Appendix to

The cost effectiveness and optimal configuration of HIV self-test distribution in South Africa: A model analysis

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Section 1: Modelling self-testing in Thembisa

Previous versions of Thembisa have not included self-testing. This supplementary material describes extensions made to the Thembisa model to include different forms of self-testing.

We define the following variables:

$\tau_{g,i,s}(x,t)$ is the rate of health worker-administered testing in sexually experienced individuals of age x and sex g, in HIV stage s and with HIV testing history i, in year t;
$\tau'_{g,i,s}(x,t)$ is the rate of health worker-administered testing in virgins of age x and sex g, in HIV stage s and with HIV testing history i;
$S_{g,i,s}(x,t)$ is the rate of self-testing in sexually experienced individuals of age x and sex g, in HIV stage s and with HIV testing history i;
$Z_{g,i,s}(x,t)$ is the rate of any HIV testing (health worker-administered or self-administered) in sexually experienced individuals of age x and sex g, in HIV stage s and with HIV testing history i, in year t.

In HIV-negative individuals ($s = 0$) and acutely-infected individuals ($s = 1$), the total rate of testing is simply

$$Z_{g,i,s}(x,t) = \tau_{g,i,s}(x,t) + S_{g,i,s}(x,t).$$

However, in HIV-seropositive individuals it is necessary to take into account that some of the HIV-positive self-testers seek confirmatory testing, i.e. there could be double-counting of the individuals diagnosed by self-testing and by health worker-administered testing. The total rate of testing is therefore calculated as

$$Z_{g,i,s}(x,t) = \tau_{g,i,s}(x,t) + S_{g,i,s}(x,t)(1 - \gamma \mathrm{I}(s > 1))$$

for $s > 0$, where γ is the fraction of individuals diagnosed through self-testing who seek confirmatory testing by health workers, and $\mathrm{I}(s > 1)$ is an indicator of whether the individual has detectable HIV antibodies (0 if HIV-seronegative, 1 if HIV-seropositive). We set γ to 68%, based in part on the STAR study, in which the proportion of individuals testing positive on self-testing who reported going for confirmatory testing varied between 48% and 74% across modalities. The assumption is also consistent with our previous assumption that the relative rate of linkage to ART services in people who self-test positive, when compared to that in people who test positive in a health facility, is 0.68 [1].

We consider five types of self-testing:

1. Self-testing through fixed point distribution (a form of community-based distribution)
2. Self-testing kits distributed at taxi ranks
3. Self-testing kits distributed to partners of pregnant women
4. Self-testing kits distributed to partners of ART patients
5. Self-testing kits distributed to employees in workplace settings

The symbol $c_j(t)$ represents the coverage/uptake of self-testing method j (indexed as 1 for fixed point distribution, 2 for taxi ranks, 3 for pregnant women's partners, 4 for partners of ART patients and 5 for employees).

Fixed point distribution

In the case of self-testing through fixed point distribution, our analyses of initial programme data suggest that the age and sex profile of individuals receiving self-testing roughly matches the age and sex profile of people who receive 'general' HIV testing in the Thembisa model (i.e. after excluding testing in antenatal clinics and people with HIV-related symptoms). We therefore set the self-testing rate to

$$\lambda^1_{g,i,s}(x,t) = c_1(t)\, A_g(x,t)\, r^*_i(t),$$

where $A_g(x,t)$ is the same age and sex adjustments that applies in the case of 'general' testing, and $r^*_i(t)$ is the relative rate of testing in individuals with HIV testing history i (1 for individuals who have never been tested or who have only tested negative, 0.5 for untreated HIV-diagnosed individuals and 0.15 for individuals on ART).[1] Figure S1 shows that with the standard age and sex adjustments for 'general' testing the model estimates of patterns of test uptake by age and sex are roughly consistent with the STAR data – although the STAR data suggest lower rates of HIV testing than predicted by the model in the 15-19 and 50+ age groups.

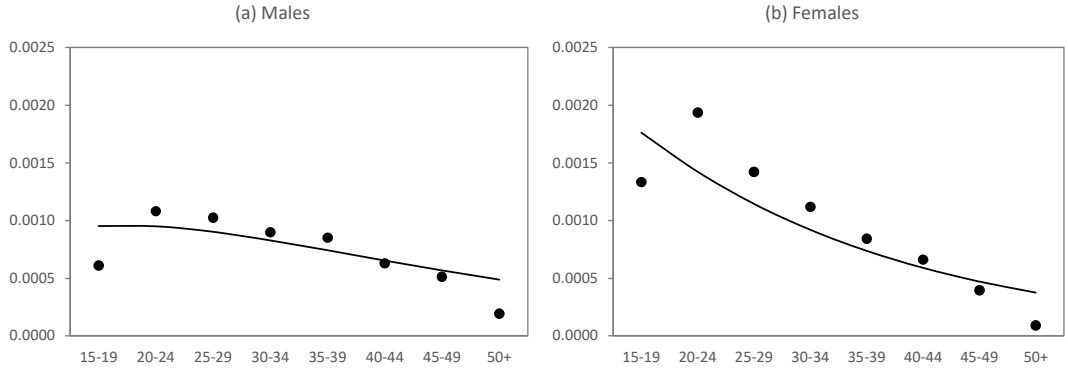

Figure S1: Rates of self-testing through fixed point distribution in Gauteng, 2017-2019
Programme data from the STAR project have been divided by the Thembisa estimates of the size of the sexually experienced population at each age in Gauteng, where most of the distribution through fixed points occurred (dots). Solid lines represent the estimates from the previous equation, scaled by an arbitrary factor to match the relative levels of testing by age and sex.

If we know the total number of self-testing kits distributed through fixed points in year t, $E_1(t)$, then we can approximate the self-testing uptake by the formula

$$c_1(t) = \frac{E_1(t)(1-W_1)}{\sum_g \sum_i \sum_s \sum_x N_{g,i,s}(x,t) A_g(x,t) r^*_i(t)},$$

where W_1 is the proportion of self-testing kits that are not used ('wastage'), and $N_{g,i,s}(x,t)$ is the size of the sexually experienced population aged x, of sex g, with HIV testing history i, at time t. In the routine data from the STAR programme, most of the self-testing kits distributed through fixed points were used 'on site' (at the point of distribution) and there was thus relatively little wastage; out of 9980 self-testing kits distributed to individuals who were interviewed, 8868 (89%) were used by the individual interviewed or (in a minority of cases) given to someone else. We therefore set W_1 to 11%.

Taxi rank distribution

We adopt a similar approach in modelling the effect of self-test kit distribution through taxi ranks. However, the STAR testing data suggest a different age and sex distribution of test recipients, with relatively high testing rates in males and in the 20-34 age group. We therefore represent the age and sex adjustment factor by the symbol $A_g'(x,t)$, which is parameterized as

$$A_g'(x,t) = B_g\, (x/25)^{\alpha - 1} \exp(-\sigma(x - 25))$$

where B_g is a scaling factor to represent the effect of sex ($B_1 = 7.5$ for men and $B_2 = 1$ for women), and α and σ are coefficients to represent the effect of age on the rate of testing. Setting α and σ to 14.1 and 0.469 respectively yields a reasonable model fit to the age-specific rates of self-testing through taxi ranks, as shown in Figure S2.

[1] This is consistent with the assumptions made about self-testing in the MicroCOSM model.

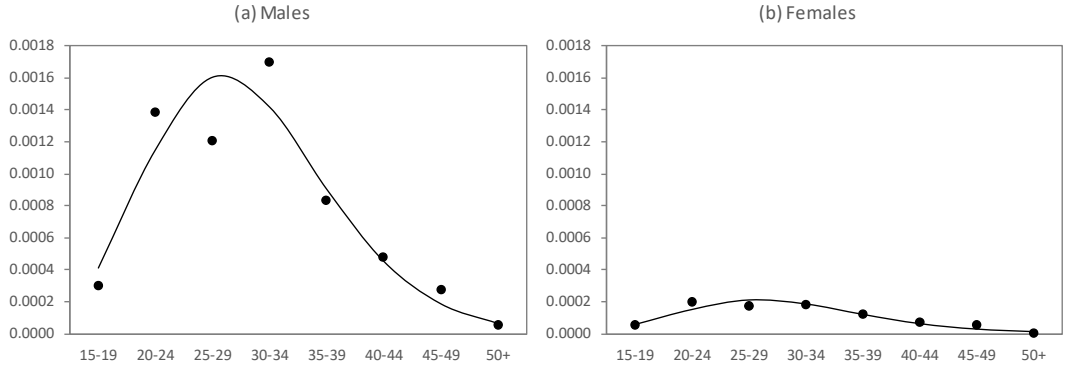

Figure S2: Monthly rates of self-testing through taxi rank distribution in Gauteng, 2018
Programme data from the STAR project have been divided by the Thembisa estimates of the size of the sexually experienced population at each age in Gauteng, where most of the distribution through taxi ranks occurred (dots). Solid lines represent the estimates from the previous equation, scaled by an arbitrary factor to match the relative levels of testing by age and sex.

We set $\lambda^2_{g,i,s}(x,t) = c_2(t)\ A_g'(x,t)\ r^*_i(t)$, where $c_2(t)$ represents the rate of self-testing through taxi ranks in females aged 25. This parameter is calculated in the same way as $c_1(t)$, using recorded numbers of tests distributed through taxi ranks ($E_2(t)$) and observed levels of wastage (W_2). Out of 5922 self-testing kits distributed to individuals who were interviewed after receiving self-testing kits through taxi ranks in the STAR project, 5028 (85%) were used by the individual interviewed or (in a small fraction of cases) given to someone else. We therefore set W_2 to 15%.

Secondary distribution to partners of pregnant women

We model the rate of self-testing in sexually experienced men, using tests distributed to them by pregnant female partners, as

$$\lambda^3_{g,i,s}(x,t) = c_3(t)\ F(x-3,\ t)\ r^*_i(t)\ (1 - W_3),$$

where $F(x,\ t)$ is the fertility rate in HIV-negative women aged x in year t. The $c_3(t)$ parameter is defined here as the proportion of HIV-positive pregnant women who are given self-testing kits to give to their partners. For the sake of simplicity, we do not incorporate effects of female HIV status and ART use on fertility, which would depend on the male's HIV status. We also assume, for the sake of simplifying the self-testing calculations, that men are on average three years older than their female partners, and that each sexually experienced male has one heterosexual partner (this assumption is made only for the purpose of approximating the effect of secondary distribution through antenatal clinics and does not apply to the rest of the Thembisa model). With these assumptions the modelled relative rates of HIV testing in men, by age, approximate those observed in the STAR data (Figure S3).

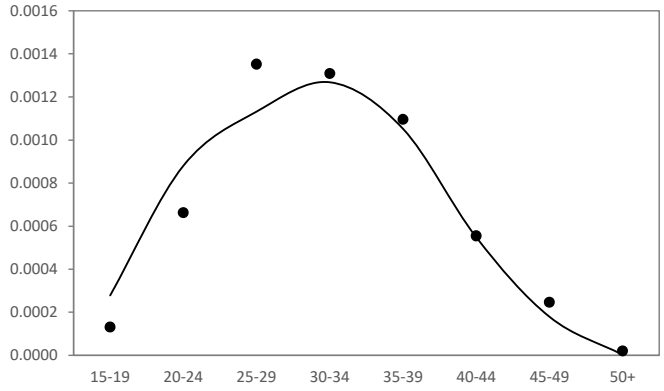

Figure S3: Male rates of self-testing through pregnant partners in Gauteng, 2017-2019
Programme data from the STAR project (numbers of men who were known to have used self-testing kits given to them by their pregnant partners) have been divided by the Thembisa estimates of the size of the sexually experienced male population at each age in Gauteng, where most of the distribution through pregnant women occurred (dots). Solid lines represent the estimates from the previous equation, scaled by an arbitrary factor to match the relative levels of testing by age.

In the STAR data, 9777 pregnant women who were given self-testing kits to give to their partners were interviewed; all reported that they gave the test(s) to at least one partner, but only 3783 (39%) reported knowing that the partner had actually used the test.

This is probably an under-estimate of actual test use, since some men may have used the test without informing their female partners, so we optimistically set W_3, the fraction of tests that are not used by HIV-negative male partners, to 0.12, consistent with the parameters estimated for the previous testing modalities. (It is worth noting that if the male partner is HIV-positive, the probability of the test not being used is $1 - r^*_i(t) \times (1 - 0.12)$.) If we know the total number of self-testing kits distributed through pregnant women in year t, $E_3(t)$, then we can estimate $c_3(t)$ by dividing $E_3(t)$ by the total number of pregnancies in year t.

Secondary distribution to partners of ART patients

We model the rate of self-testing in sexually experienced individuals, following secondary distribution of self-testing kits by sexual partners on ART, as

$$\lambda^4_{g,i,s}(x,t) = c_4(t)\, H_s(g \mid p_0, p_1)\, K_g(x, t)\, r^*_i(t)\, (1 - W_4),$$

where $H_s(g \mid p_0, p_1)$ is the probability that an individual of HIV status s and sex g has an HIV-positive partner (given HIV prevalence levels of p_0 in male partners and p_1 in female partners), and $K_g(x, t)$ is the ART coverage in year t in HIV-positive sexual partners of individuals aged x and of sex g. $H_s(g \mid p_0, p_1)$ is calculated using a formula given in the appendix, based on South African data on levels of seroconcordance in heterosexual relationships. The coverage parameter, $c_4(t)$, is defined as the proportion of ART patients who are given self-testing kits to give to their sexual partners, and W_4 is the proportion of self-test kits distributed that do not get used by sexual partners. Out of 4153 HIV-diagnosed individuals who were given self-testing kits to give to their sexual partners through the STAR project, all reported giving the test to sexual partners, but only 1871 (45%) reported knowing that the test was used. Again, this is likely to be an under-estimate of the fraction of tests actually used. We have therefore set W_4 to 0.12, the same value as assumed for secondary distribution of self-testing kits to partners of pregnant women. If we know the total number of self-testing kits distributed through index partners in year t, $E_4(t)$, then we can approximate the self-testing uptake by the formula

$$c_4(t) = \frac{E_4(t)}{\sum_i \sum_s \sum_x N_{g,i,s}(x,t) H_s(g \mid p_0, p_1) K_g(x,t)}$$

Note that in this equation (as in the equation for $c_3(t)$) we do not have a wastage term or a testing history adjustment, because the uptake parameter is inclusive of tests that are not used. In contrast, the uptake parameters for the fixed point and taxi rank distribution strategies were exclusive of wastage, and the associated formulas for $c_1(t)$ and $c_2(t)$ therefore excluded wastage.

Distribution through workplaces

Our approach to modelling distribution through workplaces is similar to that for taxi ranks, with a different age distribution from that for general HIV testing. As with fixed point and taxi rank self-test distribution, the STAR data suggest that almost all tests distributed are used by the individuals who receive the tests, and a relatively small fraction are given to others. We therefore ignore secondary distribution, in the interests of simplicity. We model the rate of self-testing in sexually-experienced individuals, through workplace distribution programmes, as

$$\lambda^5_{g,i,s}(x,t) = c_5(t)\, \mathrm{Q}(x, g)\, A^*_g(x,t)\, r^*_i(t),$$

where $\mathrm{Q}(x, g)$ is the rate of employment in individuals aged x, of sex g, and $A^*_g(x,t)$ determines the relative rates of testing uptake by age and sex among employed individuals. The $\mathrm{Q}(x, g)$ parameters are estimated from the 2015 Quarter 3 Labour Force Survey [2], and are shown in Table S1. (We assume rates of employment are zero below age 15 and at ages 65 and older.)

Table S1: Proportion of individuals employed, by age and sex

	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64
Male	2.6%	26.7%	48.3%	54.3%	57.7%	60.3%	59.3%	51.1%	44.9%	24.1%
Female	1.5%	17.4%	35.6%	44.1%	49.0%	48.7%	47.0%	41.4%	35.4%	16.3%

Source: South African Labour Force Survey 2015, Quarter 3 (authors' own calculations).

Similar to the modelling of the age and sex pattern of testing uptake through taxi ranks, we use the following function to represent the age and sex pattern of self-testing in employed populations:

$$A^*_g(x,t) = B^*_g(x/25)^{\alpha^*_g - 1} \exp(-\sigma^*_g(x - 25))$$

where B^*_g is a scaling factor to represent the effect of sex ($B^*_1 = 0.95$ for men and $B_2 = 1$ for women), and α^*_g and σ^*_g are coefficients to represent the effect of age on the rate of testing. Setting α^*_1 and σ^*_1 to 4.59 and 0.153 respectively in men, and setting α^*_2 and σ^*_2 to 2.94 and 0.122 respectively in women, yields a reasonable model fit to the age-specific rates of self-testing through workplaces, as shown in Figure S4. The peak testing rates in males are higher than those in females, despite the B^*_g adjustment being slightly lower for men than for women, which is because of the higher rates of employment in men.

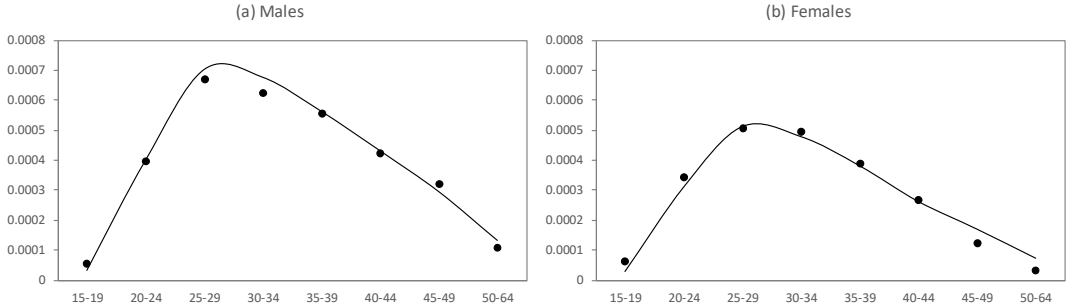

Figure S4: Rates of self-testing through workplaces
Programme data from the STAR project (2017-2020) have been divided by the Thembisa estimates of the size of the sexually experienced population at each age in South Africa (dots). Solid lines represent the estimates from the $\lambda^5_{g,i,s}(x,t)$ equation, scaled by an arbitrary factor to match the relative levels of testing by age and sex.

The coverage parameter $c_5(t)$ is defined as the rate of self-testing through workplace programmes, in employed women aged 25 in year t. We estimate this parameter from the total number of self-tests distributed through campaigns in workplaces in year t, $E_5(t)$, and the assumed fraction of test kits that are not used, W_5:

$$c_5(t) = \frac{E_5(t)(1-W_5)}{\sum_g \sum_i \sum_s \sum_x N_{g,i,s}(x,t) \mathrm{Q}(x,g) A^*_g(x,t) r^*_i(t)}.$$

In the STAR programme, out of 13 308 tests distributed to interviewed individuals, 12 321 (93%) were reported to have been used or given to someone else. We therefore set $W_5 = 0.07$.

Total testing rates and index testing

Table S2 summarizes the data from the STAR programme for the 2017-2020 period, on total numbers of self-testing kits distributed. We assume that this represents the total number of self-test kits distributed, although the STAR programme has also distributed kits through other distribution channels (data forthcoming), and some self-testing kits may be distributed through other providers, or sold through pharmacies.

Table S2: Total self-testing kits distributed in South Africa

Year	Fixed point distribution	Taxi rank distribution	ANC client distribution	Index testing	Workplace testing
2017-18	57701	155643	1107	859	84713
2018-19	117215	225107	9847	3798	165624
2019-2020*	68720	74531	10183	4923	128951

ANC = antenatal clinic. * Results for 2020 are only available up to the end of March so are an under-estimate of the true total.

The total rate of self-testing is calculated as

$$S_{g,i,s}(x,t) = \sum_j \lambda^j_{g,i,s}(x,t).$$

The annual rate at which sexually experienced individuals get tested by health workers is calculated as

$$\tau_{g,i,s}(x,t) = b(t)A_g(x,t)r_i(t) + \Omega_s d_i(t) + F_{g,s}(x,t)v_i(t) + S_{g,i,s}(x,t)\gamma \mathrm{I}(s>1)$$

where $b(t)$ is the base rate of 'general' HIV testing in year t, in individuals who do not have any HIV symptoms and are not pregnant; $A_g(x,t)$ is the adjustment factor to represent the effect of age and sex on the base rate of test uptake; $r_i(t)$ is the adjustment factor to represent the effect of testing history; Ω_s is the annual incidence of OIs in CD4 stage s; $d_i(t)$ is the fraction of OI patients who are tested for HIV in year t; $F_{g,s}(x,t)$ is the fertility rate in sexually experienced women aged x, in HIV stage s, during year t (set to zero for men); and $v_i(t)$ is the proportion of pregnant women who receive HIV testing in year t. The first three terms on the right-hand side of this equation correspond to the three HIV testing modalities previously modelled in Thembisa, and the associated symbols are the same as defined previously [3].

The rate of HIV testing in asymptomatic virgins is assumed to be a multiple φ of the rate of HIV testing in asymptomatic girls aged 15 who are sexually experienced and non-pregnant, i.e.

$$\tau'_{g,i,s}(x,t) = b(t)A_2(15,t)r_i(t)\varphi + \Omega_s d_i(t).$$

For virgins we are therefore excluding antenatal testing (since they would not be pregnant) and self-testing.

Suppose that $G(t)$ is the total number of HIV tests performed by health workers in adults aged 15 and older, in year t. If $V_{g,i,s}(x,t)$ is the number of virgins, at the start of year t, then

$$G(t) \approx \sum_g \sum_i \sum_s \sum_x N_{g,i,s}(x,t)\tau_{g,i,s}(x,t) + V_{g,i,s}(x,t)\tau'_{g,i,s}(x,t).$$

(The relation is not exact because the numbers of individuals in the different strata change over the course of the year, so relying only on the values at the start of the year may lead to some bias.) We use the above calculation to estimate the base rate of testing in year t:

$$\hat{b}(t) = \frac{G(t) - \sum_g \sum_i \sum_s \sum_x N_{g,i,s}(x,t)\{\Omega_s d_i(t) + F_{g,s}(x,t)v_i(t) + S_{g,i,s}(x,t)\gamma I(s>1)\} + V_{g,i,s}(x,t)\Omega_s d_i(t)}{\sum_g \sum_i \sum_s \sum_x N_{g,i,s}(x,t)A_g(x,t)r_i + V_{g,i,s}(x,t)A_2(15,t)r_i\varphi}$$

Sensitivity and specificity of self-testing

Based on a previous review, we assume that self-testing is 100% specific [4] [Figueroa]. We further assume that self-testing sensitivity depends on the recency of HIV infection: self-testing is assumed to have 0% sensitivity during the acute phase of HIV infection (approximately the first 3 months after HIV acquisition) and 100% sensitivity thereafter. With these assumptions the average sensitivity across all HIV testers is around 96% [5], roughly consistent with sensitivities reported in various studies [Figueroa]. These sensitivity and specificity assumptions are the same as for conventional HIV testing in Thembisa.

Linkage to ART after diagnosis

In the previous version of Thembisa we assumed that the probability of ART initiation soon after diagnosis depended on the setting in which diagnosis occurred, with the probability being highest in antenatal care settings (95% in the period after 2015), lower in people diagnosed when seeking treatment for HIV-related OIs (78%), and lowest for individuals diagnosed in other settings (40%).

In the new version of the model, we apply the same 40% probability of linkage to individuals who seek confirmatory testing after a positive self-testing result. This means that the actual proportion of all individuals diagnosed through self-testing who link to ART is 27% (40% × 68%, where 68% is the assumed proportion of positive self-testers who seek confirmatory testing). This is consistent with the assumption made in MicroCOSM (also 27%), which was based on rates of linkage observed in other models of community-based testing, prior to the availability of local data on linkage to care after self-testing [1]. However, rates of linkage to ART after diagnosis through self-testing are difficult to estimate reliably, and these estimates should be treated with caution [6].

Model results and calibration

Table S3 compares the model estimates of the yield on self-testing with the yields estimated from the STAR data. The model estimates of yield are based only on the tests that were used (i.e. the denominator does not include unused test kits). In the case of the secondary distribution testing modalities (index testing and testing of male partners of pregnant women), there is uncertainty regarding the true yield, because individuals only reported on whether they knew that their partner used the test and whether they knew their partner tested positive. In these cases, a conservative lower bound on the yield would be the total number of known positive results divided by the total numbers of tests distributed to sexual partners. An upper bound on the yield would be the total number of known positive tests divided by the numbers of tests that were known to have been used (although one might argue that this is not an upper bound if partners who test positive are less likely to tell their partners that they used the test, or if they are likely to misreport that they are negative). For both secondary testing modalities, the model estimate of the testing yield falls between the lower and upper bounds estimated from the STAR data, which is reassuring.

Table S3: HIV testing yields, averaged over the 2017-2020 period

	Fixed point distribution	Taxi rank distribution	ANC client distribution	Index testing	Workplace testing
Model estimate	5.73% (5.36-6.09%)	5.18% (4.86-5.45%)	3.91% (3.66-4.15%)	19.9% (19.3-20.4%)	6.44% (6.05-6.74%)
STAR data	3.05%	8.98%	-	-	4.23%
Lower bound	-	-	2.22%	11.0%	-
Upper bound	-	-	5.74%	24.4%	-

ANC = antenatal clinic.

In the case of the fixed point distribution, taxi rank distribution and workplace distribution modalities, however, the yields estimated by the model are very inconsistent with the STAR data. While the model estimates that the three modalities should have relatively similar testing yields (5.2-6.4%), the STAR data suggest that the testing yields on these three modalities are very different. Previous studies have identified taxi ranks as 'hotspots' or locations with high HIV prevalence [7, 8], but our model assumes HIV prevalence in taxi ranks is no different from that in the general population (after controlling for age and sex), which may be unrealistic.

Table S4 summarizes the estimates of the testing coverage in each year, for each modality, based on the numbers in Table S1. For all modalities, there was a substantial increase in coverage/uptake between 2017-18 and 2018-19. However, coverage either increased minimally or dropped substantially in the following year, which may be a reflection of the 2019-20 data being incomplete at the time of this analysis.

Table S4: Coverage/uptake of self-testing in South Africa

Year	Fixed point distribution $c_1(t)$	Taxi rank distribution $c_2(t)$	ANC client distribution $c_3(t)$	Index testing $c_4(t)$	Workplace testing $c_5(t)$
2017-18	0.00259	0.00185	0.00099	0.00022	0.01166
2018-19	0.00523	0.00265	0.00803	0.00088	0.02258
2019-20	0.00305	0.00087	0.00833	0.00106	0.01741
Average*	0.00362	0.00179	0.00578	0.00072	0.01722

ANC = antenatal clinic. * The average coverage is assumed to apply in the post-2020 period.

Limitations

The results shown in Tables S3 and S4 are the results obtained using the national version of the Thembisa model. However, almost all of the STAR data come from Gauteng province, and one could argue that it would be more meaningful to run the Gauteng version of the Thembisa model.

Another limitation is that there is substantial uncertainty regarding the relative rates of testing in previously diagnosed individuals, and these assumptions affect the estimated yield on self-testing (Table S3). We assume that individuals who retest positive are no more likely to initiate ART than individuals who were previously diagnosed and did not get tested, i.e. there are no modelled benefits to retesting individuals who have already been diagnosed. This assumption is unrealistic, as evidence suggests that previously-diagnosed individuals who retest positive are as likely to link to HIV care as individuals who are diagnosed positive for the first time [9, 10]. However, the assumption is consistent with the assumption made for health worker-administered testing. In future versions of Thembisa we plan to revise these assumptions about linkage to ART after re-diagnosis, to better reflect the benefits of repeat testing.

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Appendix A: Predicting HIV seroconcordance in South African couples

For the purpose of modelling index testing, it is necessary to be able to estimate the probability that an individual who tests positive has a positive partner. Suppose that we consider a population of n heterosexual couples. We further define a to be the number who are concordant positive, b the number who are serodiscordant with the female partner positive and the male negative, c the number who are serodiscordant with the male partner positive and d the number who are concordant negative (Figure A1).

		Male HIV status: Positive	Male HIV status: Negative
Female HIV status	Positive	a	b
	Negative	c	d

Figure A1: Numbers of couples by HIV status

We define θ to be the odds ratio relating the odds of HIV infection in the individual to the odds of HIV infection in their partner, i.e. $\theta = ad / bc$. We also define π_0 to be the HIV prevalence in male partners $((a + c) / n)$ and π_1 to be the HIV prevalence in female partners $((a + b) / n)$. These quantities can be estimated from various South African studies, as summarized in Table A1. Estimates of θ appear highly heterogeneous across studies, varying between 2.5 and 32, with the odds ratios generally being highest in the studies in which HIV prevalence is lowest. This is because as HIV prevalence increases in the general population, individuals are relatively more at risk of having acquired HIV from partners other than their current partner, and the strength of association between the individual's HIV status and their partner's status thus becomes weaker.

Table A1: South African studies of seroconcordance in heterosexual couples

Study	a	b	c	d	π_0	π_1	θ (95% CI)
Mbulawa *et al* [11]	112	158	44	155	33.3%	57.6%	2.50 (1.62-3.87)
de Bruyn *et al* [12]	302	126	326	671	44.1%	30.0%	4.93 (3.83-6.37)
Kilembe *et al* [13]	245	175	93	394	37.3%	46.3%	5.93 (4.36-8.08)
Lurie *et al* [14]	16	10	25	117	24.4%	15.5%	7.49 (2.78-20.53)
Doherty *et al* [15]	26	50	12	200	13.2%	26.4%	8.67 (3.87-20.06)
2016 DHS [16]	61	44	21	293	19.6%	25.1%	19.34 (10.35-36.55)
Simbayi *et al* [17]	124	134	57	1378	10.7%	15.2%	22.37 (15.37-32.64)
Naik *et al* [18]	11	7	10	201	9.2%	7.9%	31.59 (8.72-115.52)

For the sake of developing a predictive model, we performed a meta-regression on the data in Table A1, using the natural log of the female HIV prevalence as the explanatory variable. (The meta-regression was also done using the log of the male HIV prevalence as the explanatory variable, but this was found to not fit the data as well, so the results of this analysis are not presented here.) The best-fitting model was of the form $\theta(\pi_1) = \exp(0.536) \times \pi_1^{-1.218}$. Figure A2 shows the meta-regression model fit to the data in Table A1.

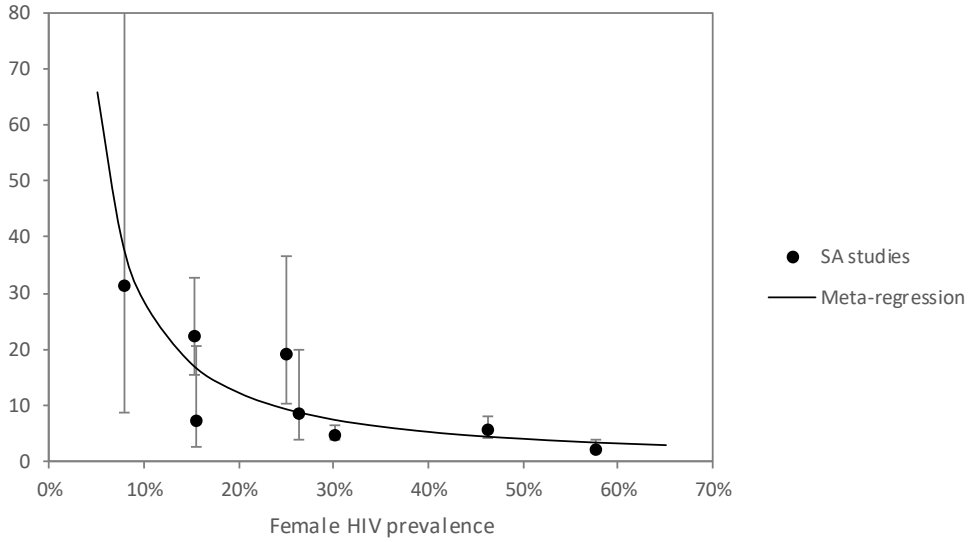

Figure A2: Odds of infection if partner is HIV-positive, relative to odds of infection if partner is HIV-negative

For the purpose of developing a predictive model, we need to be able to estimate a, b, c and d from the parameters $\theta(\pi_1)$, π_0 and π_1. For the sake of simplicity, we will re-express a, b, c and d as proportions that sum to 1, so that $n = 1$, $d = 1 - a - b - c$, $\pi_0 = a + c$, and $\pi_1 = a + b$. Substituting these equations into the odds ratio formula gives

$$\theta(\pi_1) = \frac{a(1-a-(\pi_0-a)-(\pi_1-a))}{(\pi_0-a)(\pi_1-a)}.$$

This can be expressed as a quadratic in a; solving for a gives

$$a = \frac{1+(\theta-1)(\pi_0+\pi_1)-\sqrt{(1+(\theta-1)(\pi_0+\pi_1))^2-4(\theta-1)\theta\pi_0\pi_1}}{2(\theta-1)}.$$

The probability that the female partner is positive, given that the male partner is positive, is then $a / (a + c) = a / \pi_0$. Similarly, the probability that the male partner is positive, given that the female partner is positive, is a / π_1. We thus have formulas for predicting partner concordance as a function of the HIV prevalence in males and females, in a population of heterosexual couples.

Section 2: Supplementary results

Table S1. Description of HIVST modalities and feasible maximum number of target populations

Fixed point	
Description	HIV self-test (HIVST) kits distributed at pre-selected locations within local communities. Testing tents are set up near areas of congregation (eg. hostels, taverns and brothels); demonstration of HIVST kit use provided, HIVST kits are distributed to consenting clients. Clients can choose option of self-testing in the tent or can take kit home for private use. For clients screening positive on site, confirmatory testing conducted by a professional provider was offered on site.
Target population description	HIV- adults and undiagnosed HIV+ adults (assuming fixed point distribution will be concentrated in 5 largest metropolitan municipalities)
Feasible maximum number of people	~14 million[1]
Taxi ranks	
Description	Distribution of HIVST kits to commuters, taxi drivers and street vendors in densely populated taxi ranks and train stations, with high foot traffic. Distribution agents provided a demonstration of HIVST kit use and offered kits to interested clients for private use off site.
Target population description	Adults accessing taxis who are HIV negative or undiagnosed PLHIV
Feasible maximum number of people	~3.9 million[2]
Secondary PHC (ANC)	
Description	Women attending their first antenatal care (ANC) visit at a primary healthcare (PHC) clinic were offered HIVST kits, to take home to their current male sexual partner(s) – defined as secondary distribution.
Target population description	Women attending ANC care
Feasible maximum number of people	~1.2 million[3]
Secondary PHC (ART patients)	
Description	HIVST kits offered by to ART patients and newly diagnosed HIV positive adults at a PHC clinic to share with their sexual partner(s) or family members who were unaware of their HIV status.
Target population description	Adults on antiretroviral treatment (ART) + newly diagnosed HIV-positive adults
Feasible maximum number of people	~5.4 million[4]
Workplace	
Description	Workplace distribution was predominantly conducted in a number of male-dominated sectors such as manufacturing, mining, construction, security, petroleum and agriculture. Two types of workplaces included: a) Larger companies without formalised HIV testing programmes or those with low HIV testing uptake were contacted before the distribution event for sensitisation; b) Distribution also took place more ad-hoc and without prior arrangement with management to employees of smaller workplaces such as petrol stations or construction sites.
Target population description	Employed population
Feasible maximum number of people	~10 million[5]
Primary PHC	
Description	This modality involved primary distribution of HIVST for on-site screening of clients attending the clinic for different services including family planning and treatment for sexually transmitted infections.
Target population description	Existing patient population seeking conventional HTS at PHC
Feasible maximum number of people	~15 million[6]

Footnotes:

1. Statistics South Africa Mid-year Population Estimates 2020 in the five largest metro municipalities (City of Cape Town, Ekurhuleni, Johannesburg, Tshwane, eThekwini), combined with provincial-level Thembisa 4.3 estimates of % diagnosed and district-level HIV prevalence statistics from the Naomi model (https://www.hivdata.org.za/)
2. Estimated from worker and higher education population using minibus taxis (Statistics South Africa National Household Travel Survey 2013), combined with HIV prevalence and known diagnosis estimates from Thembisa 4.3
3. Estimates of women attending antenatal care in 2020 from Thembisa 4.3
4. Estimates of adult population on antiretroviral treatment and newly diagnosed HIV+ adults in 2020 from Thembisa 4.3
5. Estimates of employed population from Statistics South Africa. Statistical Release P0277. Quarterly Employment Statistics. December 2019.

Table S2: Unit costs used in the costing of the HIV programme

Intervention	Cost unit	Unit cost (2019 USD)
ART provision per adult (first line regimen, first year)	per person	299.15
ART provision per adult (first line regimen, follow-up years)	per person	196.48
ART provision per adult (second line regimen, follow-up years)	per person	323.64
ART provision per child (first year)	per person	322.39
ART provision per child (follow-up year)	per person	229.20
Early infant male circumcision	per person	43.24
Medical male circumcision (MMC)	per person	86.47
Condom provision (per condom distributed)	per condom	0.05
Prevention of mother-to-child transmission	per person	21.03
Conventional HTS: general (negative)	per test	3.75
Conventional HTS: general (positive)	per test	5.52
Conventional HTS: antenatal care (negative)	per test	3.26
Conventional HTS: antenatal care (positive)	per test	5.01
Conventional HTS: provider-initiated testing and counselling (negative)	per test	3.75
Conventional HTS: provider-initiated testing and counselling (positive)	per test	5.52
Conventional HTS: Mobile testing (negative)	per test	5.76
Conventional HTS: Mobile testing (positive)	per test	6.66
Conventional HTS: Home based testing (negative)	per test	5.76
Conventional HTS: Home based testing (positive)	per test	6.28
Conventional HTS: Partner notification (negative)	per test	3.41
Conventional HTS: Partner notification (positive)	per test	5.32
HIVST: fixed point	per test	5.70
HIVST: taxi ranks	per test	4.74
HIVST: partners of pregnant women	per test	13.04
HIVST: partners of ART patients	per test	12.31
HIVST: primary PHC	per test	8.24

Figure S1. A) number of HIV infections averted over the status quo, and B) incremental cost (2019 USD) per HIV infection averted; distributing up to 1 million HIVST distributed per year. Status quo distribution of 1 million HIVST kits: fixed point (5% of HIVST), taxi ranks (5%), secondary PHC (ANC) (7%), secondary PHC (ART patients) (3%), workplace (20%) and primary PHC distribution (60%).

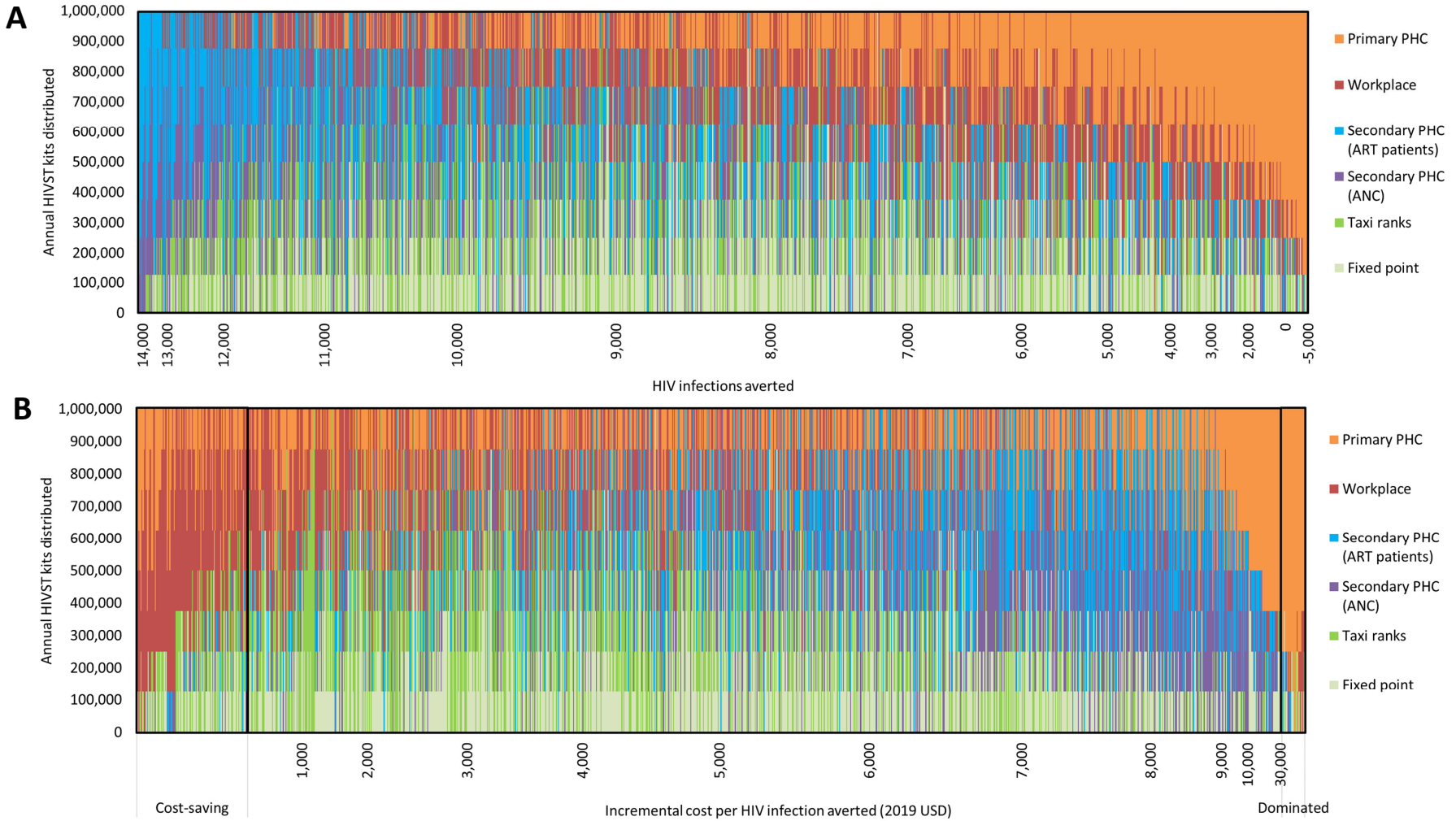

Figure S2. A) number of new HIV infections averted over the status quo, and B) incremental cost (2019 USD) per HIV averted; distributing up to ~6.7 million HIVST per year by 2030. Status quo distribution of 1 million HIVST kits: fixed point (5% of HIVST), taxi ranks (5%), secondary PHC (ANC) (7%), secondary PHC (ART patients) (3%), workplace (20%) and primary PHC distribution (60%)

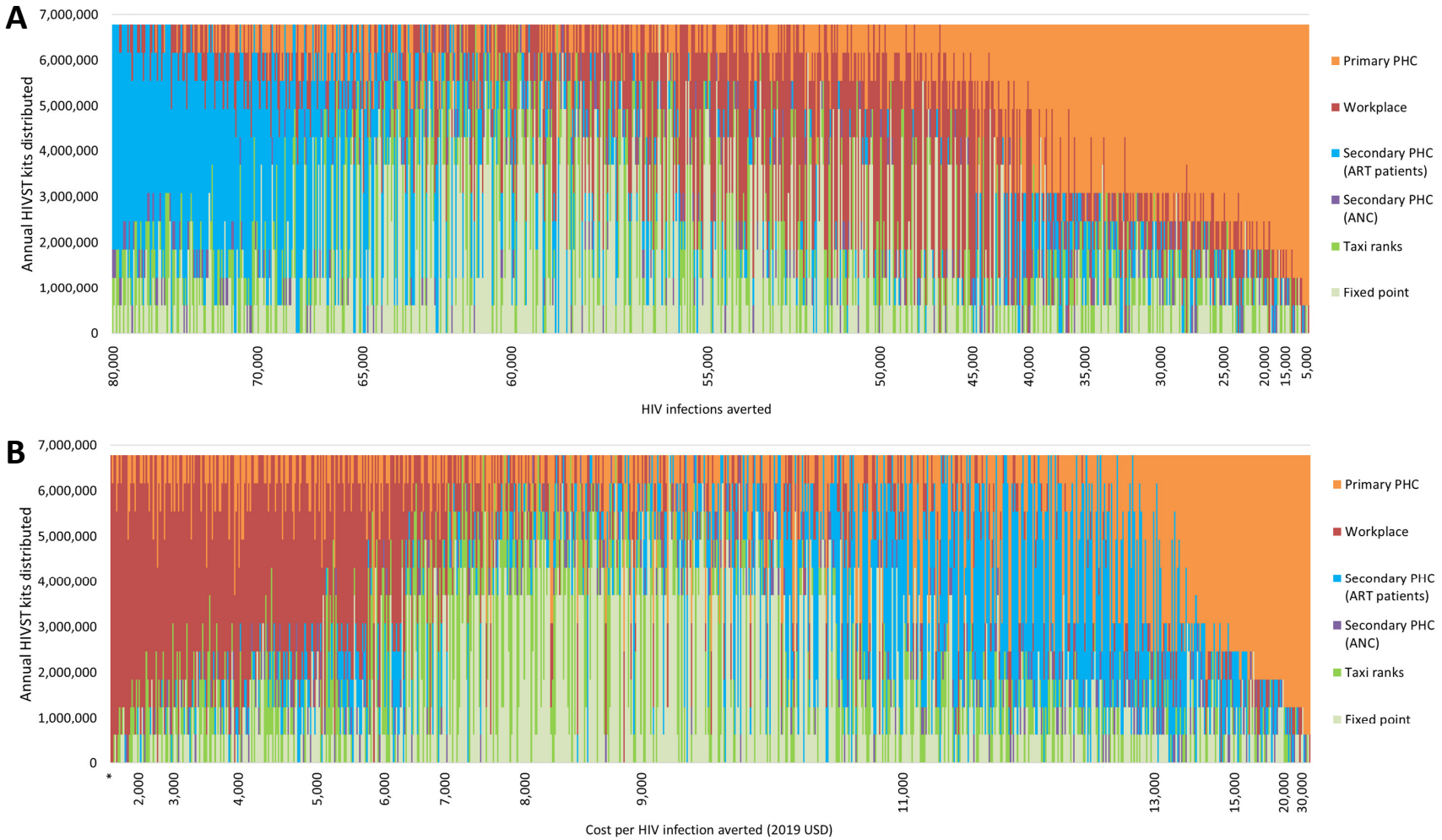

Figure S3. A) number of life years saved over baseline of no HIVST, and B) incremental cost (2019 USD) per life year saved; distributing up to 1 million HIV-ST distributed per year.

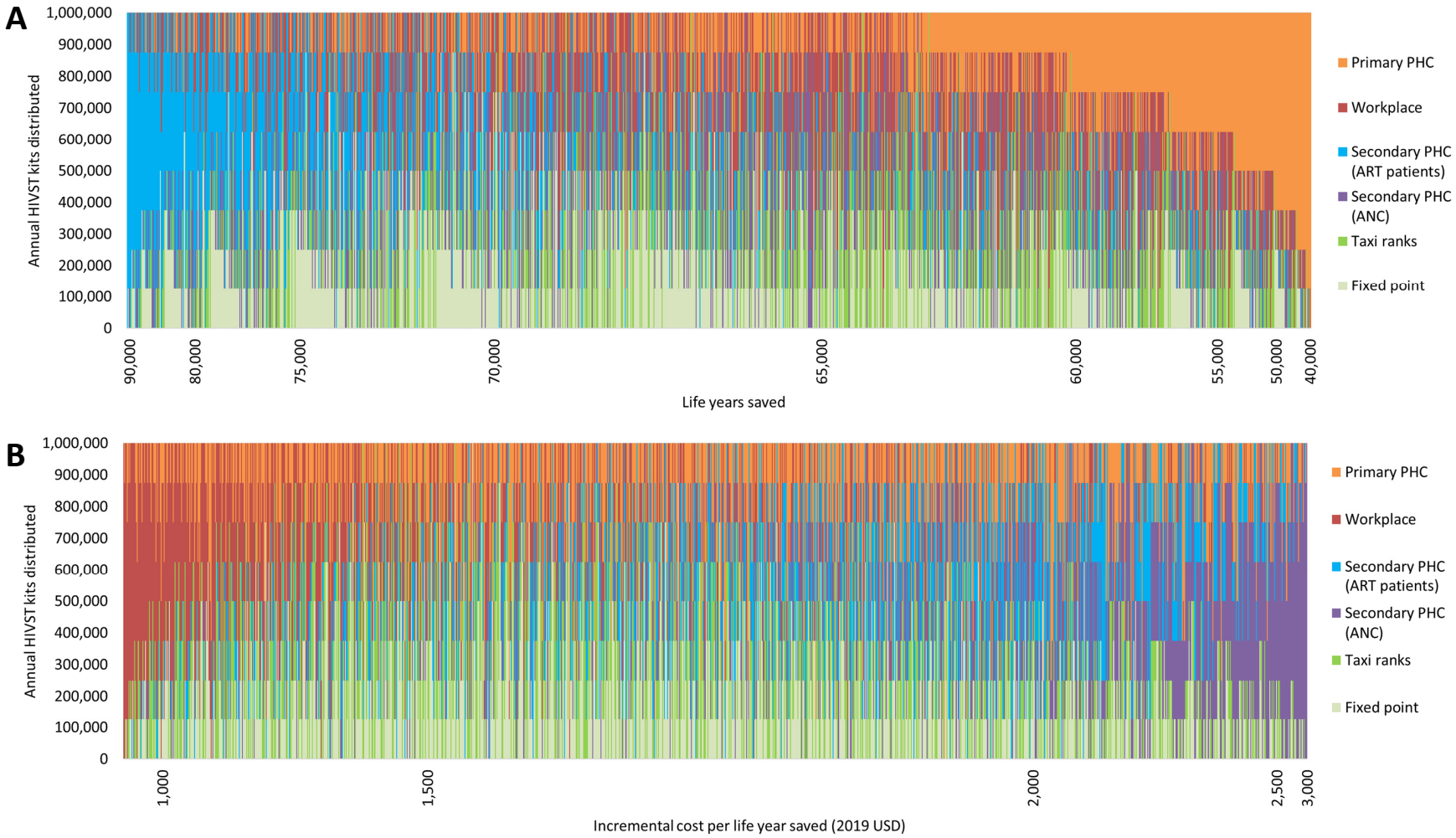

Figure S4. A) number of life years saved over baseline of no HIVST, and B) incremental cost (2019 USD) per life year saved; distributing up to ~6.7 million HIV-ST distributed per year.