The potential impact of expanding antiretroviral therapy and combination prevention in Vietnam: Towards elimination of new HIV infection
Appendix: Supporting Information

Model structure

A schematic diagram of the transmission model is given in Figure S1. The most important routes of transmission are among injection drug users (IDUs) [1] or people who inject drugs (PWID) some of whom may also be men who have sex with men (MSM) and some of whom may also be female sex workers (FSW). The IDUs who are also MSM connect to the group of MSM who are not IDUs and the FSW who are also IDUs connect to their male clients (MCF). These male clients of female sex workers connect to the female sex workers who are or who are not IDUs. A proportion of the men in each of the male groups also have female partners (LRW). These low risk women are assumed to be an epidemiological dead end and do not infect anyone else.

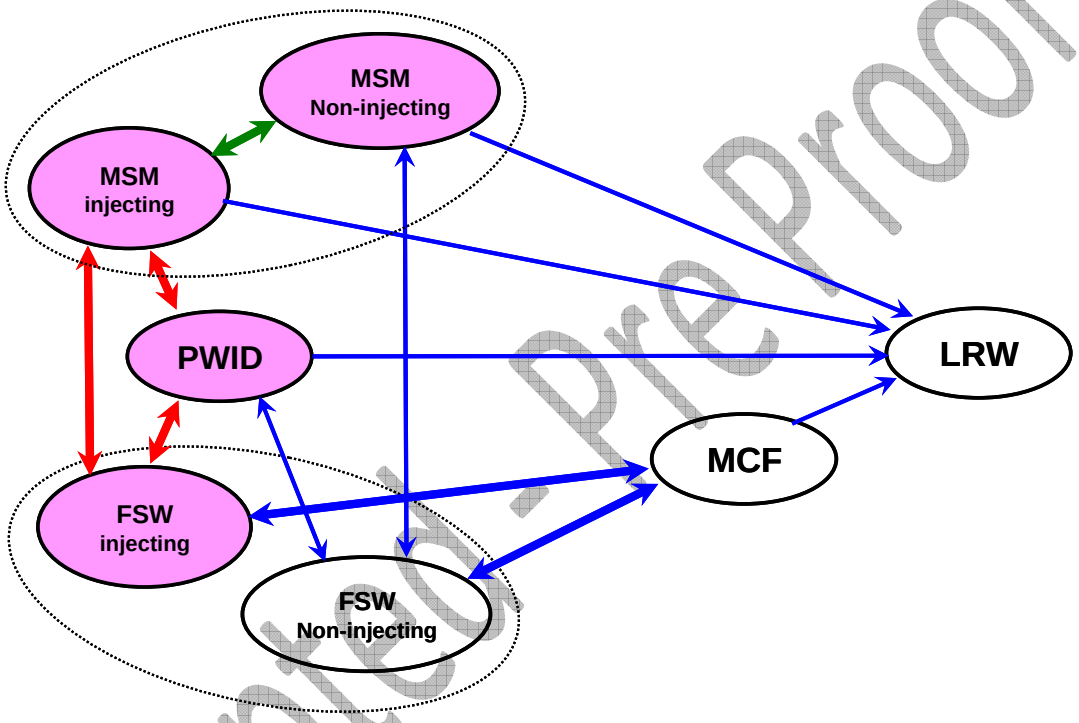

Figure S1. Schematic diagram of the transmission model. Circles define groups. Arrows indicate directions and extent of transmission between groups. LRW: low risk women; MSM: men who have sex with men; PWID: people who inject drugs (IDUs); FSW: female sex workers; MCF: male clients of female sex workers. Groups coloured pink indicate that HIV transmission happens within the group.

In Figure S1 the epidemic is sustained by the transmission routes indicated by the heavy arrows. The red arrows correspond to transmission among PWID, the green arrow transmission among MSM, and the blue arrows indicate heterosexual transmission. We assume LRW are an epidemiological cul de sac - while LRW can be infected by their male sexual partners, they do not infect other adults. It is assumed that a certain proportion of men in all male groups visit FSW or have regular female partners. For FSWs and MSM who inject drugs, we assume that they can be infected either sexually or through needle sharing while keeping the relevant parameters fixed to the values used in each of the separate groups.

Each sub-population has one infected class so that the survival function is exponential, not Weibull. Although this removes the delay of approximately four years between changes in prevalence and in mortality, this analysis is mainly concerned with long-term effects so that this approximation is justified. The model does not explicitly include age but allows people to remain in different risk groups for predetermined average times after which they stop engaging in the

[1] In the main text IDUs, injection drug users, are referred to as 'people who inject drugs' or PWID.

risk behaviour (Table 1), but are retained in the model if they are infected with HIV in order to determine the number of people on ART.

The key parameters for each risk group are: 1) the initial size of the group; 2) the length of time for which a person remains in that risk group; 3) the force of infection for transmission within that risk group, which determines the rate at which HIV spreads through the risk group; 4) a heterogeneity parameter which allows for the variation in risk behaviour within each group and controls the steady state prevalence of HIV within that group. In all the groups, it is assumed that the group size, before the introduction of HIV, is constant so that the rate at which people are recruited to each group is equal to the rate at which they leave it. Once the HIV epidemic starts the recruitment rate remains constant but because people in that risk group have an increased mortality the size of the risk group will fall.

The model is illustrated as a compartmental model in Figure S2. In Figure S2 $P_{\Sigma i}$ indicates the prevalence averaged over all those in group *i* so that:

$$P_{\Sigma d} = \frac{I_d + I_{md} + I_{sd}}{N_d + N_{md} + N_{sd}} \quad (1)$$

$$P_{\Sigma m} = \frac{I_{md} + I_{sd}}{N_{md} + N_{sd}} \quad (2)$$

$$P_{\Sigma c} = \frac{I_c + I_{cd} + I_{cm} + I_{cmd}}{N_c + N_{cd} + N_{cm} + N_{cmd}} \quad (3)$$

$$P_{\Sigma s} = \frac{I_s + I_{sd}}{N_s + N_{sd}} \quad (4)$$

$$P_{\Sigma p} = \frac{p_c I_c + p_d I_d + p_m I_m + p_{md} I_{md}}{p_c N_c + p_d N_d + p_m N_m + p_{md} N_{md}} \quad (5)$$

where I_j is the number of infected people and N_j is the total number of people in group *j*. p_i is the proportion of people in group *i* who have regular female partners since not all the MCFs, IDUs and MSM have regular female partners.

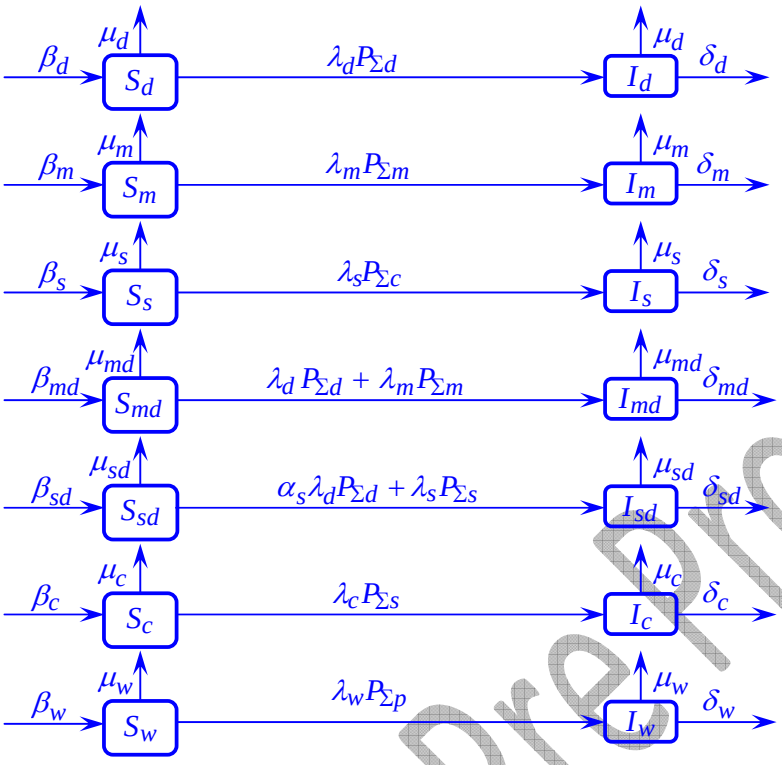

Figure S2. Model for IDUs, FSWs, MCFs, LRWs. *S*: susceptible people; *I*: infected people; Subscripts indicate the different groups: *d*: IDU; *m*: MSM; *s*: FSW; *md*: MSM&IDU; *sd*: FSW&IDU; *c*: MCF; *w*: LRW. We use $P_{\Sigma i}$ to indicate the prevalence averaged over all those in group *i* where *i* may be IDU, MSM, FSW, MCF or PLW (partners of low risk women) as described further in the text and Equations 1 to 5. λ_i is the *per capita* rate at which people in group *i* acquire infection. μ_i is the rate at which people leave group *i* (1/duration of stay in that group); δ_i gives the rate at which people die of AIDS in each group. Because FSW who use drugs appear to be at much greater risk than other drug users we include the factor α_s in the transmission from FSW who use drugs. We assume initially that the system is in a steady state so the $\beta_i = \mu_i$, *i* = *d*, *m*, *s*, *md*, *sd*, *c* and *w*.

Model equations

The equations corresponding to the model in Figure S2 are:

$$S_d^{\bullet} = \mu_d S_d^0 - \left(\lambda_d P_{\Sigma d} + \lambda_c P_{\Sigma s} + \mu_d\right) S_d \qquad 6$$

$$I_d^{\bullet} = \left(\lambda_d P_{\Sigma d} + \lambda_c P_{\Sigma s}\right) S_d - \left(\mu_d + \delta_d\right) I_d \quad 7$$

$$S_m^{\bullet} = \mu_m S_m^0 - \left(\lambda_m P_{\Sigma m} + \lambda_c P_{\Sigma s} + \mu_m\right) S_m \quad 8$$

$$I_m^{\bullet} = \left(\lambda_m P_{\Sigma m} + \lambda_c P_{\Sigma s}\right) S_m - \left(\mu_m + \delta_m\right) I_m \quad 9$$

$$S_s^{\mathrm{g}} = \mu_s S_s^0 - \left(\lambda_s P_c + \mu_s\right) S_s \quad 10$$

$$I_s^{\mathrm{g}} = \lambda_s P_c S_s - \left(\mu_s + \delta_s\right) I_s \quad 11$$

$$S_{md}^{\bullet} = \mu_{md} S_{md}^0 - \left(\lambda_d P_{\Sigma d} + \lambda_m P_{\Sigma m} + \lambda_c P_{\Sigma s} + \mu_{md}\right) S_{md} \quad 12$$

$$I_{md}^{\bullet} = \left(\lambda_d P_{\Sigma d} + \lambda_m P_{\Sigma m} + \lambda_c P_{\Sigma s}\right) S_{md} - \left(\mu_{md} + \delta_{md}\right) I_{md} \quad 13$$

$$S_{sd}^{\bullet} = \mu_{sd} S_{sd}^0 - \left(\lambda_d P_{\Sigma d} + \lambda_s P_{\Sigma c} + \mu_{sd}\right) S_{sd} \quad 14$$

$$I_{sd}^{\bullet} = \left(\lambda_d P_{\Sigma d} + \lambda_s P_{\Sigma c}\right) S_{sd} - \left(\mu_{sd} + \delta_{sd}\right) I_{sd} \quad 15$$

$$S_c^{\bullet} = \mu_c S_c^0 - \left(\lambda_c P_{\Sigma s} + \mu_c\right) S_c \quad 16$$

$$I_c^{\bullet} = \lambda_c P_{\Sigma s} S_c - \left(\mu_c + \delta_c\right) I_c \quad 17$$

$$S_w^{\bullet} = \mu_w S_w^0 - \left(\lambda_w I_{\Sigma p} + \mu_w\right) S_w \quad 18$$

$$I_w^{\bullet} = \lambda_w I_{\Sigma p} S_w - \left(\mu_w + \delta_w\right) I_w \quad 19$$

where

$$P_{\Sigma j}^{i} = \frac{N_i}{\sum_j N_j} \quad 20$$

gives the proportion of all those in groups j that are also in i, $i \in j$, so that $P_{\Sigma d}^{md}$, for example, gives the proportion of all drug users that are also MSM, that are in the group md. P_c is the prevalence in MCFs. S_i^0 is the number of uninfected (susceptible) people in group i before the HIV epidemic starts.

In order to allow for heterogeneity in risk, which effectively controls the steady state prevalence of infection, each of the transmission terms λ in Equations 6 to 19 is multiplied by a corresponding exponential term so that

$$\lambda_i = \lambda_i^* \, \mathrm{e}^{-\alpha_i P_i} \quad 21$$

where $P_i = I_i/N_i$. In the early stage of the epidemic the prevalence is low but those at highest risk will be infected first. As the prevalence rises, those that are not yet infected will be at lower risk and the average value of the transmission parameter will decrease as the prevalence of infection increases.

Data sources

The trend data for HIV prevalence in each sub-population in Can Tho are drawn from Vietnam's national technical working group on estimation and projection (TWG) data set, [1-2] which are derived from annual National Sentinel Surveillance from 1994 to 2010 (unpublished data) and Integrated Biological and Behavioural Surveillance (IBBS) in 2006 [3] and 2009. [4] To estimate the sub-population sizes (Table 1, main text), the data were triangulated using numbers used for the national estimation and projection, [1-2] data from various Ministries, mapping exercises conducted by various projects, and HIV case reports.

IDU

No adjustment was made to prevalence data used by the National TWG.

FSW

Sentinel surveillance does not distinguish between those who do and do not inject drugs but prevalence estimates from IBBS 2009 [4] and population size estimates from the pre-assessment for IBBS2009 were used to calibrate the prevalence in those two groups, as follows. (Table S1)

Table S1

	Populations size (adjusted)	%injectors	#injectors	%HIV prevalence in injectors	# HIV+ in injectors	# non-injectors	%HIV prevalence in non-injectors	# HIV+ in non-injectors
Data source	IBBS pre-assessment	IBBS 2009		IBBS 2009			IBBS 2009	
Venue-based SW (VSW)	1800	1.20%	22	40.0	9	1778	2.9	52
Street-based SW (SWS)	240	16.70%	40	78.3	31	200	7.8	16
Total	2040		62		40	1978		67
% HIV in VSW+SSW				64.9%			3.4%	

MSM

Sentinel surveillance had not included MSM until 2010, and data related to MSM had been extremely limited. The National Technical Working Group on Estimation and Projection (TWG) had thus relied on following four studies and surveys from Ho Chi Minh City, two ad hoc studies and two rounds of IBBS, to generate the shape of HIV trend for this group with or without scaling factor depending on the province (Table S2). For Can Tho, no scaling was applied. It should also be noted that the most recent analysis indentified that MSM who inject drugs were over-represented in IBBS 2009 sample which translated into an over estimation of HIV prevalence among MSM in IBBS 2009. Given this issue with the 2009 data, we used the most recent survey findings to down scale the 2009 data points.

Table S2

Year	Data sources
2000	Cao, H.N. Knowledge, attitudes and practices on HIV/AIDS among men who had sex with men and visited the Consultation Unit of the Pasteur Insitute in Ho Chi Minh City, Vietnam, 2000.
2004	Tuan, N.A. Sexual behavior and risk factors of HIV transmission among men who have sex with men in Ho Chi Minh City, Vietnam, NIHE 2004.
2006	IBBS 2006
2009	IBBS 2009 – scaled down to 8%.

It has been recognized that not all MSM are exposed to the same level of HIV risk, and the risks largely depends on their risk behaviors. To account for the heterogeneity of risk behaviors among the MSM community, the MSM population were further stratified as follows (Table S3).

1) Vietnam's National Technical Working Group on Estimation and Projection (TWG) uses 0.75% of male (age 15+) as medium estimates for MSM size in Can Tho, which gives 3290.
2) Can Tho Provincial AIDS Center reports estimated number of MSM who are engaged in risk behaviour as 1500, and thus we used this number as the size of MSM who are at risk of HIV infection.

3) Then, we disaggregated those groups into three groups, a) MSM with drug injecting behaviour, b) Male sex workers, and c) MSM who neither inject nor sell sex, but are engaged in at-risk male-to-male sex. We used IBBS2009 data to obtain HIV prevalence and proportional size of those three MSM sub-groups, as follows. We assumed MSM sample in IBBS2009 are those with at least moderate risk and do not include low-risk MSM.

Table S3

	HIV prevalence	% size of MSM in IBBS sample	# Estimated MSM engaged in risk behaviour	# total MSM (including low risk MSM)
Data source	IBBS 2009	Sample composition in IBBS2009	Total number 1500 from Provincial AIDS Center via Partners in Health Research	MSM size estimates used for National estimation and projection
a) MSM with drug injecting behaviour	28.0	21.6%	324	
b) Male sex workers	9.74	6.43%	96	
c) MSM who neither inject nor sell sex, but are engaged in at-risk male-to-male sex	3.01	71.95%	1079	
Low risk MSM (not reachable)	NA	NA	NA	
Total			1500	3290

4) With an aim to develop simple model structure that could still project key epidemic dynamics, it was decided to further re-categorize the above three groups into two groups: injecting MSM (sexual + injecting risk) and non-injecting MSM (only sexual risk). That is, b) Male sex workers and c) MSM who neither inject nor sell sex, but are engaged in at-risk male-to-male sex, were merged as non-injecting MSM. Therefore, we used the following data to calibrate the two MSM groups in our model (Table S4).

Table S4

	HIV prevalence	Population size
Injecting MSM	28.0%	324
Non-injecting MSM (excluding low risk MSM)	3.5%	1176

5) For low risk MSM, whose size was estimated as 1,790 (= 3290 – 1500), it was assumed that their contribution to HIV epidemic is likely to negligible, and thus low risk MSM were excluded them from the model.

MCF

For MCF, the model uses the HIV prevalence among clients at sexually transmitted infection (STI) clinics multiplied by 0.31 on the assumption that they represent a fraction of MCFs who do not use condoms consistently.[5] Size of MCF was based on the assumption that 12% of general males (age 15+) have sex with FSW, taking into account National TWG estimates [1-2] and male clients survey results [5], and to reach plausible value of the number of sex acts per FSW and the number of MCF per FSW. IDU who have sex with FSWs (22% of IDU, IBBS 2009) was deducted.

LRW

Antenatal care (ANC) surveillance data were collected at urban ANC services where the prevalence of HIV is about twice that in rural areas and where about half of the population of Can Tho lives [1]; the prevalence among women attending ANC was therefore multiplied by 0.75 to get an overall estimate of the prevalence in LRW.

Model fit

To fit the model to the data, we fix the group sizes, the average length of time for which people remain in any compartment, and the AIDS related mortality. We then vary the starting prevalence, the transmission parameters and the heterogeneity parameter for each group to get the maximum likelihood fit to the trend data shown in Figure S3. The best

fit of the model to the data is also given in Figure S3. For IDUs the model was fitted to the data up to and including 1996 and after and including 2000. If the remaining points were included in the fit the epidemic in IDUs increases unreasonably quickly but the prevalence in the other groups then rises correspondingly quickly and one cannot get satisfactory fits to any of the other groups. It is likely that when monitoring of HIV started there was a tendency to underestimate the prevalence and the fitted curve is more reasonable.

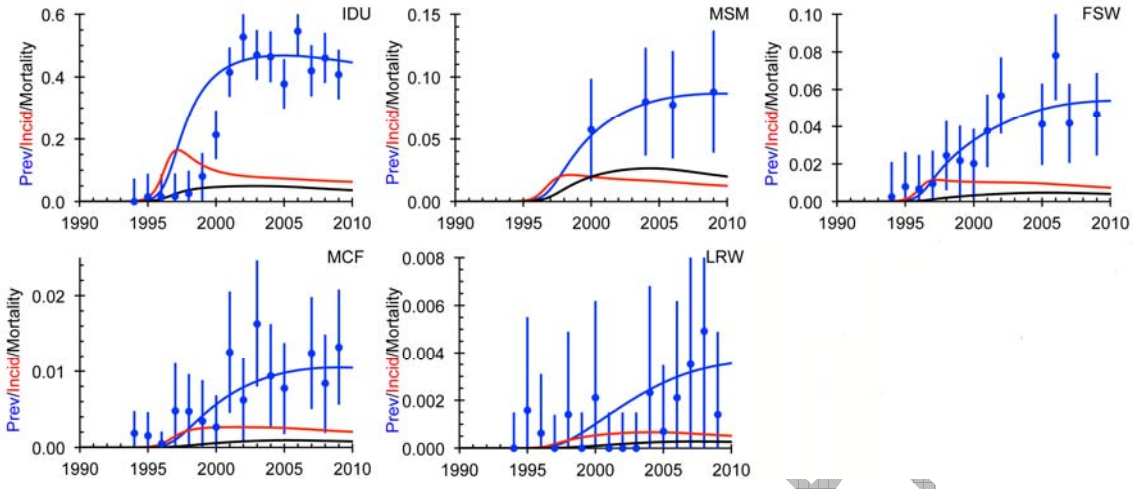

Figure S3. Fits of the model (blue line) to the data (blue dots and error bars) for the prevalence of HIV in Can Tho, Vietnam. Red lines: implied incidence; black lines: implied mortality. IDU: intravenous drug users; MSM: men who have sex with men; FSW: female sex workers; MCF: male clients of female sex workers; LRW: low risk women.

Implied rates in sub-groups

Since we only have data for various combined groups such as all FSWs but without separate data on those that do and do not use drugs, we have to impute these values from the model fits. The trends in the various HIV-related rates in each risk group are given in S4. The trends in S4 are for the scenario in which all interventions are maintained at their 2010 level and there is not further expansion.

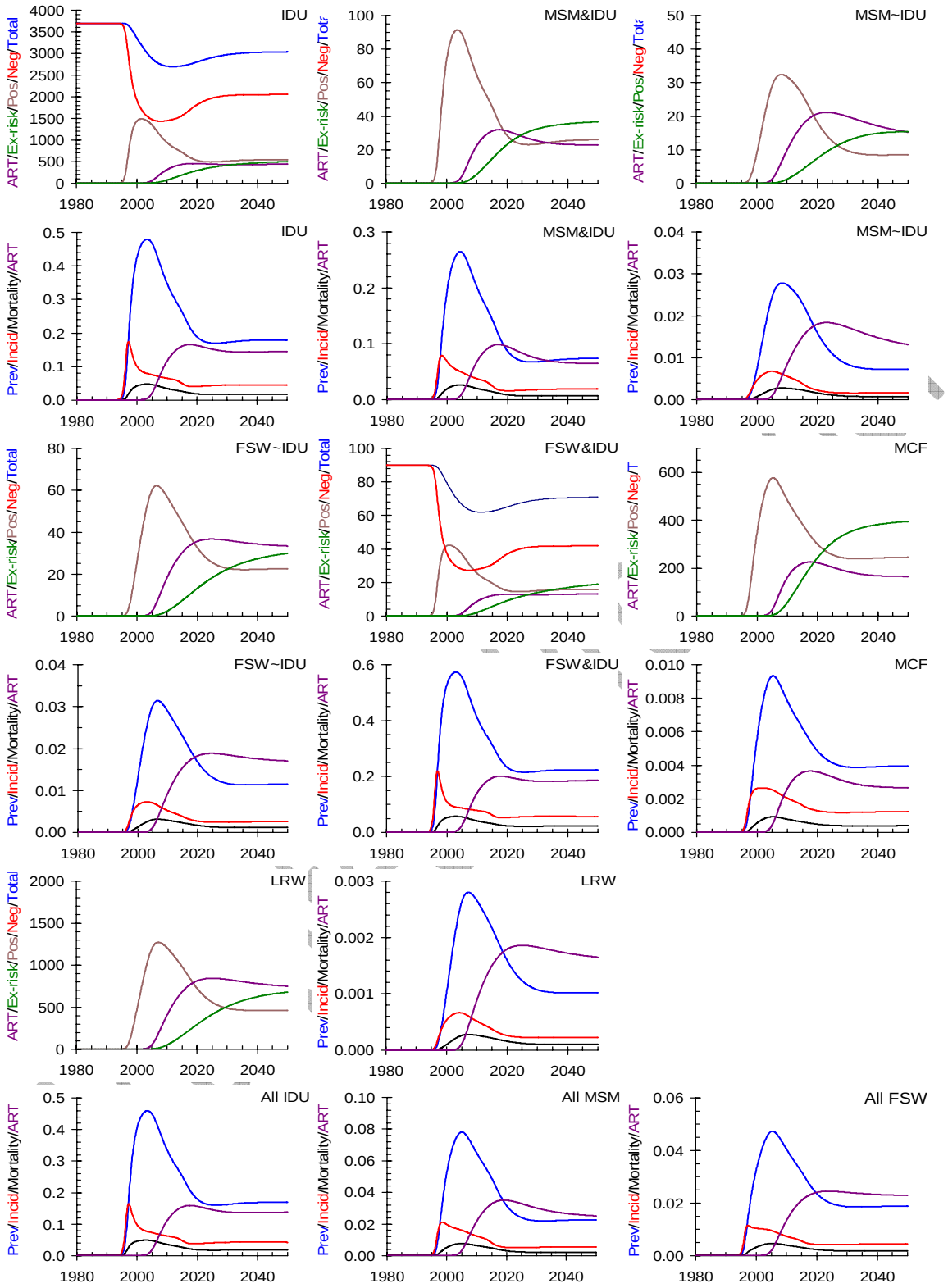

Figure S4. Graphs giving the number of people on ART, HIV-positive but no longer at risk, HIV-positive, HIV-negative and total number and the prevalence, incidence, mortality and ART coverage expressed as proportions of the total population for each of the risk groups as defined in the text. For MSM (with and without IDU) and MCF we do not plot the numbers that are HIV-negative or the total numbers since the prevalence in both cases is low.

References

1. VAAC. *Viet Nam HIV/AIDS Estimates and Projections 2007-2012.* Hanoi, Viet Nam: Viet Nam Authority of HIV/AIDS Control, Ministry of Health;2009.
2. VAAC. *Viet Nam HIV/AIDS estimates and projections 2011-2015.* Hanoi, Viet Nam: Viet Nam Authority of HIV/AIDS Control, Ministry of Health;2012.
3. VAAC. *Results from the HIV/STI integrated biolgoical and behavioral surveillance (IBBS) in Viet Nam 2005-2006.* Hanoi, Viet Nam: Ministry of Health - Viet Nam;2006.
4. VAAC. HIV/STI Integrated biological and behavioral sureillance (IBBS) in Viet Nam 2009. 2012.
5. PSI. *Behavioral survey of male clients of female sex workers across seven provinces in Viet Nam.* Hanoi, Viet Nam: Population Service International Viet Nam;2009.

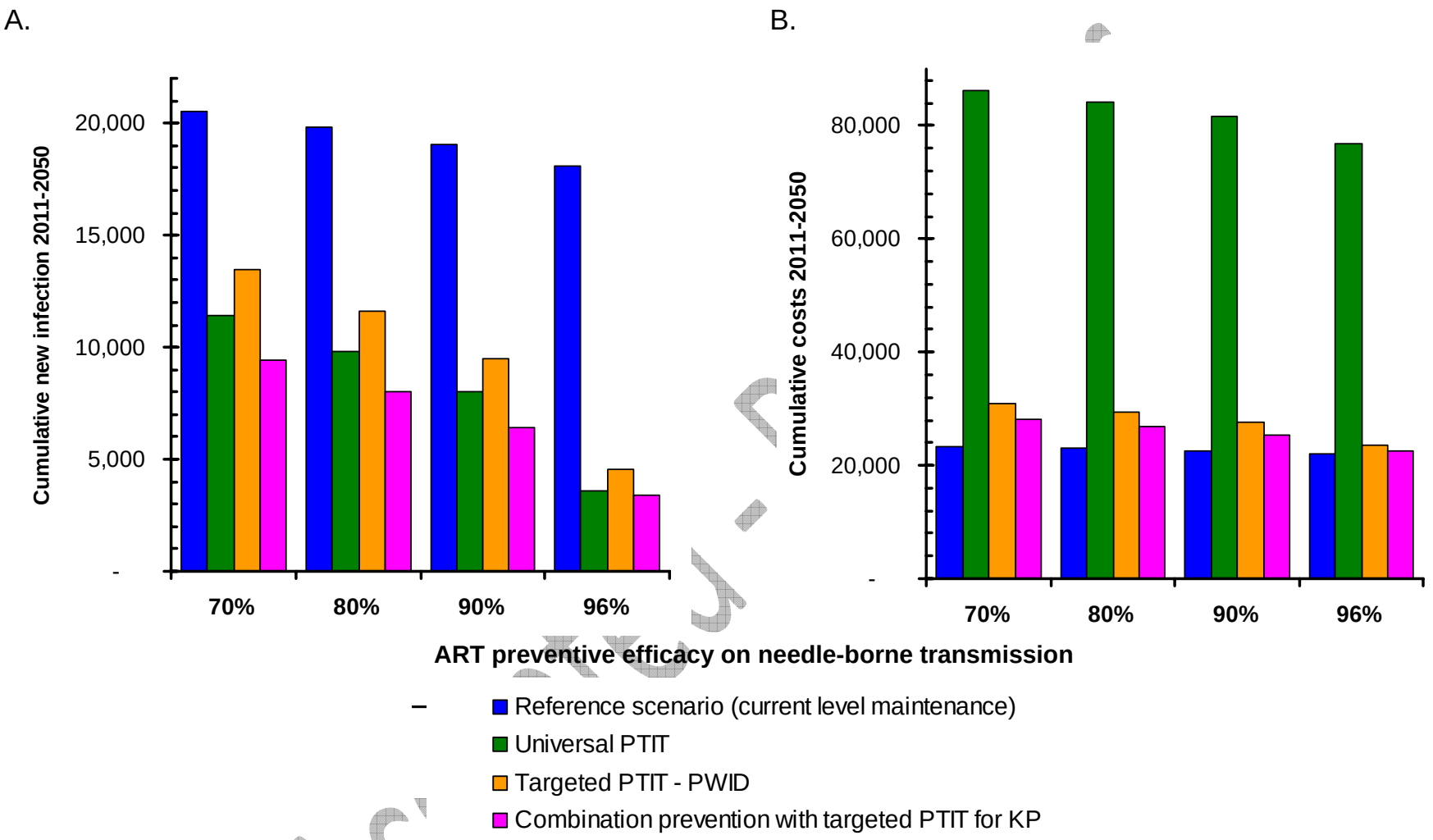

Figure S5. Effect of ART preventive efficacy on needle-borne transmission on cumulative new infections and costs from 2011 to 2050. The efficacy was changed step-wise from 70% to 96% in the four scenarios.

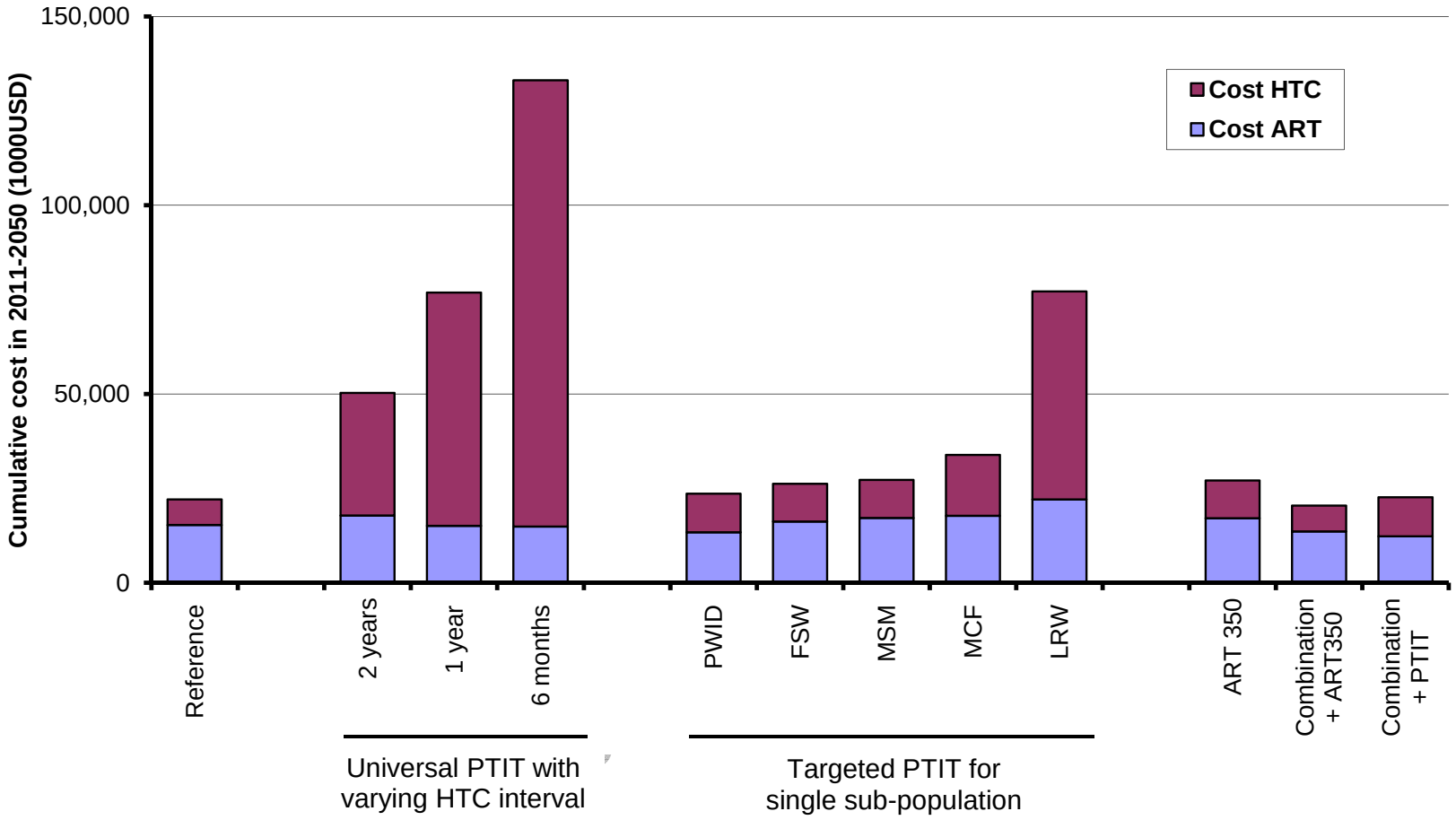

Figure S6. Breakdown of the cumulative cost in 2011-2050 period by HTC and ART costs. PTIT are offered to all adult populations (universal PTIT) or to selected sub-populations (targeted PTIT). Reference assumes current coverage of ART and other prevention interventions are maintained at the level in 2010. SA, standard ART scale-up in which ART is expanded to 90% of those with CD4 count below 350 cells/mm^3 by 2020. CP, combination prevention scale-up. In the last scenario, PTIT focusing on three key populations, i.e. PWID, FSW and MSM, was added to combination prevention scale-up.