76.0–81.5%)		[4, 5, 17-19]
Circumcision probability	10.0% (8.0-12.0%)											[20]
Average number of injections per year	562 (511–851)		514 (385–642)		217 (162–642)		684 (513–855)			637 (478–796)		[4, 5, 17-19]
Percentage of shared injections			22.8% (21.3–24.3%)		16.1% (14.1–18.1%)		17.8% (16.1–19.4%)			12.5% (11.4–13.6%)		[4, 5, 17, 19]
Percentage of reused syringes that are cleaned					4.8% (2.1–10.7%)	11.9% (7.7–18.1%)						[21]
HIV testing rate per year							8.9% (7.6–10.1%)			20.3% (19.0–21.6%)		[4, 5]
Prevalence of syphilis							1.8% (1.3–2.5%)			0.8% (0.6–1.2%)		[4, 5]
Men who have sex with men												
Estimated population size (in thousand [min-max]										385 (177–393)		[11]
Average number of sexual acts with non-commercial female partners per year							25 (19–31)			29 (22–36)		[4, 5]
Average number of sexual acts with non-commercial male partners per year							52 (39–65)			47 (35–59)		[4, 5]
Average number of sexual acts with commercial male partners per year							29 (22–36)			45 (34–56)		[4, 5]
Condom use percentage for last sex act with non-commercial female partner							43.7% (37.3–50.1%)			43.0% (39.1–46.8%)		[4, 5]
Condom use percentage for last sex act with non-commercial male partner							63% (58.5–67.5%)			56.1% (53.0–59.3%)		[4, 5]
Condom use percentage for last sex act with commercial male partner							57.5 (48.4–66.6%)			58.9% (52.8–65.0%)		[4, 5]
Circumcision probability	10.0% (8.0-12.0%)											[20]

Average number of injections per year							23 (22–24)			20 (19–21)			[4, 5]
Percentage of shared injections							29.1% (17.1–41.1%)			23.3% (15.8–30.7%)			[4, 5]
HIV testing rate per year							5.0% (3.4–6.5%)			21.9% (20.1–23.8%)			[4, 5]
Prevalence of sexually transmitted infections							22.9% (20.0–25.8%)			13.6% (12.1–15.1%)			[4, 5]
Low risk females (excluding female sex workers)													
Estimated population size (in thousand [min-max]										32,960 (32,918–33,002)			[11, 12]
Average number of regular sexual acts per year						52 (36–65)							[15]
Average number of casual sexual acts per year						0 (n/a)							[15]
Condom use percentage for last regular sex act						14.5% (12.9–16.3%)							[15]
Condom use percentage for last casual sex act						7.1% (0.8–22.7%)							[15]
HIV testing rate per year						2.1% (1.8–2.5%)							[15]
Street-based female sex worker													
Estimated population size (in thousand [min-max]										29 (13–45)			[11]
Average number of non-commercial sexual acts per year							36 (29–43)			29 (22–35)			[4, 5]
Average number of commercial sexual acts per year	658 (558–728)		664 (580–748)		424 (308–540)		655 (558–745)			834 (753–916)			[4, 5, 17-19]
Condom use percentage for last sex act with non-commercial partner	31.6% (23.7–39.5%)		34.2% (31.7–36.8%)		60.5% (56.4–64.6%)		41.3% (37.7–44.8%)			40.4% (37.4–53.7%)			[4, 5, 17-19]
Condom use percentage for last sex act with commercial partner	88.5% (86.9–90.1%)		81.4% (79.7–83.1%)		90.3% (87.9–92.7%)		92.1% (90.6–93.6%)			87.5% (86.1–89.0%)			[4, 5, 17-19]
Average number of injections per year							49 (37–61)			57 (43–71)			[4, 5]
Percentage of shared injections							25.6% (18.1–33.3%)			13.6% (8.7–18.5%)			[4, 5]
HIV testing rate per year							7.4% (6.1–8.7%)			26.5% (24.8–28.2%)			[4, 5]
Prevalence of sexually transmitted infections			22.8% (18.6–26.9%)		17.8% (14.3–21.4%)		7.1% (5.9–8.4%)			3.4% (2.7–4.1%)			[4, 5, 22]
Entertainment-based female sex worker													

Estimated population size (in thousand [min-max]										36 (16–56)		[11]
Average number of non-commercial sexual acts per year							36 (30–42)			34 (28–40)		[4, 5]
Average number of commercial sexual acts per year	377 (325–431)		327 (238–417)		365 (286–440)		591 (521–661)			730 (661–801)		[4, 5, 17-19]
Condom use percentage for last sex act with non-commercial partner	48.6% (36.5–60.8%)		45.3% (42.3–48.2%)		60.1% (57.2–62.9%)		37.8% (34.8–62.9%)			40.1% (37.5–42.7%)		[4, 5, 17-19]
Condom use percentage for last sex act with commercial partner	90.3% (89.1–91.5%)		69.6% (66.9–72.3%)		85.6% (83.6–87.7%)		93.4% (92.2–94.6%)			88.0% (86.7–89.3%)		[4, 5, 17-19]
Average number of injections per year							19 (14–24)			17 (13–21)		[4, 5]
Percentage of shared injections							15.4% (7.1–19.6%)			31.7% (29.9–33.5%)		[4, 5]
HIV testing rate per year							8.4% (7.1–9.6%)			31.7% (29.9–33.5%)		[4, 5]
Prevalence of sexually transmitted infections			20.4% (16.9–24.0%)		15.1% (12.0–18.1%)		3.7% (2.8–4.5%)			2.3% (1.8–2.9%)		[4, 5, 22]

*Note: * internal communications with an experienced epidemiologist in Vietnam*

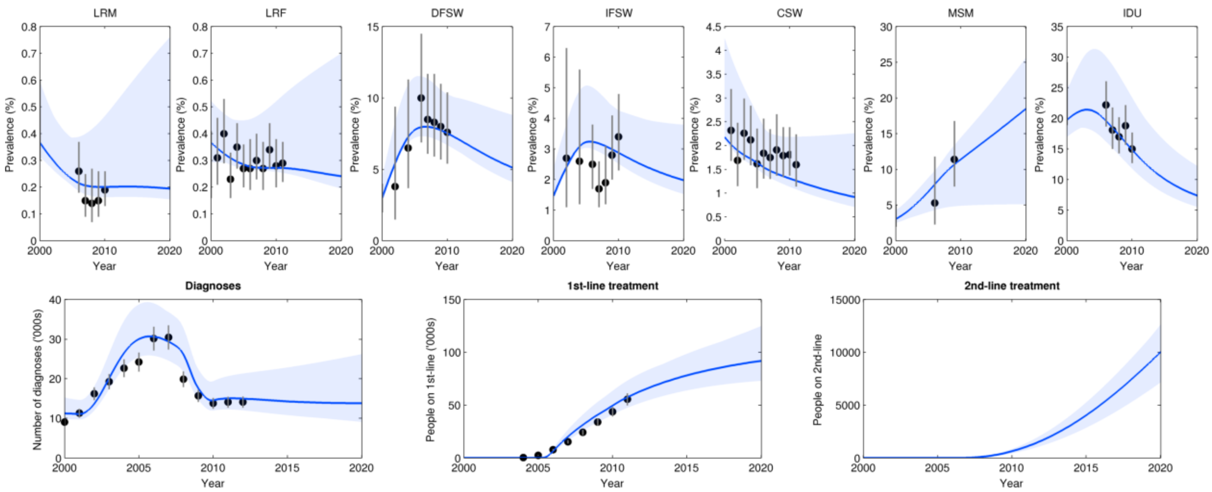
Appendix 3: Calibration of model to the HIV epidemic in Vietnam

Prevtool was calibrated to HIV prevalence in each population group Vietnam over 2000-2011. While primarily calibrated to match HIV prevalence, Prevtool also optimized input parameters to match available behavioral data for this period, as well as data on diagnoses and treatment.

The figure below shows the modeled HIV prevalence for each population group (blue lines) compared to prevalence data (black dots), along with a 95% confidence interval (gray shading).

The calibrated input parameters and resulting model simulation represent the baseline conditions for the 2000 to 2011 period. The values of each parameter in 2011 represent current conditions.

Figure S. 13: Calibrated input parameters by Prevtool



Appendix 4: Relationships between HIV/AIDS spending and behavioral parameters

In this analysis, a logistic function was used to describe the relationship between a behavioral parameter affected by a HIV prevention program and the level of spending on that program. Seven HIV prevention programs were evaluated and details of selected key behaviors that are more likely influenced by an intervention are summarized in Table S4.1. Using this function with assumed uncertainties bounds, we obtained logistic curve fits to available datasets for overall program spending and associated behaviors. We assume the behavioral indicators in 2000 correspond to the background behavioral patterns in the absence of HIV prevention programs in Vietnam.

In the following figures, black dots represent the actual empirical data, whereas the blue line represents the fitted curve. It is important to note that each plot shows the level of behaviour changes in relation to our presumed financial investments at the national level for the five key HIV interventions in Vietnam.

Table S. 6: Selected behaviors affected by HIV prevention programs

HIV prevention program	Targeted behavior
1. Needle-syringe exchange program (NSP)	Percentage of IDUs who report sharing injections in the past month Average number of injections per year
2. Methadone maintenance therapy (MMT)	Percentage of IDUs receiving MMT
3. 100% condom use for FSWs	Percentage of condom use in the last sex acts with commercial partners in FSWs Percentage of condom use in the last sex acts with non-commercial partners in FSWs
4. 100% condom use and lubricant for MSM	Percentage of condom use in the last sex acts with commercial male partners in MSM Percentage of condom use in the last sex acts with non-commercial male partners in MSM
5. Mass communication and untargeted condom promotion	Percentage of condom use in the last sex acts with spouse/lover in general population aged 15-49 years
6. STI management and treatment	STI prevalence among FSWs STI prevalence among MSM
7. HIV voluntary counseling and testing (VCT)	Percentage of HIV testing in the past 12 months in FSWs Percentage of HIV testing in the past 12 months in MSM Percentage of HIV testing in the past 12 months in IDUs Percentage of HIV testing in the past 12 months in FSWs

Figure S. 14: Relationships between IDU behavioral parameters and spending on NSP and MMT in Vietnam, 2006-2010

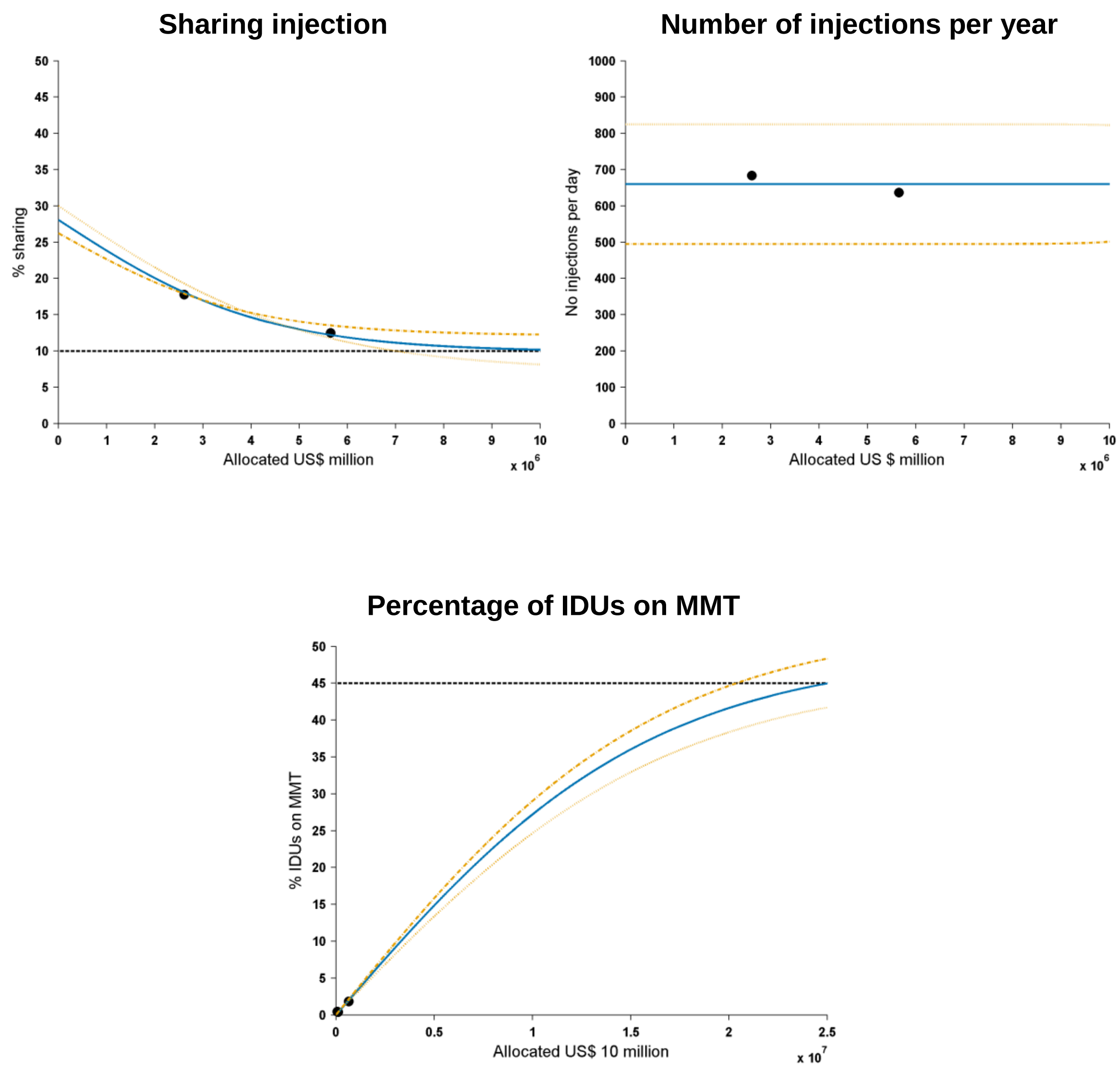
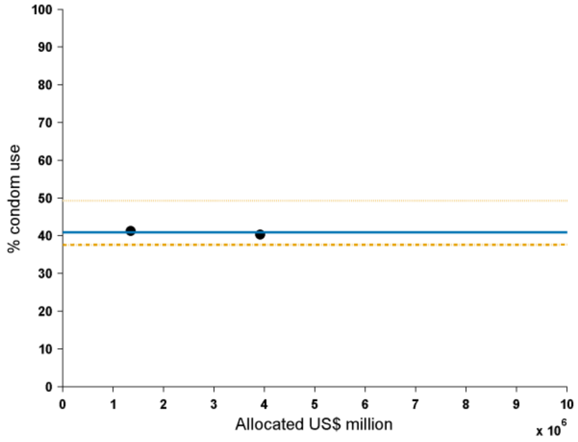


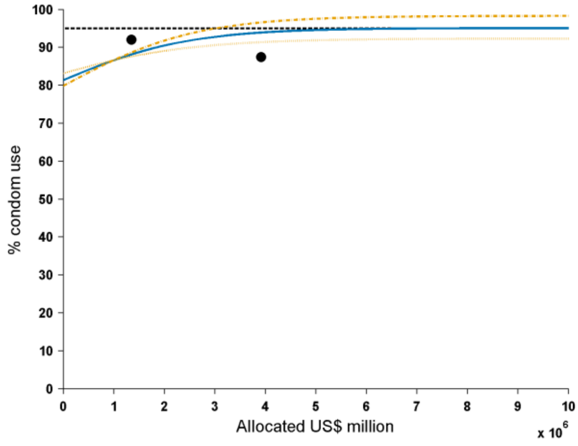
Figure S. 15: Relationships between FSW behavioral parameters and spending on condom promotion program targeting FSW in Vietnam, 2006-2010

Street-based FSW

Condom use with non-commercial partners

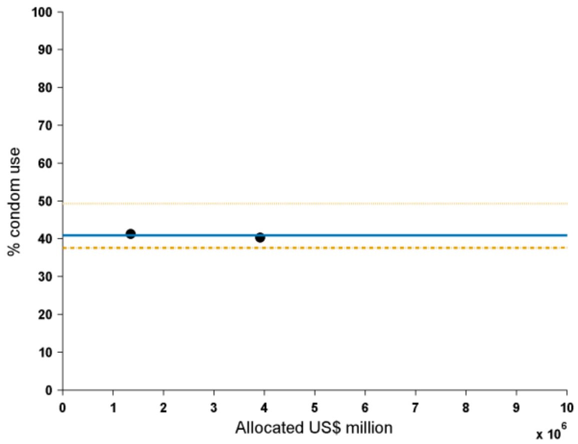


Condom use with commercial partners



Entertainment-based FSW

Condom use with non-commercial partners



Condom use with commercial partners

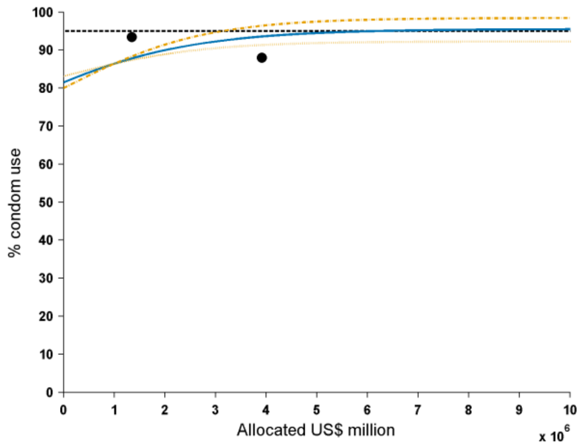


Figure S. 16: Relationships between MSM behavioral parameters and spending on condom promotion program targeting MSM in Vietnam, 2006-2010

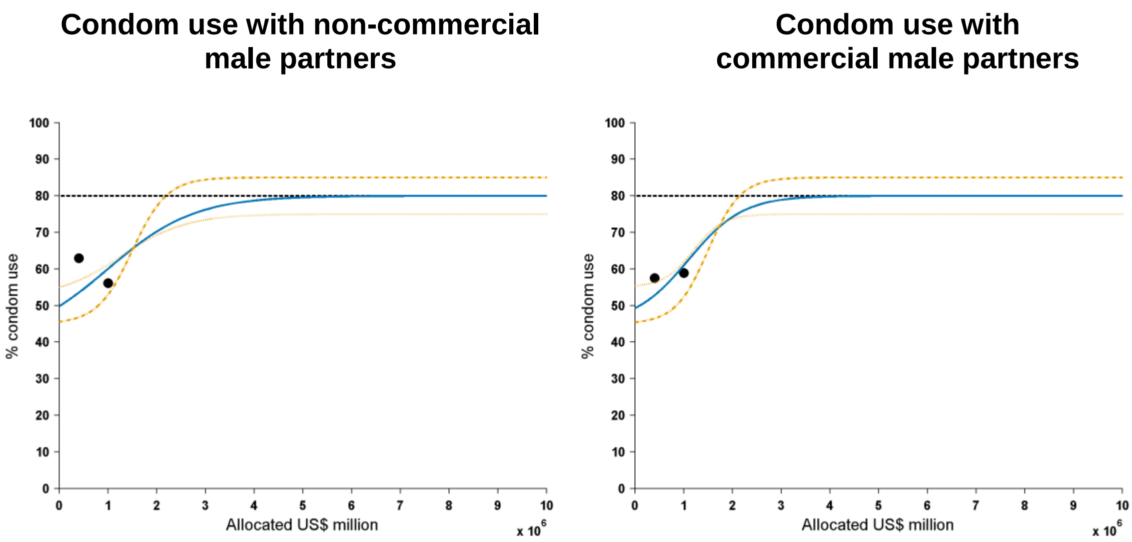


Figure S. 17: Relationships between condom use and spending on mass information education communication and untargeted condom promotion program in general population in Vietnam, 2006-2010

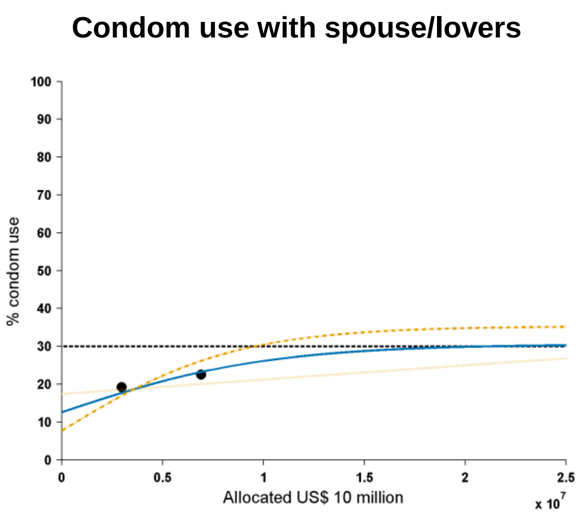


Figure S. 18: Relationships between STI prevalence and STI spending in Vietnam, 2006-2010

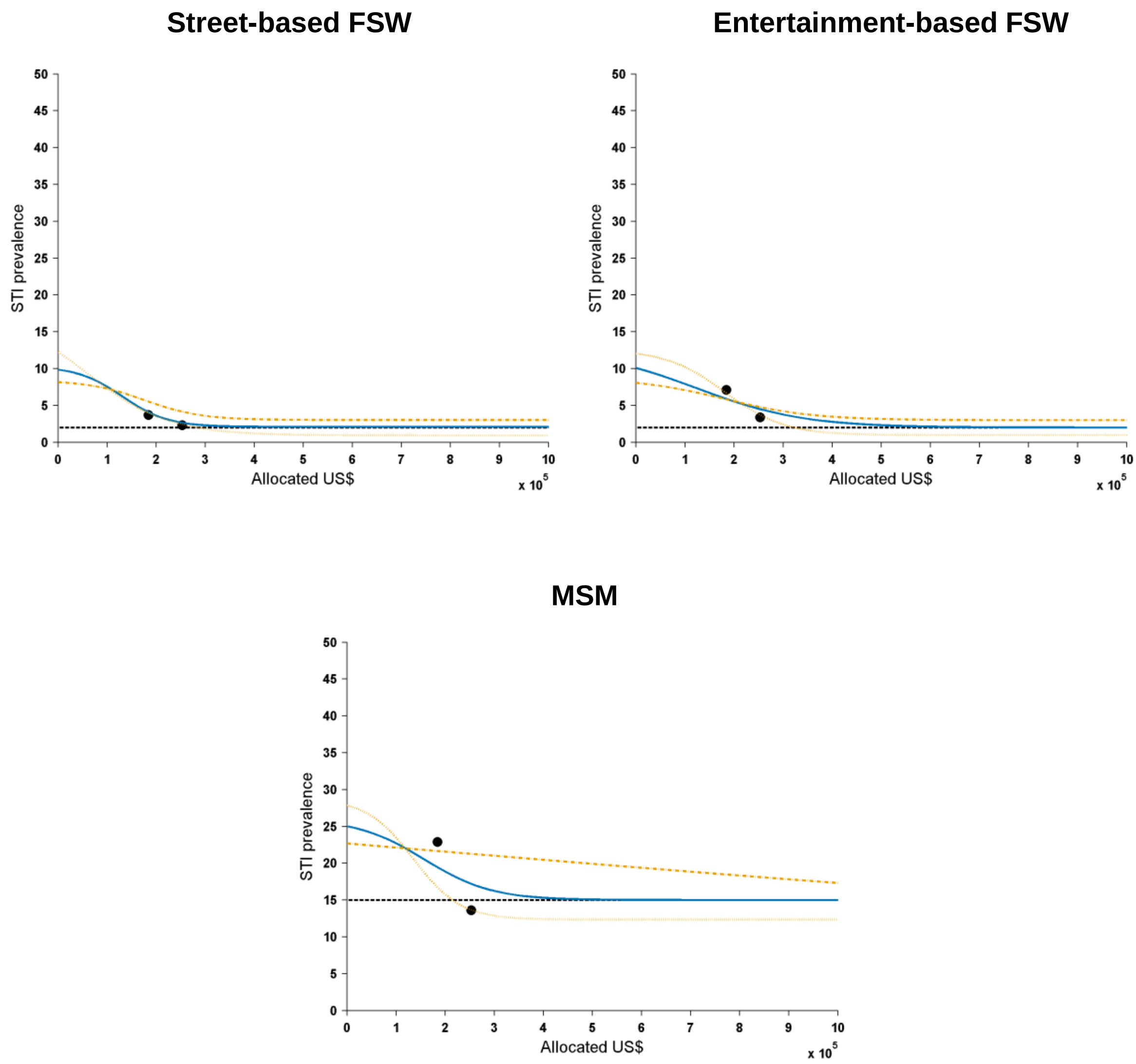
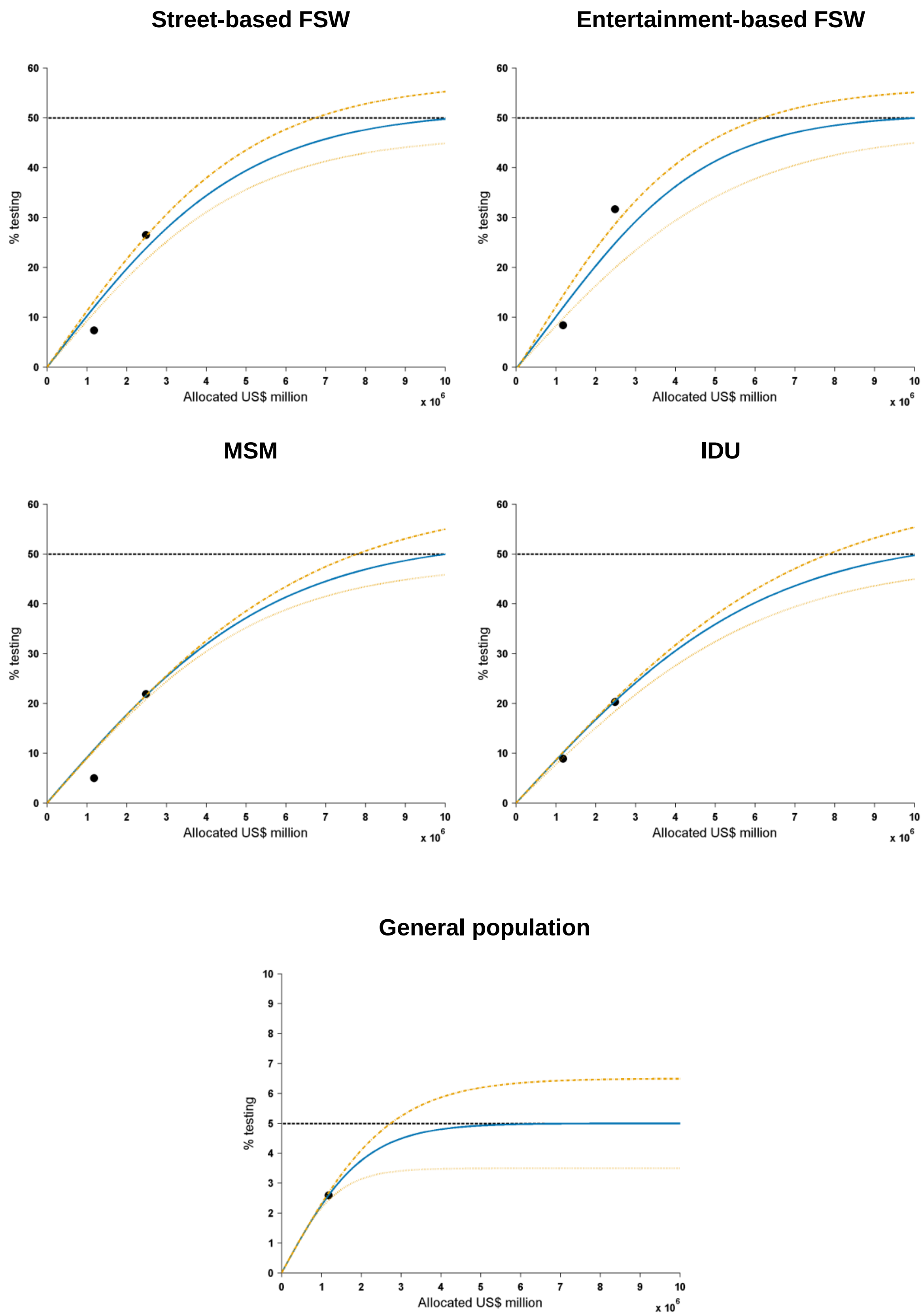


Figure S. 19: Relationships between HIV testing and VCT spending in Vietnam, 2006-2010



Appendix 5: Counterfactual scenarios in the absence of HIV interventions

Using a generalized 4-parameter logistic function, for each at-risk populations and general population we calibrated the behavioral parameters from 2000 to 2015 affected by prevention programs targeting that population in a counterfactual scenario to determine the cost-effectiveness of HIV program funding in Vietnam. These scenarios were based on the assumed effect of the removal of specific programs. The initial values are assumed parameters in 2000 and the saturate/stable values of scenario at 2015 are assumed to be at the similar levels as the staring year of each implementations or locations in the absence of the intervention programs. All counterfactual scenarios are plotted below. In these plots, the black dots represent the actual empirical data. The blue curves represented the best-fitted curve to the empirical data obtained during calibration process using a generalized logistic function, whereas the red curves represent scenario in the absence of interventions.

Figure S. 20: Counterfactual of NSP and MMT for IDU

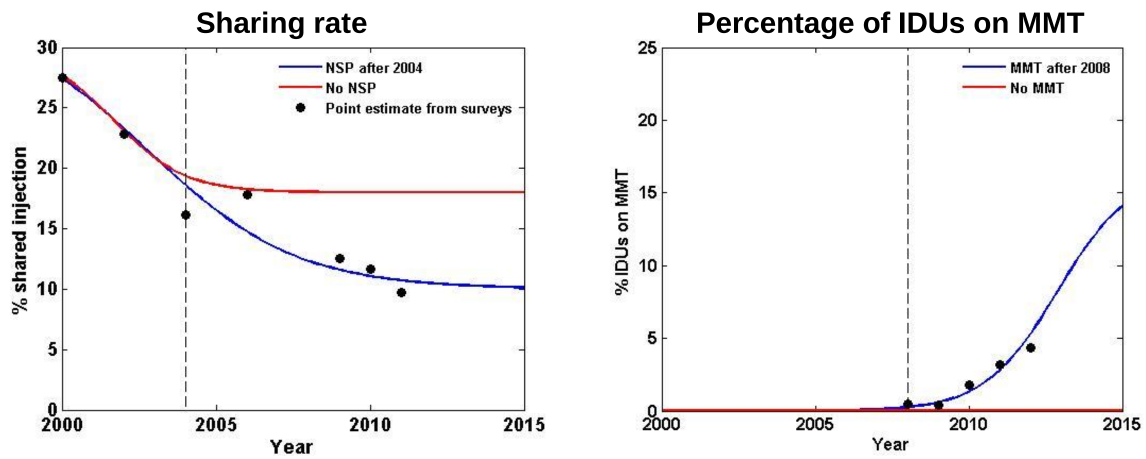


Figure S. 21: Counterfactual of condom use program for FSW

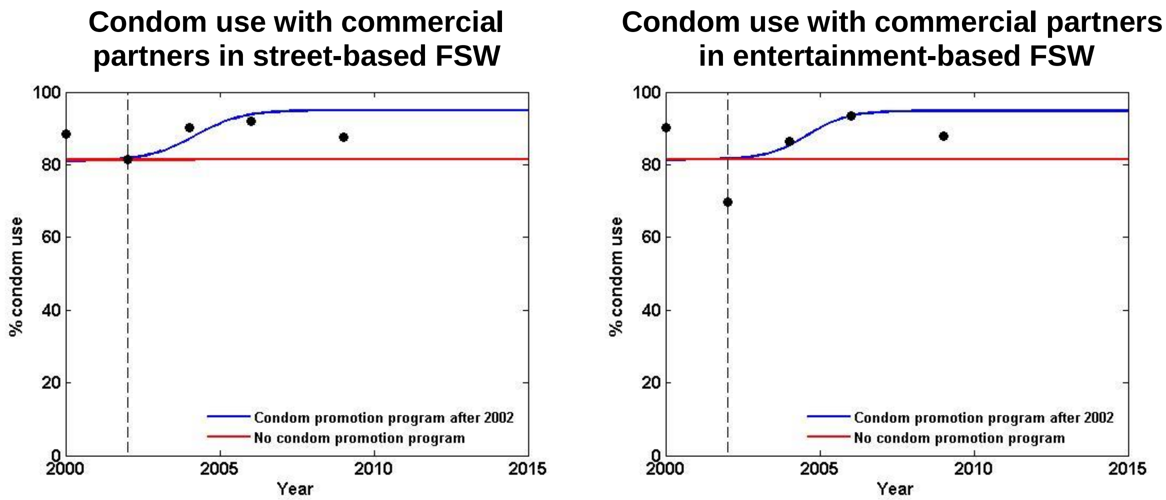


Figure S. 22: Counterfactual of condom use program for MSM

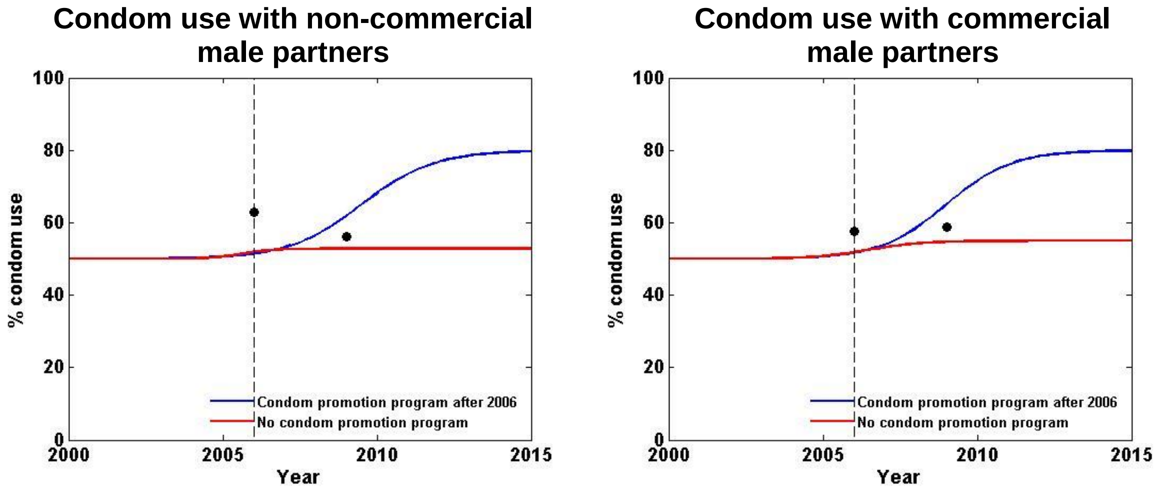


Figure S. 23: Counterfactual of on mass information education communication and untargeted condom promotion program for general population

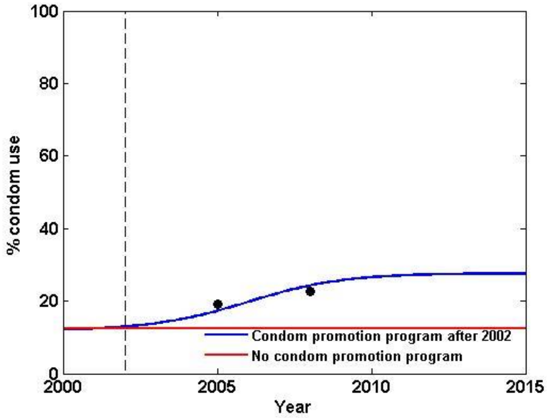


Figure S. 24: Counterfactual of STI program for different groups

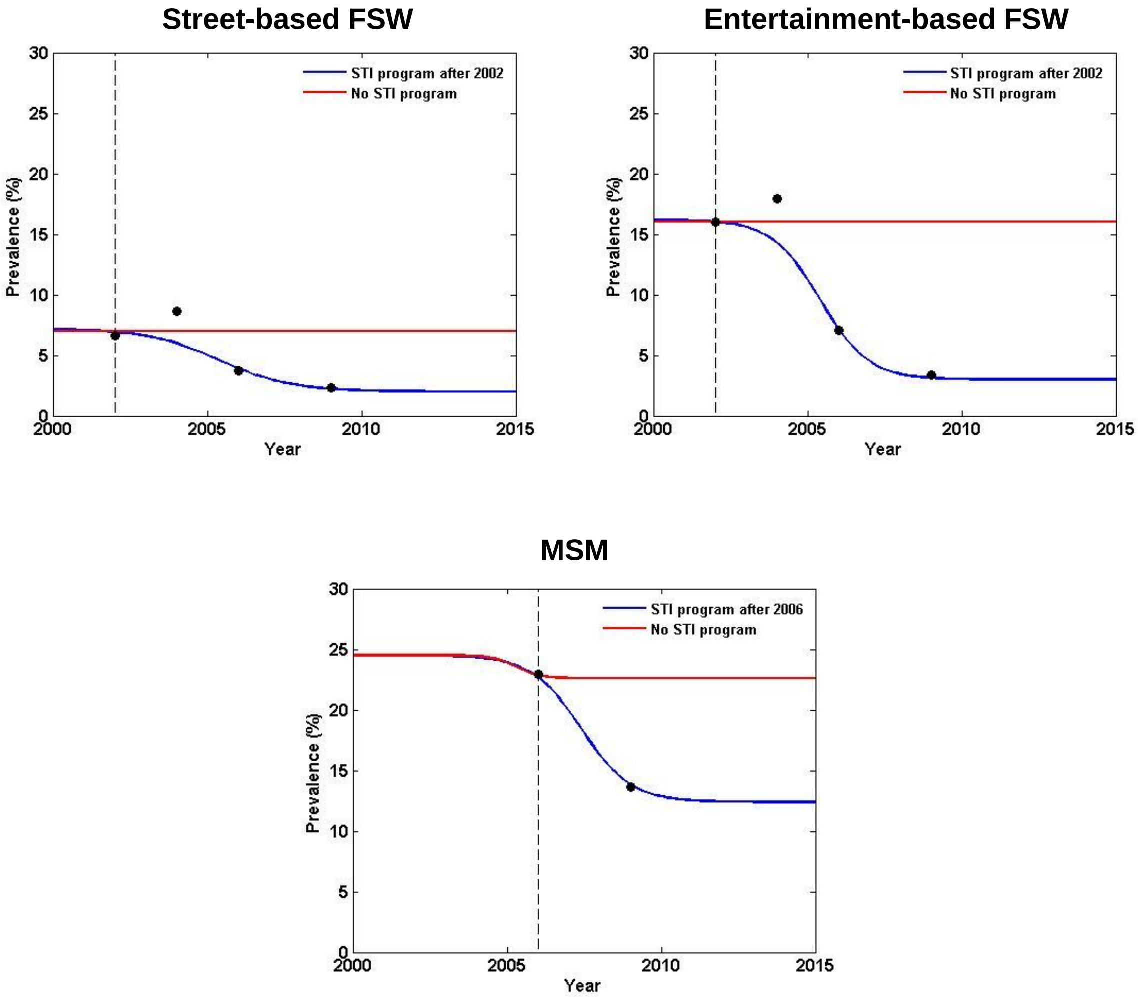
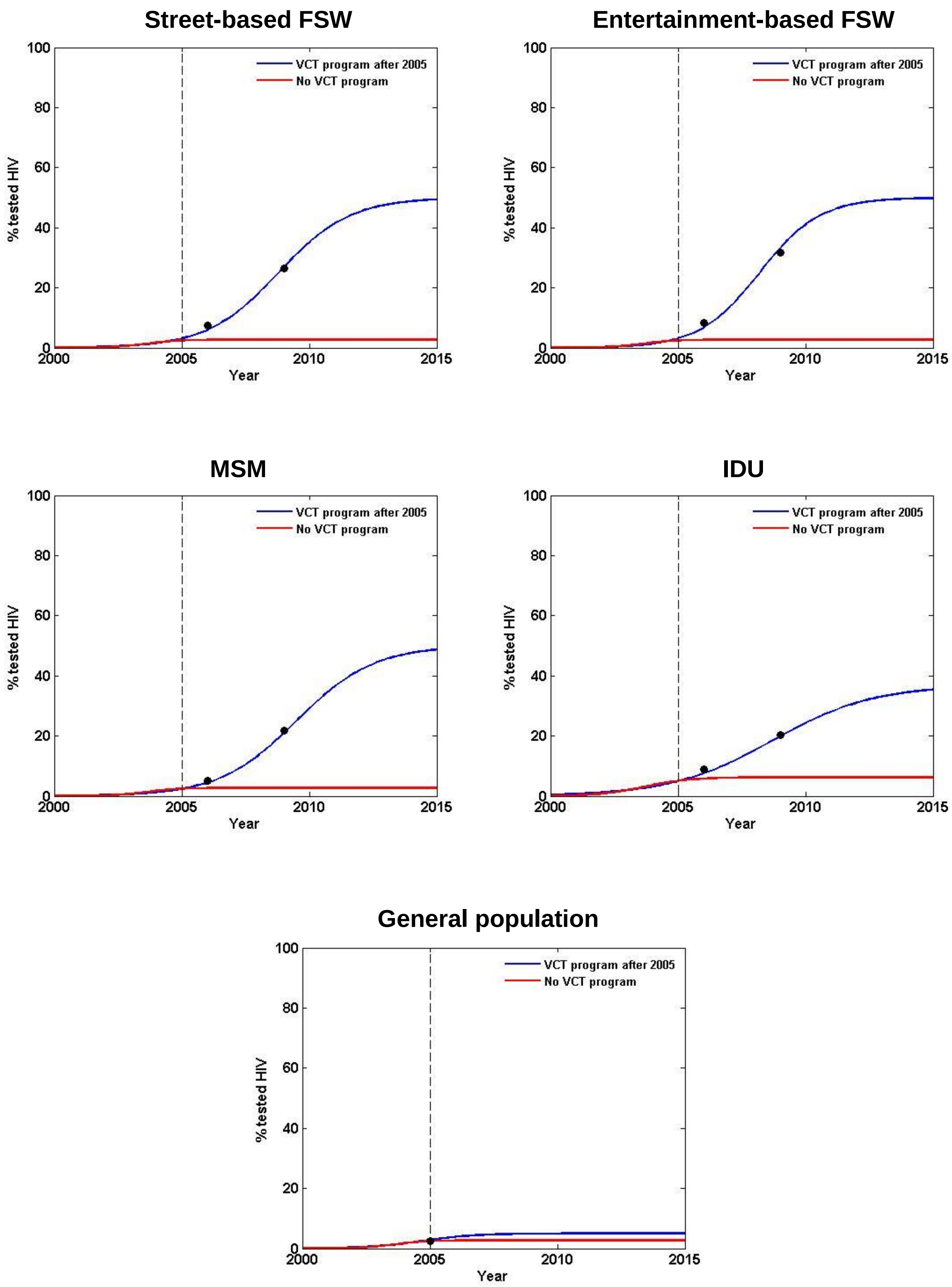


Figure S. 25: Counterfactual of VCT program for different groups



References

1. Vietnam Administration of HIV/AIDS Control, *Vietnam HIV/AIDS Estimates and Projections, 2007-2012. Hanoi: Ministry of Health.* 2009. Available at: http://www.unaids.org.vn/sitee/images/stories/EPP%20report%20EN.pdf.

2. Vietnam National Committee for AIDS, D., and Prostitution Prevention and Control, , *The Fourth Country Report on Following Up the Implementation to The Declaration of Commitment on HIV and AIDS.* 2011. Available at: http://www.unaids.org.vn/sitee/images/stories/ungass_2010/UNGASS_2010_en.pdf.

3. Morrow, M., K.T.H. Oanh, and N.N.N. Trang, *Women who inject drugs: Beyond the numbers. Hanoi, Vietnam. 2011. Available at: http://ni.unimelb.edu.au/__data/assets/pdf_file/0010/515827/Final_Book_FIDU.pdf.*

4. Vietnam Ministry of Health, *Results from HIV/STI integrated behavioral and biological surveillance (IBBS) in Vietnam - Round II (2009). Hanoi, Vietnam. 2011. Available at: http://aidsdatahub.org/en/reference-librarycols2/surveillance-situational-analysis-assessments/item/24471-results-from-the-hiv-sti-integrated-biological-and-behavioral-surveillance-ibbs-in-vietnam-round-ii-2009-hoang-tv-tuan-na-vi-lnl-et-al-2011*

5. Vietnam Ministry of Health, *HIV/STI integrated biological and behavioral surveillance (IBBS) in Vietnam, 2005 – 2006. Hanoi, Vietnam. 2006. Available at: http://www.fhi360.org/en/HIVAIDS/pub/survreports/res_IBBS_2005-6_Vietnam.htm*

6. Tran, B.X., et al., *Cost-effectiveness of integrating methadone maintenance and antiretroviral treatment for HIV-positive drug users in Vietnam's injection-driven HIV epidemics.* Drug and Alcohol Dependence, 2012. **125**(3): p. 260-266.

7. Government of Socialist Republic of Viet Nam, *Declaration of commitment on HIV and AIDS adopted at the 26th United Nations General Assembly Special Session in June 2001 (UNGASS): Reporting periode: January 2008 - December 2009. Hanoi, Vietnam. 2012. Available at: http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2010countries/vietnam_2010_country_progress_report_en.pdf*

8. The Joint United Nations Programme on HIV/AIDS (UNAIDS), *Viet Nam national AIDS spending assessment, 2008-2010. Hanoi: Vietnam. 2012. Available at: http://aidsdatahub.org/en/whats-new/316-vietnam/953-viet-nam-national-aids-spending-assessment-2008-2010-unaids-2012.*

9. Schwartländer, B., et al., *Towards an improved investment approach for an effective response to HIV/AIDS.* The Lancet. **377**(9782): p. 2031-2041.

10. Vietnam Authority of HIV/AIDS Control (VAAC), World Bank, and University of New South Wales, *Evaluation of the epidemiological impact of harm reduction programs on HIV in Vietnam. Hanoi, Vietnam. 2011. Available at:*

http://www.med.unsw.edu.au/NCHECRweb.nsf/resources/vietnam/$file/FinalVietnamImpactEvaluationReport.pdf.

11. Vietnam Ministry of Health, *Estimated size of mots-at-risk populations in Vietnam* 2012.

12. General Statistics Office (GSO), *Monthly statistical information on population and employment. 2012. Available at: http://www.gso.gov.vn/default_en.aspx?tabid=467&idmid=3*.

13. General Statistics Office (GSO), National Institute of Hygiene and Epidemiology (NIHE), and ORC Macro, *Vietnam population and AIDS indicator survey 2005. 2006. Calverto, Maryland, USA: GSO, NIHE, and ORC Macro.*

14. Pasteur Institute of Ho Chi Minh City, *Survey's HIV/STI and knowledge, attitudes, behavior among people aged 15-49 in Dong Nai, Hau Giang, and Vinh Long.* 2008.

15. Tuan, N.A., et al., *Household survey in two provinces in Viet Nam estimates HIV prevalence in an urban and a rural population.* AIDS Research and Human Retroviruses, 2008. **24**(8): p. 1017-1026.

16. Nguyen, N.T., et al., *Clients of female sex workers as a bridging population in Vietnam.* AIDS and Behavior, 2009. **13**(5): p. 881-891.

17. Asian Development Bank (ADB), *Final project report "Community action for preventing HIV/AIDS" in five provinces in Vietnam: Dien Bien, Quang Tri, An Giang, Kien Giang and Dong Thap. Hanoi, Vietnam. 2006. Available at: www.gms-cdc.org/*.

18. National AIDS Standing Bureau, *HIV/AIDS behavioral surveillance survey Vietnam 2000. Hanoi, Vietnam. Hanoi, Vietnam. 2001. Available at: http://www.fhi360.org/en/hivaids/pub/survreports/bssvietnam2000.htm*.

19. National Committee for Population Family and Children and Community Action fot Preventing HIV/AIDS Project, *Baseline survey report: Community action for preventing HIV/AIDS in Lai Chau, Quang Tri, Dong Thap, An Giang, and Kien Giang. Hanoi, Vietnam. 2002. Available at: http://www.inthealth.ku.dk/reach/resources/baselinesurvey_vn.pdf/*.

20. Ruan, Y., et al., *Willingness to be circumcised for preventing HIV among chinese men who have sex with men.* AIDS Patient Care and STDs, 2009. **23**(5): p. 315-321.

21. Pasteur Institute of Ho Chi Minh City, *Evaluating a HIV prevention program for injecting drug users in Soctrang, Vietnam.* 2006.

22. Vu Thuong, N., et al., *Impact of a community sexually transmitted infection/HIV intervention project on female sex workers in five border provinces of Vietnam.* Sexually Transmitted Infections, 2007. **83**(5): p. 376-382.