Time to scale up PrEP beyond the highest-risk populations? Modelling insights from high-risk women in sub-Saharan Africa

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Short summary: A study exploring strategies for scale-up of PrEP for women at population-level across sub-Saharan African countries spanning a range of HIV burden, weighing individual cost-effectiveness with population impact.

Abstract

Objectives: New HIV infections remain higher in women than men in sub-Saharan Africa. PrEP is an effective HIV prevention measure, currently prioritized for those at highest risk, such as female sex workers (FSW), for whom it is most cost-effective. However, the greatest number of HIV infections in sub-Saharan Africa occur in women in the general population. As countries consider wider PrEP scale-up, there is need to weigh the population-level impact, cost and relative cost-effectiveness to inform priority-setting.

Methods: We developed mathematical models of HIV risk to women and derived tools to highlight key considerations for PrEP programming. The models were fitted to South Africa, Zimbabwe and Kenya, spanning a range of HIV burden in sub-Saharan Africa. The impact, cost and cost-effectiveness of PrEP scale-up for adolescent girls and young women (AGYW), women 25-34 years and women 35-49 years were assessed, accounting for differences in population sizes and the low program retention levels reported in demonstration projects.

Results: PrEP could avert substantially more infections a year among women in general population than among FSW. The greatest number of infections could be averted annually among AGYW in South Africa (24-fold that for FSW). In Zimbabwe, the greatest number of infections could be averted among women 25-34 years (8-fold that for FSW), and in Kenya similarly between AGYW and women 25-34 years (3-fold that for FSW). However, the unit costs of PrEP delivery for AGYW, women 25-34 years and women 35-49 years would have to reduce considerably (by 70.8-91.0% across scenarios) for scale-up to these populations to be as cost-effective as for FSW.

Conclusions: PrEP has the potential to substantially reduce new HIV infections in HIV-endemic countries in sub-Saharan Africa. This will necessitate PrEP being made widely available beyond those at highest individual risk, and continued integration into a range of national services and at community level to significantly bring down the costs and improve cost-effectiveness.

Key words: HIV, pre-exposure prophylaxis, female sex workers, adolescent girls and young women, scale-up, women, impact, cost-effectiveness, sub-Saharan Africa

Introduction

Women remain the most affected by the global HIV epidemic. In sub-Saharan Africa, the region with the greatest HIV burden, 59% of new adult infections are among women[1]. In 2018, a quarter of all new infections were among adolescent girls and young women (AGYW) aged 15-24 years[2], whilst female sex workers (FSW) are up to 20 times more likely to be HIV positive than women in the general population[3].

Oral pre-exposure prophylaxis (PrEP) has shown HIV prevention efficacy in randomised controlled trials (up to 99% risk reduction, depending on drug adherence and study population)[4,5]. It is hoped PrEP will address some of the drivers of HIV in women, which include lack of agency to negotiate sex and condom use[1]. Aside from women in sero-discordant relationships[6], PrEP demonstration projects have faced challenges in retaining women[7–9], raising concerns about the ability of programs to avert infections when scaled-up[1]. A recently completed PrEP demonstration project among FSW in South Africa reported 22% 12-month program retention rates[7]. Early results from programming in Kenya[9,10,11] and Zimbabwe[12] show even lower retention rates in AGYW than FSW.

As PrEP is rolled out in countries in sub-Saharan Africa in line with 2016 normative guidance, its use has been prioritised for populations at substantial risk of HIV[13], including FSW, AGYW and individuals with history of low condom use, STIs, multiple concurrent partnerships and transactional sex[14–23]. PrEP programs are being hosted by services tailored for groups at highest risk of infection, or in general services with screening tools used to identify those most at risk. There have been challenges with the sensitivity and specificity of screening tools, which may serve better as an initiator of client-provider dialogue rather than as a determinator of eligibility[13,24–27]. Increasingly, there is pressure for countries to move towards universal access to PrEP as part of a rights-based approach to health[28]. The rights-based language of PrEP programming is shifting to refer to populations who could benefit from PrEP, rather than focus on an individual's level of risk[28].

Whilst FSW are typically women at highest HIV risk[2], HIV incidence among women in the general population varies significantly by age range across countries in sub-Saharan Africa[2], To date, six of the eight finalised population-based HIV impact assessments (PHIA) undertaken in sub-Saharan African countries reveal higher levels of incidence in women 25-34 years or 35-49 years than in AGYW 15-24 years[29–36]. Policy makers are having to weigh the potential benefits and challenges of scaling up PrEP for groups of women at lower individual levels of risk, but in whom the total number of new infections is greater due to differences in population sizes[1].

Decisions around PrEP scale-up are taking place in a context of limited external resources for HIV, constraints in domestic budgets and a global push for countries to prioritize resources to reach the 90-90-90 treatment targets[1]. These decisions mirror those previously faced by policy makers in determining whether to scale up antiretroviral treatment (ART) for individuals at higher CD4 counts, balancing comparatively lower benefits for individuals with potential for greater population-level prevention effects[13].

Several modelling studies have evaluated the cost-effectiveness and impact of PrEP for high-risk populations in sub-Saharan Africa[37–41]; between key populations and men/ women in the general population[42,43]; between groups in the general population[44–47]; relative to other HIV prevention interventions and ART[40,44,45,48–51]. Studies typically find PrEP to be less cost-effective than other established prevention interventions or scaling up ART, but cost-effective as part of a combination prevention approach for those at greatest risk. To date no study has assessed the scale-up of PrEP from highest-risk populations (e.g. FSW) to groups of women across the general population at comparatively lower risk, weighing cost-effectiveness on an individual basis with the need to avert the greatest number of infections at a population level.

Our study aims to build simple mathematical models to highlight key considerations to feed into policy making, as countries consider scaling-up PrEP across a more broadly defined group of women at risk in sub-Saharan Africa. It aims to present decision makers with a range of important considerations, including PrEP cost-effectiveness, cost and estimated number of HIV infections averted on PrEP for different groups of women at population-level. We use case studies of three HIV-endemic countries: South Africa, Zimbabwe and Kenya. These countries, spanning a range of HIV burden levels in the region, have each adopted a national PrEP strategies[19–21], and been at the forefront of PrEP roll-out in sub-Saharan Africa[28]. This study makes a first attempt to address a gap in the literature, given the limited use of real-world PrEP retention and use-effectiveness data in parameterizing modelling studies[52].

Materials and Methods

As the contexts in which the models are being applied are stable generalised high prevalence HIV epidemics[1], we adopted static mathematical models of HIV risk[53–55]. Static models are a comparatively easier tool for use and communication with policy makers, and have been shown to be robust to inform policy making around the introduction of new HIV interventions over short-medium time horizons in stabilised epidemics[56].

The mathematical models take the Bernoulli formulation of HIV risk[56]. In this model formulation, women's sexual partners are assumed to come from one or more population groups, each with a given level of HIV prevalence. Women are assumed to have a certain number of partners from each of these population groups per year, with whom they have an average number of sex acts each per year. Sex acts are assumed to be peno-vaginal, which is the predominant pathway of HIV transmission to heterosexual women in sub-Saharan Africa[1]. Condoms are assumed to be used with partners from each population group with a given level of consistency (% of time that they are used). The risk-reduction efficacy of condoms is taken to be 85% (range 80-90%)[57,58]. We used estimates for women from the Partners Demonstration Project[59] to relate levels of PrEP adherence to levels of HIV risk reduction. We used the 12-month PrEP programme retention levels reported in the South African TAPS demonstration project in FSW[7] (the only study to date from which there is empirical evidence of 12-month PrEP retention levels in women in sub-Saharan Africa). The models also account for STI levels, levels of viral load suppression due to ART in HIV positive partners, and male circumcision. Analyses were conducted over a one-year timeframe, as PrEP is intended to cover 'seasons' of HIV risk, and few PrEP demonstration programs have achieved significant retention in women in this context beyond the first 12 months[7,9]. The mathematical models, basic rules derived from them, and data used to parameterise and calibrate the models are given in the *Supplementary Materials: Supplementary Methods* section*.* All models were programmed in R version 3.3.2.

Tools to help guide PrEP programme decision making

Heatmaps were developed to help guide programme decision making using a basic set of information typically available to PrEP programmes[60]. They are intended to apply to women from any age group, to help programmers understand their underlying HIV risk and evaluate whether PrEP may be of benefit to them. The first set of heatmaps helps decision makers estimate the annual HIV incidence in women by number of monthly sex acts, average condom use and underlying epidemic setting (i.e. HIV prevalence in the partner population). The number of monthly sex acts, average condom use and HIV prevalence in the partner population are simulated over a range of possible levels in the sub-Saharan African context – spanning women who have very low to very high risk behaviours.

The second set of heatmaps helps decision makers estimate the relative unit cost at which it will be cost-effective to scale up PrEP from a comparatively higher- (e.g. FSW) to comparatively lower-risk woman (e.g. AGYW). The cost-effectiveness ratio is defined as the incremental cost of PrEP per infection averted, per year. It accounts for the level of PrEP program retention and average PrEP adherence. The cost-effectiveness ratio and further details are given in *Supplementary Materials: Supplementary Methods section 2.2* and *equation S2.5.* In the absence of willingness-to-pay thresholds, relative cost-effectiveness was assessed by comparing estimates of cost per infection averted between populations. It was assumed that the higher-risk group had 22% PrEP program retention levels and all women retained had PrEP adherence levels of 70-85% (corresponding to risk-reduction of 73-99%[59]), consistent with the South African TAPS demonstration project in FSW[7]. Given this paucity of empirical data, PrEP program retention for the lower-risk group was simulated between $\pm$25% of the 22% retention levels of the higher-risk group (i.e. 16.5%-27.5%), consistent with the difference between 6-month AGYW and FSW retention in Kenya[9] for the lower bound, and for the upper bound to account for data uncertainty. For lower-risk women retained in the PrEP program, it was assumed that PrEP adherence was the same as the higher-risk group.

Country case studies

In order to highlight key considerations to feed into decision making as countries consider scaling-up PrEP beyond those at highest-individual risk, we assessed the cost-effectiveness, cost and impact of scaling-up PrEP for women across a spectrum of high HIV risk in South Africa, Zimbabwe and Kenya. Given their significantly higher individual HIV risk[1], FSW were taken as the benchmark for assessment. In comparison, we considered the scale-up of PrEP to three groups of women at high HIV risk in the general population[61–63]: AGYW, women 25-34 years and women 35-49 years. No further targeting of PrEP was assumed. Women aged 50+ were not evaluated given paucity of information available to parameterise and fit the models in all three country contexts[29,64–67].

FSW were assumed to have partners drawn from two populations: regular partners and clients. AGYW were assumed to have partners drawn from their own age group (15-24 years) and the 25-34 years age group, given that 17% and 14% women 15-19 years report relationships with men at least 10 years older in Zimbabwe[65] and Kenya[66] respectively, and 36% South African women 15-19 years report relationships with men at least 5 years older[61]. Women 25-34 years and women 35-49 years were assumed to have partners drawn from their own age groups given lack of data to suggest otherwise. This assumption was explored further through structural sensitivity analysis (see below section). Data to parameterise the models were drawn from the literature and fitted to the latest national estimates of HIV incidence[29,68–75] using Bayesian Monte Carlo Filtering with Latin Hypercube Sampling. See *Supplementary Materials: Table S2* for all data used in parameterising and fitting the models.

FSW were assumed to have 12-month PrEP program retention and adherence levels consistent with the TAPS demonstration project[7]. All other women were assumed to have program retention levels between $\pm$25% of these 12-month FSW retention levels[9], and the same adherence levels as FSW retained in the program. To explore the role of adherence, the parametric uncertainty analyses were repeated with 1) 25% lower HIV risk-reduction across all groups, and 2) 25% lower HIV risk-reduction across AGYW, women 25-34 years and women 35-49 years (unchanged among FSW).

As a comparison, we estimated the current unit costs of PrEP program delivery per person retained after 12-months (Table 1). We assumed FSW were offered PrEP through programmes with outreach and community mobilisation components and all other women were offered PrEP through sexual and reproductive health services, with AGYW having larger counselling components. Further information on the methodology and assumptions are set out in *Supplementary Materials: Supplementary Methods section 2.2* and in the assumptions column in Table 1.

Structural sensitivity analysis

We explored how the model outcomes change if women aged 25-34 years have an additional partner group from an older male population (35-49 years); illustratively assuming 50% the number of partners a year from this age group as had by women 35-49 years.

Further details on the methods are set out in *Supplementary Materials: Supplementary Methods,* and all data used in the study in *Supplementary Materials: Table S2.*

Results

Figure 1 shows the estimated annual HIV incidence in women, according to their number of monthly sex acts and their average condom use. The estimates are shown for four cases: underlying HIV prevalence in partner population of 5%, 10%, 20% and 40%.

Figure 1 shows that where women's partners come from a population with HIV prevalence of up to 5%, women will be below the 3%[13] WHO-recommended annual HIV incidence threshold for PrEP where the number of sex acts a month is up to 10 and average condom use is at least 50% (areas shaded yellow). As the underlying HIV prevalence in the partner population increases, women will need higher levels of condom consistency or to engage in fewer sex acts a month to be below the WHO incidence threshold for PrEP (areas shaded orange-red). Where women's partner population have a prevalence of 40%, women will almost uniformly be above the threshold for PrEP.

The relative cost at which PrEP will be equally as cost-effective to be scaled-up in the lower-risk group as it will be in the higher-risk group, is demonstrated in Figure 2 for four scenarios: underlying HIV prevalence in the lower-risk women's partner population of 10%, 20%, 30% and 40%, with HIV prevalence in the higher-risk women partner population of 40%. The equivalent figure corresponding to 20% HIV prevalence in the higher-risk women's partner population is given in *Supplementary Materials: Figure S4.* The relative cost at which PrEP will be equally as cost-effective is shown by the relative average condom use in the lower-risk group compared to the higher-risk group (x-axis), and the relative number of sex acts a month for women in the lower-risk group compared to the higher-risk group (y-axis).

Where HIV prevalence in the lower-risk women's partner population is 10%, the results show that the unit cost of PrEP in the lower-risk group will have to be much lower than in the higher-risk group for PrEP roll-out to be equally as cost-effective (areas shaded yellow), other than where the numbers of monthly sex acts in the lower-risk group exceeds that of the higher-risk group (areas shaded green). This is independent of the levels of condom use by either the higher- or lower-risk women. As HIV prevalence increases in the lower-risk women's partner population relative to the higher-risk women's partner population, PrEP will be equally cost-effective between the two groups at increasingly higher unit costs for the lower-risk group relative to the higher-risk group. Relative cost-effectiveness does not, however, imply affordability at either individual or population level[40].

In Figure 2, 100% on the axes represents the point at which condom use or the number of sex acts per month in the "lower-risk" woman goes from being lower than to the same as in the "higher-risk woman". This may represent the case that, for example, an AGYW engaging in transactional sex has higher risk behaviours (e.g. lower condom use) than a FSW (e.g. with relatively high levels of condom use).

Country case studies

The model fits to HIV incidence for South Africa, Zimbabwe and Kenya are given in *Supplementary Materials: Figures S1-S3.*

Figure 3 shows the maximum unit cost of PrEP for AGYW, women 25-34 years and women 35-49 years, relative to the unit cost of PrEP for FSW, for scale-up to be equally as cost-effective as it is in FSW. This is shown for South Africa (blue), Zimbabwe (orange) and Kenya (green). As comparators, the estimated current relative unit costs are shown (cream). The underlying data for Figure 3 are given in Table 2.

For example, in the case of AGYW in South Africa, Figure 3 shows that PrEP will be equally cost-effective for AGYW as for FSW at a maximum median relative unit cost of 23.3 % (95% CrI: 13.3%, 36.8%) (furthest left blue boxplot). The current estimated unit cost of PrEP in AGYW relative to FSW in South Africa is median 79.8 % (95% CrI: 73.0%, 87.0 %) (furthest left cream boxplot). If the cost of PrEP for AGYW in South Africa dropped by median 70.8% (95% CrI: 53.2%, 83.4 %) it would be equally as cost-effective as for FSW.

Otherwise, across all other scenarios in all three countries, the current unit cost of PrEP for AGYW, women 25-34 years and women 35-49 years would have to drop between median 71.8-91.0% (95% CrIs spanning: 50.8%, 96.5%) to be equally as cost-effective.

Figure 4 illustrates the estimated number of infections that could be averted a year due to PrEP in each high-risk women population group, in each country, for every $100,000 available for PrEP programming.

Given the differences in relative population sizes, Figure 5 demonstrates the relative number of infections that could be averted a year with PrEP at equal coverage levels in AGYW, women 25-34 years and women 35-49 years as in FSW. In comparison to the number of infections averted annually in FSW in South Africa, a median 24 times (95% CrI:12, 45) the number of HIV infections could be averted in AGYW, median 14 times (95% CrI:7, 27) in women 25-34 years, and median 8 times (95% CrI:4, 17) in women 35-49 years, if PrEP were rolled out at the same coverage levels across populations. However, the cost of these programmes relative to the cost of programmes for FSW would be a median 28.3-, 26.7- and 18.7-fold higher for AGYW, for women 25-34 years and for women 35-49 years, respectively *(Supplementary Materials: Table 4a).*

In Zimbabwe, a median 4 times (95% CrI:2, 9) the number of annual HIV infections could be averted in AGYW, median 8 times (95% CrI:3, 14) in women 25-34 years, and median 3 times (95% CrI:2, 5) in women 35-49 years, in comparison to FSW with equal PrEP program coverage. However, the cost of these programmes relative to the cost of programmes for FSW would be a median 21.9-, 15.2- and 7.0-fold higher for AGYW, for women 25-34 years and for women 35-49 years, respectively.

In Kenya, a median 3 times (95% CrI:2, 8) the number of HIV infections could be averted in AGYW, median 3 times (95% CrI:1, 5) in women 25-34 years, and median 1 times (95% CrI:1, 3) in women 35-49 years, in comparison to FSW with equal PrEP program coverage. However, the cost of these programmes relative to the cost of programmes for FSW would be a median 27.4-, 16.4- and 8.5-fold higher for AGYW, for women 25-34 years and for women 35-49 years, respectively.

Sensitivity analyses

Repeating the analyses shown in Figures 3 and 5 with 25% reduced adherence-related HIV risk-reduction across all female groups led to <0.01% change across the scenarios (*Supplementary Materials: Tables S9 and S10)*. Repeating these analyses with 25% reduced adherence-related HIV risk reduction among all non-FSW women groups led to <0.3% change across the scenarios (*Supplementary Materials: Tables S11 and S12).* Repeating these analyses under the structural sensitivity analysis led to <1% change across scenarios (*Supplementary Materials: Tables S13 and S14).*

Discussion

This is the first study to assess the potential impact and relative cost-effectiveness of PrEP scale-up from FSW to groups of women in the general population groups among countries in sub-Saharan Africa, using updated data from PrEP programming to highlight key considerations for decision making. Our findings may be of interest to national policy makers as they consider adopting PrEP policies based on more inclusive definitions of people at risk in line with conclusions from other studies that PrEP will only have substantial effect on generalised epidemics if scaled-up beyond highest-risk groups[40,45,46]. PrEP should be offered to women at highest HIV risk, such FSW, for whom it is most cost-effective. However, only by extending PrEP to women at comparatively lower risk will new HIV infections reduce substantially.

We developed tools to guide PrEP programming: heatmaps to estimate the annual HIV incidence in women (Figure 1) and relative cost-effectiveness between higher- and lower-risk women (Figure 2). By adapting the models to three countries spanning the spectrum of high HIV burden contexts in sub-Saharan Africa, we have shown that the unit costs of PrEP delivery for AGYW, women 25-34 years and women 35-49 years would have to reduce considerably (by median 70.8-91.0% across scenarios) for scale-up to these populations to be as cost-effective as for FSW.

Rolling out PrEP for women in the general population has potential to substantially impact on the countries' HIV epidemics. In South Africa, PrEP has the potential to avert approximately 24 times the number of infections annually in AGYW as in FSW when scaled up at equal coverage levels, and approximately 14 and 8 times the number in women 25-34 and 35-49 years respectively. In Zimbabwe approximately 8 times the number of infections could be averted annually in women 25-34 years as in FSW, and approximately 4 and 3 times the number in AGYW and women 35-49 years respectively. In Kenya, approximately 3 times the number of infections could be averted annually in AGYW and in women 25-34 years as in FSW, and around the same number in women 35-49 years as in FSW.

However, scaling up PrEP programs among the general population is likely to be costly and pose challenges of affordability. This study has shown that scaling up PrEP programs for AGYW, women 25-34 years and women 35-49 years would cost a median 18.7-28.3 times (across scenarios) the cost of programmes with equal coverage levels among FSW in South Africa. In Zimbabwe, programmes for these groups of women with equal coverage would cost a median 7.0-21.9 times the cost of programmes for FSW, and in Kenya, a median 8.5-27.4 times the cost of programmes for FSW.

Policy makers will need to weigh these prospects for population-level impact against affordability, in view of current program costs, budget constraints and program sustainability (although PrEP is for seasons of risk, rather than long-term use, so may be more feasibly scaled back as population incidence decreases). Relative cost-effectiveness does not indicate affordability at individual or population level[40]. Scaling up PrEP for women in the general population has the potential to drive cost reductions through economies of scale. This will require countries to continue to integrate PrEP into a range of health, non-health and community services for women in the general population[19–21], which in some instances (e.g. education) may be challenging in local cultural contexts. Future long-acting PrEP formulations under investigation[76–78], may also help improve cost-effectiveness, if they increase HIV prevention use-effectiveness through improved product adherence and retention. This study complements the ongoing effort to use mathematical models as tools to understand PrEP scale-up in other countries outside of South Africa[37–43],[44–51,79,80].

Limitations

This study was conducted using static mathematical models, given their comparative ease for use in policy making and they require a narrower and more readily available set of data in comparison to the more complex dynamic models typically used to HIV decision making. However, these models do not assess long-term cost-effectiveness[81] or capture downstream infections averted in partner populations. Studies have shown that introducing HIV prevention interventions to high-risk groups has greatest impact on reducing onwards transmission early in epidemics when prevalence is low and the basic reproductive rate is high, than in endemic high-burden contexts[82,83], such as those in which our model is applied[1]. Therefore, if the study were extended to look at the impact of PrEP beyond its recipients, the estimated number of infections averted would likely increase, the costs per infection averted would likely decrease, and modest changes would be expected comparing the relative impact between high-risk populations.

The heatmap tools in Figures 1 and 2 were developed to help PrEP programmers estimate women's HIV risk using a basic set of information typically available to PrEP programmes (number of sex acts/ month, condom use, estimated HIV prevalence in partner population)[60]. They do not account for more granular information, such as the presence of STIs in sexual partnerships, ART use or viral suppression among HIV positive partners, and male circumcision levels. Such information is needed to estimate a woman's HIV risk more accurately. As such, the heatmap tools should be taken to be indicative, rather than precise, tools for estimating a woman's HIV risk.

Much of the data used to characterise women are limited by age and lack of reliable data on numbers of partners and sex acts. Sexual behaviour data is subject to under-reporting, and when collected through demographic health surveys, reporting as percentages makes it difficult to derive meaningful limits or statistic distributions for the underlying data. Cost estimates are limited by assumptions on how subgroups are reached and scarcity of empirical data. Data uncertainty is addressed to some extent through the uncertainty analysis.

This study was parameterised using population averages for broadly defined groups. It does not account for significant behavioural heterogeneity that exists within each of these groups nor in differences in HIV burden at local-levels, potentially masking important risk groups and population interactions. Accordingly, reported population mixing between women 15-19 years and men 5-10 years older in these countries was represented by AGYW (15-24 years) drawing partners from male populations 15-24 years and 25-34 years. Lack of available data to parameterize women 50 years+ meant it was not possible to explore the scale-up of PrEP to this population group.

This assessment is limited by a paucity of empirical 12-month PrEP programme retention data for women in sub-Saharan Africa[7,11]. Potential differences in PrEP programme retention by female population group were accounted for to some extent in the sensitivity analyses. Should future PrEP programmes be able to retain women for longer than 12-months, it is possible that greater programme efforts will be needed to maintain programme retention and drug adherence (e.g. retention support, client follow up), which may reduce the cost-effectiveness of programmes over longer time horizons. This study also does not explicitly account for other PrEP program cascade factors, such as uptake. Doing so would affect the relative estimates of PrEP effectiveness where at least one female population has materially different program uptake than the others.

Conclusion

PrEP has the potential to significantly reduce the numbers of new HIV infections in HIV-endemic countries in sub-Saharan Africa, even considering low levels of PrEP program retention in women. This will necessitate PrEP being made widely available beyond those at highest individual risk, including to women in the general population. Wide-scale roll out will require integration of PrEP into a wide range of national services and at community level, in order to significantly bring down the costs and improve cost-effectiveness.

Country	Population	**Current unit cost (min - max)**	Service delivery excl. drugs	Drugs only (min - max)	**Specific Assumptions**
South Africa	FSW	190 – 210	130	57 - 80	Unit costs measured during a demonstration project in Johannesburg and Pretoria via FSW clinics. Costs reported by Eakle et al[7] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment) and indirect costs (eg, management, utilities, and transportation). We allocated outreach, demand creation and HCT costs to a unit cost of per person-year on PrEP as these were reported separately.
South Africa	AGYW (15-24 years)	149 – 169	89	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[84] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors' estimation of costs among female adolescents.
South Africa	Women (25-34 years)	128 – 148	68	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[84] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors' estimation of costs among young women.
South Africa	Women (35-49 years)	87 – 107	27	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[84] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors estimation of costs among pregnant women - we assumed for this lowest risk population, the cost will be similar to those attending ANC.
Zimbabwe	FSW	293 – 317	237	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[85]
Zimbabwe	AGYW (15-24 years)	219 – 243	163	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[85]

Zimbabwe	Women (25-34 years)	181 - 204	124	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[85]
Zimbabwe	Women (35-49 years)	106 - 130	50	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[85]
Kenya	FSW	399 - 423	343	57 - 80	Unit costs measured in preparation for a demonstration project in Nairobi via SWOP clinics (for FSW). Costs reported by Cremin et al[86] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), related costs (eg, outreach and demand creation), and indirect costs (eg, management, utilities, and transportation).
Kenya	AGYW (15-24 years)	358 - 382	302	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[87] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs, laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among the highest risk subpopulation in the general population.
Kenya	Women (25-34 years)	294 - 318	238	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[87] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs, laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among all women.
Kenya	Women (35-49 years)	185 - 209	129	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[87] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs,

			laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among all women excluding screening costs.

Table 1: Current unit cost estimates per person retained on PrEP after 12-months by population and country.

The estimated current unit costs for FSW, AGYW, women 25-34 years and women 35-49 years are shown disaggregated by the portion that is service delivery costs and the portion that is drug costs. The costs were calculated in line with the methodology set out in Supplementary Materials: Methods section 2.2. Service delivery costs were taken from demonstration projects and previous costing publications in Kenya[86,87] and South Africa[7]. For Zimbabwe, non-tradable components of the South African estimates were transferred using purchasing power parities[88]. Costs in USD 2017. Ranges were only available for drug unit costs. The far right hand side column of the table sets out specific assumptions made in the calculations.

**For these calculations, we replaced reported drug costs by a range of USD57-80. The low bound is the internationally traded value of USD3.75 (https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf) plus 25% top up of freight and distribution costs in country (15% shipping and handling charges, and 10% for drug distribution costs). The high bound is the highest reported price for drugs in the demonstration projects - 30 days TDF/FTC at USD6.75.*

***transferability of costs between countries followed standard guidelines (https://pdfs.semanticscholar.org/36ab/74fd24fb883db703c475364c34ad574a3f35.pdf)*

**** Purchasing Power Parities (PPP)*

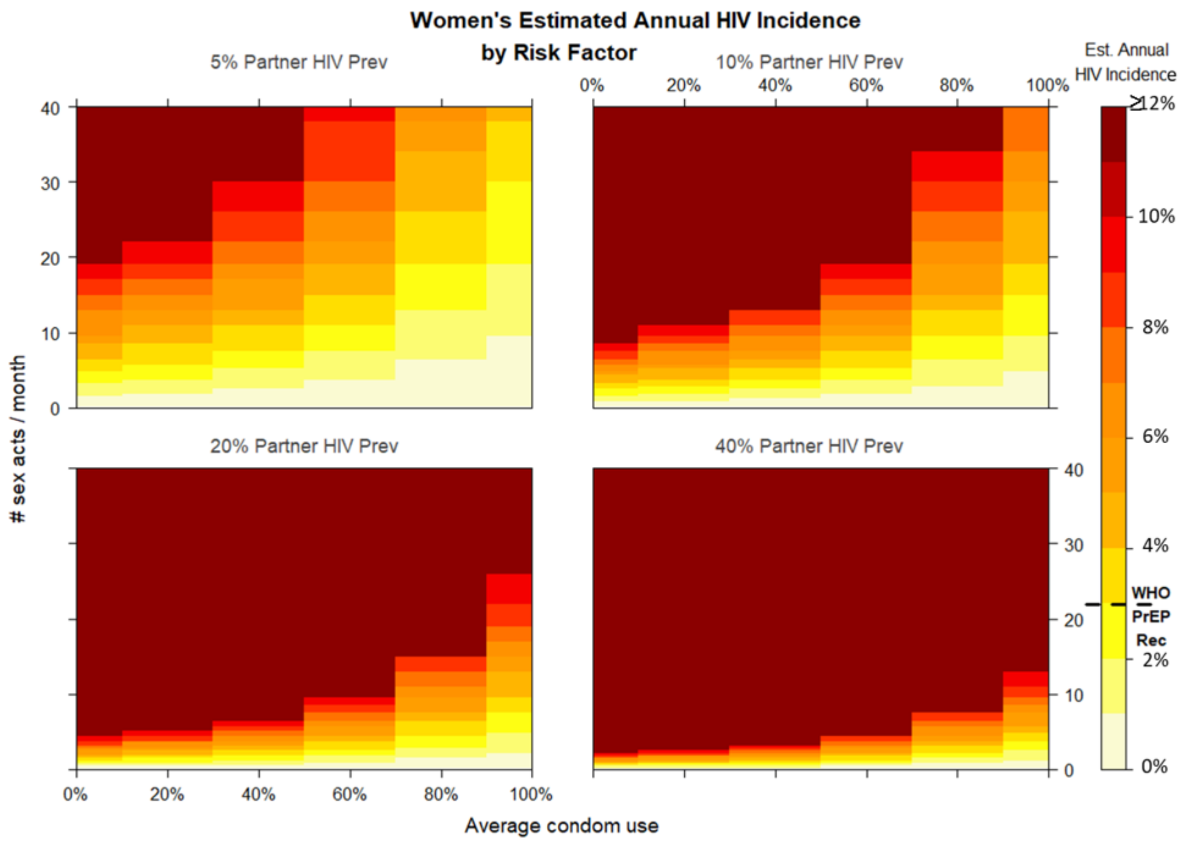

Figure 1: Women's estimated HIV incidence by risk factor.

The heatmaps show the estimated annual HIV incidence in women according to their number of sex acts per month (number of partners multiplied by average number of sex acts with each per month), and average condom use. The estimated annual HIV incidence is shown by colour (according to the colour key on the right-hand side of the graph) in incidence increments of 1% or 1 per 100 person years. An annual incidence of at least 3% or 3 per 100 person years is coloured light orange and corresponds to the WHO recommended threshold for PrEP eligibility[13]. The 4 heatmaps correspond respectively (left to right, top to bottom) to underlying partner HIV prevalence of 5%, 10%, 20% and 40%. The heatmaps are calculated using equation (S1.1) from the Supplementary Materials: Supplementary Methods, section Model Structure, assuming that a women's partners are drawn from a single population and no women are on PrEP.

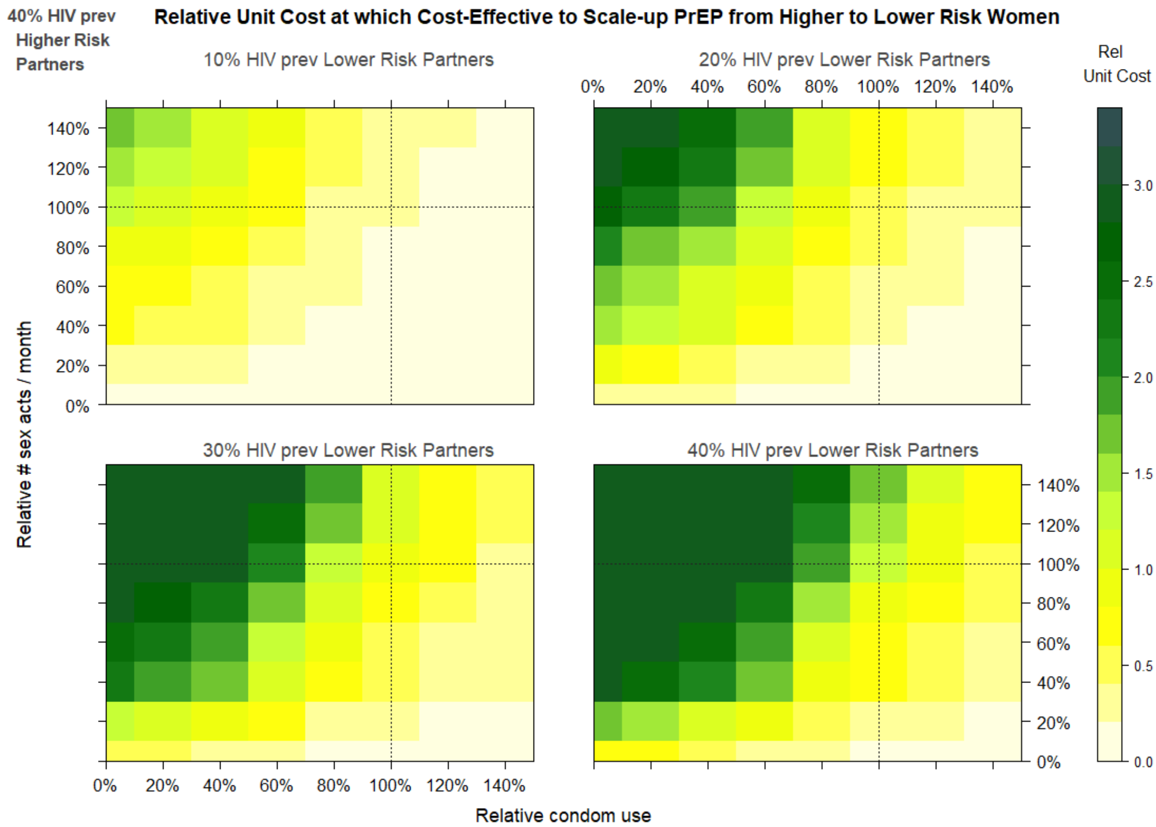

Figure 2: Relative unit cost at which it is cost-effective to scale up PrEP from a higher- to lower-risk women group.

The heatmaps show the relative unit cost at which it is cost-effective to scale up PrEP from a higher- to a lower-risk group. The relative unit cost at which PrEP is cost-effective is shown by the relative average condom use in the lower-risk group compared to the higher-risk group (x-axis), and the relative number of sex acts a month for women in the lower-risk group compared to the higher-risk group (y-axis). 100% on the axes represents the point at which the condom use or number of sex acts in the lower-risk group goes from being lower than to higher than in the levels in the higher-risk group.

The unit cost of PrEP in the lower-risk group relative to the higher-risk group at which PrEP is equally cost-effective between the two groups is shown by colour, according to the colour key on the right-hand side of the graph. A colour within the yellow spectrum denotes that the relative unit cost of PrEP in the lower-risk group relative to the higher-risk group has to be less than 1 for it to be equally as cost cost-effective. A colour within the green spectrum denotes that the relative unit cost of PrEP in the lower-risk group relative to the higher-risk group will be greater than 1 for it to be equally as cost cost-effective. The 4 heatmaps correspond respectively (left to right, top to bottom) to underlying partner HIV prevalence of 10%, 20%, 30% and 40% in the lower-risk group's partner population and all of them corresponding to 40% HIV prevalence in the higher-risk women's partner population. The heatmaps are calculated using equation (S1.5) from the Supplementary Materials: Supplementary Methods, section Model Structure, assuming that women's partners are drawn from a single population each. The higher-risk group are assumed to have 12-month PrEP program retention levels of 22%[7] and *adherence levels of 70-85% (corresponding to a risk reduction of 73-99%[59]). The PrEP program retention levels for the lower-risk group were simulated between +/- 25% the retention of the higher-risk group[9]. For those lower-risk women retained in the PrEP program, it was assumed that PrEP adherence was the same as the higher-risk group. The axes were capped at 140% relative condom use or number of sex acts/ month, in order to depict the most pertinent trends for programmers in the heatmaps.*

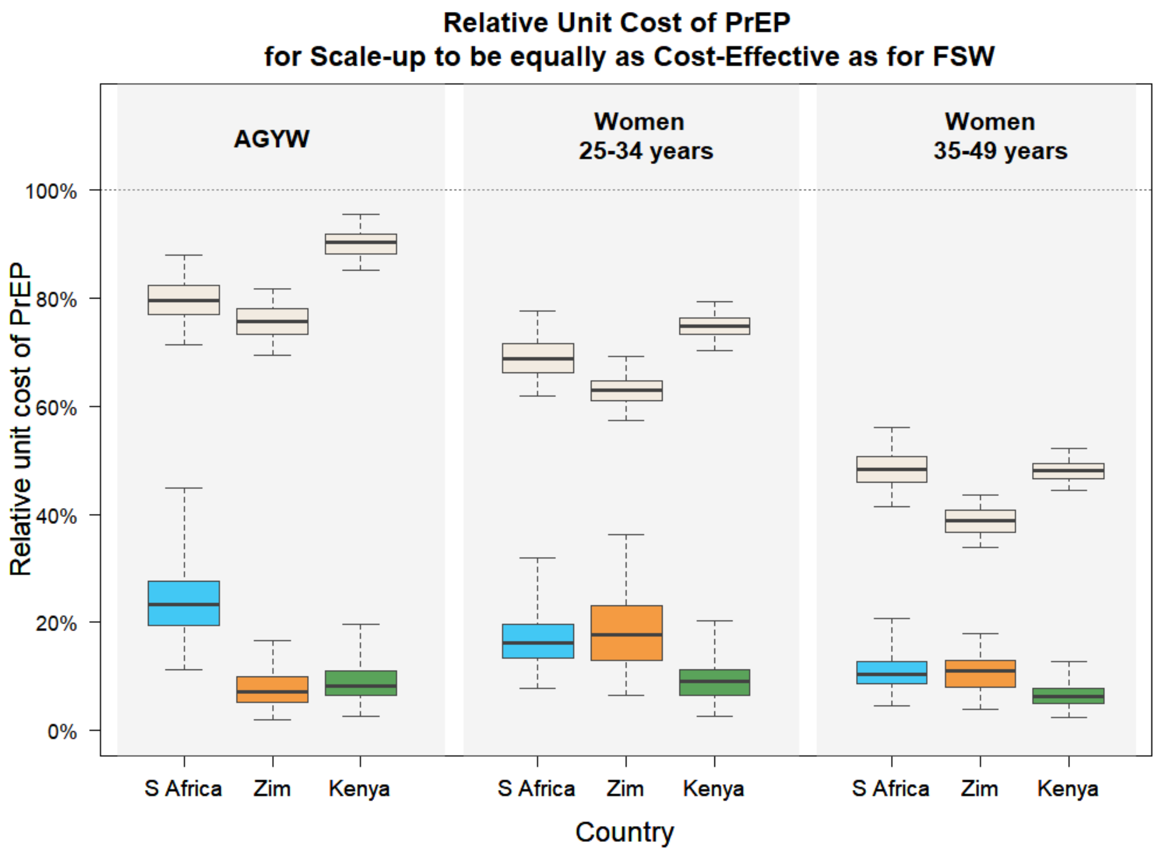

Figure 3: Relative unit cost of PrEP for scale-up to be equally as cost-effective as for FSW.

The boxplot shows the maximum unit cost of PrEP per year for AGYW, women 25-34 years or women 35-49 years relative to the unit cost of PrEP for FSW, for PrEP scale-up in these populations to be equally as cost-effective as it is for FSW (bright-coloured boxes). The maximum relative unit costs are shown, grouped left to right, for AGYW, women 25-34 years or women 35-49 years. Within each age grouping, the results are show by country, left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in green). The maximum relative unit costs are calculated using equation (S2.5) from Supplementary Materials: Supplementary Methods, section Model Structure and assume that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project[7]. As comparisons, current estimates of the unit costs of PrEP for AGYW, women 25-34 years and women 35-49 years, relative to the unit cost of PrEP for FSW are shown for all countries (in cream), calculated using data from Table 1. The abbreviations used in the graph are as follows: AGYW denotes adolescent girls and young women 15-24 years, S Africa denotes South Africa and Zim denotes Zimbabwe.

		Women Population Group		
Country	**Unit Cost Relative to FSWs**	**AGYW (15-24 years)**	**Women 25-34 years**	**Women 35-49 years**
South Africa	Maximum Relative Unit Cost to be as Cost-Effective as for FSW	23.3 % (13.3 % , 36.8 %)	16.2 % (9.1 % , 26.0 %)	10.5 % (5.7 % , 18.0 %)
	Estimated Current Unit Cost Relative to FSW	79.6 % (72.4 % , 86.7 %)	68.7 % (62.7 % , 75.8 %)	48.3 % (42.4 % , 54.7 %)
	% Reduction in Current Unit Cost Needed to be Equally as Cost-Effective as for FSW	-70.8 % (-83.4 % , -53.2 %)	-76.2 % (-87.0 % , -62.6 %)	-78.4 % (-88.1 % , -61.8 %)
Zimbabwe	Maximum Relative Unit Cost to be as Cost-Effective as for FSW	7.1 % (2.7 % , 14.9 %)	17.7 % (7.1 % , 31.2 %)	11.0 % (5.5 % , 17.2 %)
	Estimated Current Unit Cost Relative to FSW	75.6 % (70.8 % , 80.8 %)	63.0 % (58 % , 67.7 %)	38.8 % (34.1 % , 42.7 %)
	% Reduction in Current Unit Cost Needed to be Equally as Cost-Effective as for FSW	-90.4 % (-96.5 % , -80.6 %)	-71.8 % (-88.9 % , -50.8 %)	-72.0 % (-86.1 % , -53.6 %)
Kenya	Maximum Relative Unit Cost to be as Cost-Effective as for FSW	8.1 % (3.9 % , 18.5 %)	9.1 % (3.6 % , 17.7 %)	6.4 % (3.1 % , 11.6 %)
	Estimated Current Unit Cost Relative to FSW	90.3 % (86.2 % , 94.8 %)	74.9 % (71.1 % , 78.4 %)	48.1 % (45.1 % , 51.6 %)
	% Reduction in Current Unit Cost Needed to be Equally as Cost-Effective as for FSW	-91 % (-95.7 % , -79.6 %)	-88 % (-95.3 % , -76.6 %)	-86.7 % (-93.7 % , -75.4 %)

Table 2: Maximum Unit Costs of PrEP for AGYW, Women 25-34 years and Women 35-49 years to be Equally as Cost-Effective as for FSW, with Estimates of Current Relative Unit Costs.

For each country, the table displays three rows of information. The first row shows the maximum relative unit costs of PrEP in AGYW, women 25-34 years and women 35-49 years relative to the unit costs of PrEP for FSW, for PrEP to be equally as cost-effective. This is calculated using equation S1.5 in Supplementary Materials: Methods, considering the estimated relative annual HIV risk reduction on PrEP between the population groups.

The second row shows the estimated current relative unit costs between the populations, calculated using the data set out in Table 1.

The third row shows the % reduction in the current unit cost needed for PrEP to be equally as cost-effective for AGYW, women 25-34 years or women 35-49 years as for FSW, considering the data set out in Table 1.

The comparisons are shown separately for South Africa, Zimbabwe and Kenya. The values shown in the table outside the brackets are the median values, and the values shown in the brackets are the 95% credible intervals (CrIs).

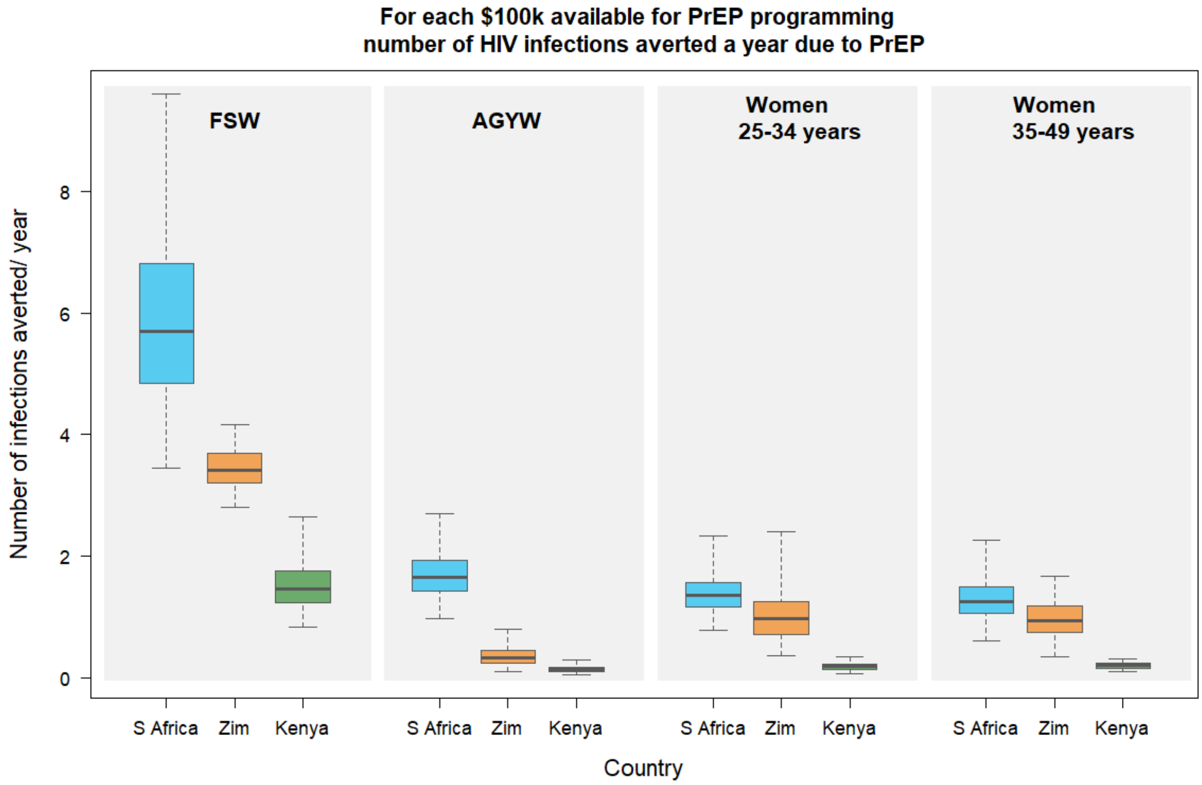

Figure 4: Boxplot of the number of HIV infections that could be averted a year due to PrEP, for each $100k available for PrEP programming.

The boxplot shows, for each $100k available for PrEP programming a year for FSW, AGYW, women 25-34 years and women 35-49 years, the total number of infections that could be averted a year due to PrEP. The number of infections that could be averted a year for each $100k available for PrEP are shown, grouped left to right, for FSW, AGYW, women 25-34 years or women 35-49 years. Within each age grouping, the results are shown by country, left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in green). The number of infections averted a year is calculated using equation (S2.10) from Supplementary Materials: Supplementary Methods, section Model Structure and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project[7]*. The unit costs of PrEP for each high-risk women group are as stated in Table 1. These estimates hold until PrEP saturation (determined by retention levels and population size) has been reached in the smallest population group – in this case, FSW. After this point, no additional financial resources will be able to reduce infections per year in this population group.*

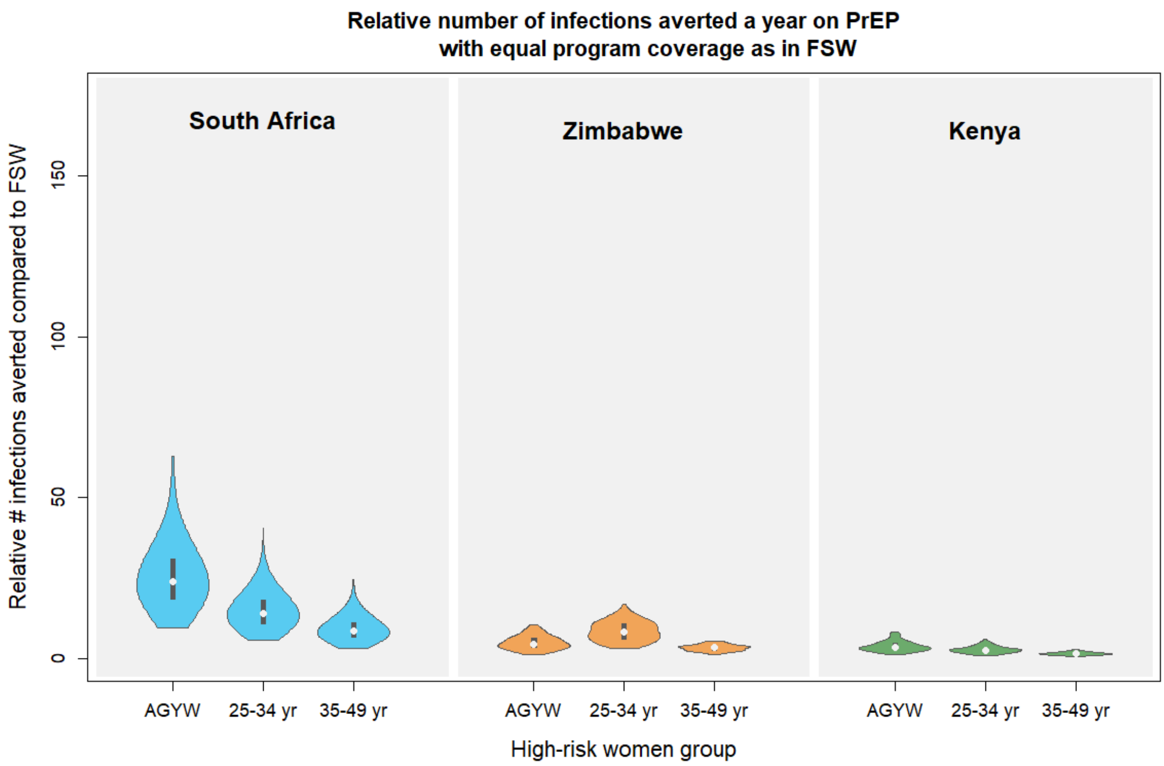

Figure 5: Violin plot of the relative number of infections averted a year on PrEP with equal program coverage as in FSW.

The violin plot shows the relative number of infections that could be averted a year in HIV negative AGYW, women 25-34 years or women 35-49 years, compared to in FSW, if PrEP were scaled up at the same coverage levels as in HIV negative FSW. The relative number of infections that could be averted are shown, grouped left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in green). In the violin plots, the white dots represent the median values, the thick black vertical lines represent the interquartile range, the vertical length of the violin represents the range of values and the width of the violin represents the frequency with which those values occur. The relative number of infections that could be averted are calculated using equation (S2.9) from Supplementary Materials: Supplementary Methods, section Model Structure and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project[7]. If these comparisons were applied to more narrowly defined sub-population groups, the wide variability in the violin plot estimates highlight that decisions around PrEP scale-up will depend on the specific characteristics of the sub-population groups under consideration. The abbreviations used in the graph are as follows: AGYW denotes adolescent girls and young women 15-24 years, 25-34 yr denotes women 25-34 years and 35-49 yr denotes women 35-49 years in each country.

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Supplementary Materials

Time to scale-up PrEP beyond the highest-risk populations? Modelling insights from high-risk women in sub-Saharan Africa

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Supplementary Materials: Supplementary Methods

Model Structure

We use a static Bernoulli formulation of HIV risk[1]. The sexual partners of high-risk women from population j are assumed to come from populations i in which the proportion HIV infected is p_i. We assume an average probability of HIV transmission, β_f, per sexual contact with an HIV infected male partner. High risk women are assumed to have C_i number of partners from each population a year, with whom they have an average of n_i sex acts a year each. Condoms are assumed to be used with partners from each population with consistency γ_{ij} and have an HIV risk reduction efficacy, ε, including slippage and breakage. Upon introduction, high-risk women from population j are assumed to adhere to PrEP at an average level α_j, which corresponds to a level of HIV risk reduction, θ_{α_j}. They are assumed to have 12-month program retention levels r_j. Sex acts are assumed to be peno-vaginal, the predominant pathway of HIV transmission to heterosexual women in sub-Saharan Africa.[2]

1.0 Individual level - Simple tools to help guide PrEP programme decision making

1.1 Assessment of HIV risk by risk factor

For the first analysis of HIV risk, we consider a simple model of HIV risk to a single high-risk woman with partners drawn from a single male population. HIV risk to an individual high-risk woman in the absence of PrEP is given by

$$\pi(0) = 1 - \left(p\left(1 - \beta_f(1 - \varepsilon\gamma)\right)^n + (1 - p)\right)^C,$$

(S1.1)

and on PrEP is

$$\pi(\theta_{\alpha_j}) = 1 - \left(p\left(1 - \beta_f\left(1 - r_j\theta_{\alpha_j}\right)(1 - \varepsilon\gamma)\right)^n + (1 - p)\right)^C$$

(S1.2)

Using equations (S1.1) and (S1.2), HIV risk reduction on PrEP is given by

$$\pi(0) - \pi(\theta_{\alpha_j})$$

(S1.3)

Heatmaps to estimate HIV incidence in women

Heatmaps were developed using equation (S1.1) to help decision makers estimate the annual HIV incidence in women by number of monthly sex acts, average condom use and underlying epidemic setting. We demonstrated four different example epidemic settings: underlying HIV prevalence in partner populations of 5%, 10%, 20% and 40%. In many sub-Saharan African contexts, 5% HIV prevalence is illustrative of HIV prevalence in males 15-24 years, 5-20% the HIV prevalence in males 25-49 years, and 20-40% the HIV prevalence in the clients of FSW (*Supporting Information: Table S2).*

In order to parameterise the model to the spectrum of HIV risk faced by women in sub-Saharan Africa, equation (S1.1) was simulated across the parameter ranges set out in *Supplementary Materials: Methods – Table S2*, yielding 720,000 distinct parameter sets.

1.2 Simple rule to estimate relative cost-effectiveness

In estimating the relative cost-effectiveness among women at risk, we considered two high-risk women of different risk. One woman is drawn from a traditionally higher-risk population (e.g. female sex workers (FSW)) and the other from a relatively lower-risk female population (e.g. adolescent girls and young women aged 15-24 years (AGYW)), denoted $H$and L respectively. For simplicity, each high-risk woman is assumed to draw their partners from one population group.

Cost-effectiveness is defined as the incremental cost of PrEP for a woman retained at level r_j in a PrEP program over a 12-month period, divided by the risk reduction achieved on PrEP when adhered to at level α with retention r_j over the 12-month period. In the absence of willingness-to-pay thresholds, relative cost-effectiveness was assessed by comparing these estimates of cost per infection averted between populations.

Analysis was conducted over a one-year timeframe, as PrEP is intended for seasons of risk, and few PrEP demonstration programs have achieved significant retention in women in this context beyond the first 12 months.[3,4] Let π_H and π_L denote the respective HIV risk for each woman, with subscripts $H$and L denoting high and low risk groups Let $\$X_H$ and $\$X_L$be the 12-month unit costs of PrEP for each woman (the incremental cost of PrEP for a woman retained in a PrEP program over a 12-month period).

Then the cost of averting one HIV infection with PrEP per year is $\frac{\$X_H}{\pi_H(0)-\pi_H(\theta_{\alpha_H})}$ and $\frac{\$X_L}{\pi_L(0)-\pi_L(\theta_{\alpha_L})}$ respectively. PrEP will become equally cost-effective in the lower-risk group as it is in the higher-risk group where:

$$\frac{\$X_L}{\pi_L(0)-\pi_L(\theta_{\alpha_L})} = \frac{\$X_H}{\pi_H(0)-\pi_H(\theta_{\alpha_H})} \tag{S1.4}$$

Equation (S1.4) can be expressed as

$$\frac{\$X_L}{\$X_H} = \frac{\pi_L(0)-\pi_L(\theta_{\alpha_L})}{\pi_H(0)-\pi_H(\theta_{\alpha_H})} \tag{S1.5}$$

To derive a simple formulation of equation (S1.5) that is intuitive for policy makers and programmers in practical real-world settings, we simplify equations (S1.1) and (S1.2) using binomial theorem. Using the example of equation (S1.2), where $\beta(1 - r\theta_\alpha)(1 - \varepsilon\gamma) \ll 1$ we have:

$$\pi(\theta_{\alpha_j}) \approx 1 - \left(p\left(1 - n\beta_f\left(1 - r_j\theta_{\alpha_j}\right)(1 - \varepsilon\gamma)\right) + (1 - p)\right)^C$$

$$\approx 1 - \left(1 - pn\beta\left(1 - r_j\theta_{\alpha_j}\right)(1 - \varepsilon\gamma)\right)^C$$

for $pn\beta\left(1 - r_j\theta_{\alpha_j}\right)(1 - \varepsilon\gamma) \ll 1$,

$$\pi(\theta_{\alpha_j}) \approx Cpn\beta\left(1 - r_j\theta_{\alpha_j}\right)(1 - \varepsilon\gamma). \tag{S1.6}$$

In other words, the HIV risk reduction to an individual on PrEP can be approximated by the total number of sex acts per unit time multiplied by the partner HIV prevalence, the basic risk of HIV transmission through peno-vaginal sex (0.0006 - 0.0011[5]), the average proportion of sex acts not protected by condoms, and the use-effectiveness of PrEP. The use-effectiveness of PrEP is defined as the HIV-risk reduction through use of PrEP at a given level of adherence, for a population with a given average program retention level.

Thus the risk reduction in equation (S1.3) is approximately

$Cpn\beta(1-\varepsilon\gamma) - Cpn\beta\left(1 - r_j\theta_{\alpha_j}\right)(1-\varepsilon\gamma)$, and simplifies to

$Cpn\beta(1-\varepsilon\gamma)r_j\theta_{\alpha_j}$.

(S1.7)

Therefore, when $\beta\left(1 - r_j\theta_{\alpha_j}\right)(1-\varepsilon\gamma) \ll 1$ and $pn\beta\left(1 - r_j\theta_{\alpha_j}\right)(1-\varepsilon\gamma) \ll 1$,the condition for equal cost-effectiveness in equation (S1.5) between two populations with different risk levels becomes:

$$\frac{\$X_L}{\$X_H} = \frac{C_L n_L p_L(1-\varepsilon\gamma_L) r_L \theta_{\alpha_L}}{C_H n_H p_H(1-\varepsilon\gamma_H) r_H \theta_{\alpha_H}}$$

(S1.8)

The relationship on relative cost of PrEP is summarised as follows.

Relative cost of PrEP ≈ Relative # sex acts **x** Relative HIV prevalence in partner population **x** Relative PrEP use-effectiveness **x** Relative % sex acts not protected by condoms

Simple rule to draw insights around relative cost-effectiveness of PrEP

This rule may help policy makers draw qualitative program insights around conditions under which it may be equally cost-effective to roll out PrEP in a lower-risk group as in a higher-risk group. This rule can be approximated based on information typically estimated by PrEP programs[6]. The relative measures stated are for lower-risk women compared to higher-risk women.

1.3 Relative risk reduction on PrEP

Heatmaps to estimate the relative unit cost at which PrEP scale-up from higher- to lower-risk women is cost-effective

Heatmaps were developed using equation (S1.5) to help decision makers estimate the relative unit cost at which it will be cost-effective to scale up PrEP from a comparatively higher- (e.g. FSW) to comparatively lower-risk woman (e.g. AGYW), also using the number of monthly sex acts, average condom use and underlying epidemic setting. Different epidemic settings were illustrated by taking HIV prevalence in the higher-risk women's partner population of either 20% or 40%. For each of these scenarios, HIV prevalence in the lower-risk women's partner population was then simulated at 1/4, 1/2, 3/4 and 1 times the prevalence of the higher-risk women's partner population (i.e. 5%, 10%, 15% and 20%; and 10%, 20%, 30% and 40% respectively). These scenarios span a range of epidemic settings in sub-Saharan Africa[7].

It was assumed that the higher-risk group had 22% PrEP program retention levels and all women retained had PrEP adherence levels of 70-85% (corresponding to risk-reduction of 73-99%[8]), consistent with the South African TAPS demonstration project in FSW[3]. PrEP program retention for the lower-risk group was simulated between ±25% of the 22% retention levels of the higher-risk group (i.e. 16.5%-27.5%), consistent with the difference between AGYW and FSW retention in Kenya[4]. For lower-risk women retained in the PrEP program, it was assumed that PrEP adherence was the same as the higher-risk group.

To obtain a spectrum of HIV risk faced by both populations reflective of the sub-Saharan African settings, we simulated across the parameter ranges set out in *Supplementary Materials: Methods – Table S2*, yielding 7,920,000 distinct parameter sets.

2.0 Population level – country case studies

We modify the risk equations (S1.1) and (S1.2) to consider HIV risk and the scale-up of PrEP at a population rather than individual level.

The total population size of high-risk women of type j is N_j, in which the prevalence of HIV is p_j. The coverage of PrEP in the population is ω_j.

In the process of parameterising the model to specific high-risk women populations, we develop the risk equations to also account for population-specific STI levels, levels of viral load suppression due to ART in HIV positive partners and male circumcision.

The parameter s_{ij} is the probability that at least one person in the partnership between high risk woman from population j and partner from population i has an STI and δ is the multiplicative increase in per sex act probability of HIV transmission in the presence of an STI.

Parameter ϑ_i is the proportion of HIV+ partners from population i that are virally suppressed on ART and ϱ models the average reduction in the probability of HIV transmission due to viral suppression on ART. The parameter τ_i is the proportion of male partner population i that are circumcised and σ is the average reduction in probability HIV transmission to women, when the male partner has been circumcised.

Where high-risk women from population j have partners drawn from a single male population, their HIV risk for a 12-month period is in the absence of PrEP is given by (leaving the j denotation to improve readability):

$$\Pi(0) = 1 - \big(p(\psi_{(1-\tau),0} + \psi_{\tau,0}) + (1-p)\big)^C$$

Where:

$$\psi_{(1-\tau),0} = (1-\tau)\big((1-\vartheta)s(1-\delta\varsigma)^n + (1-\vartheta)(1-s)(1-\varsigma)^n + \vartheta s(1-(1-\varrho)\delta\varsigma)^n + \vartheta(1-s)(1-(1-\varrho)\varsigma)^n\big)$$

$$\psi_{\tau,0} = \tau\big((1-\vartheta)s(1-(1-\sigma)\delta\varsigma)^n + (1-\vartheta)(1-s)(1-(1-\sigma)\varsigma)^n + \vartheta s(1-(1-\sigma)(1-\varrho)\delta\varsigma)^n + \vartheta(1-s)(1-(1-\sigma)(1-\varrho)\varsigma)^n\big)$$

and $\varsigma = \beta_f(1-\varepsilon\gamma)$

(S2.1)

For women on PrEP we have

$$\Pi(r\theta_\alpha) = 1 - \big(p(\psi_{(1-\tau),r\theta_\alpha} + \psi_{\tau,\ r\theta_\alpha}) + (1-p)\big)^C$$

Where:

$$\psi_{(1-\tau),\,r\theta_\alpha} = (1-\tau)\big((1-\vartheta)s(\,1-\delta\kappa)^n + (1-\vartheta)(1-s)(\,1-\kappa)^n + \vartheta s(\,1-(1-\varrho)\delta\kappa)^n + \vartheta(1-s)(\,1-(1-\varrho)\kappa)^n\big)$$

$$\psi_{\tau,\,r\theta_\alpha} = \tau\big((1-\vartheta)s(\,1-(1-\sigma)\delta\kappa)^n + (1-\vartheta)(1-s)(\,1-(1-\sigma)\kappa)^n + \vartheta s(\,1-(1-\sigma)(1-\varrho)\delta\kappa)^n + \vartheta(1-s)(\,1-(1-\sigma)(1-\varrho)\kappa)^n\big)$$

and $\kappa = \beta_f(1-r\theta_\alpha)(1-\varepsilon\gamma)$

(S2.2)

Similarly, when high-risk women from population j have partners drawn from two male populations $i = 1, 2$, their HIV risk for a 12-month period is in the absence of PrEP is given by

$$\Pi(0) = 1 - \big(p_1(\psi^1_{(1-\tau),0} + \psi^1_{\tau,0}) + (1-p_1)\big)^{C_1}\big(p_2(\psi^2_{(1-\tau),0} + \psi^2_{\tau,0}) + (1-p_2)\big)^{C_2}$$

Where

$$\psi^1_{(1-\tau),0} = (1-\tau_1)\big((1-\vartheta_1)s_1(\,1-\delta\varsigma_1)^{n_1} + (1-\vartheta_1)(1-s_1)(\,1-\varsigma_1)^{n_1} + \vartheta_1 s_1(\,1-(1-\varrho)\delta\varsigma_1)^{n_1} + \vartheta_1(1-s_1)(\,1-(1-\varrho)\varsigma_1)^{n_1}\big)$$

$$\psi^1_{\tau,0} = \tau_1\big((1-\vartheta_1)s_1(\,1-(1-\sigma)\delta\varsigma_1)^{n_1} + (1-\vartheta_1)(1-s_1)(\,1-(1-\sigma)\varsigma_1)^{n_1} + \vartheta_1 s_1(\,1-(1-\sigma)(1-\varrho)\delta\varsigma_1)^{n_1} + \vartheta_1(1-s_1)(\,1-(1-\sigma)(1-\varrho)\varsigma_1)^{n_1}\big)$$

$$\varsigma_1 = \beta_f(1-\varepsilon\gamma_1)$$

and

$$\psi^2_{(1-\tau),0} = (1-\tau_2)\big((1-\vartheta_2)s_2(\,1-\delta\varsigma_2)^{n_2} + (1-\vartheta_2)(1-s_2)(\,1-\varsigma_2)^{n_2} + \vartheta_2 s_2(\,1-(1-\varrho)\delta\varsigma_2)^{n_2} + \vartheta_2(1-s_2)(\,1-(1-\varrho)\varsigma_2)^{n_2}\big)$$

$$\psi^2_{\tau,0} = \tau_2\big((1-\vartheta_2)s_2(\,1-(1-\sigma)\delta\varsigma_2)^{n_2} + (1-\vartheta_2)(1-s_2)(\,1-(1-\sigma)\varsigma_2)^{n_2} + \vartheta_2 s_2(\,1-(1-\sigma)(1-\varrho)\delta\varsigma_2)^{n_2} + \vartheta_2(1-s_2)(\,1-(1-\sigma)(1-\varrho)\varsigma_2)^{n_2}\big)$$

$$\varsigma_2 = \beta_f(1-\varepsilon\gamma_2)$$

(S2.3)

When enrolled on a PrEP program:

$$\Pi(r\theta_\alpha) = 1 - \big(p_1(\psi^1_{(1-\tau),\,r\theta_\alpha} + \psi^1_{\tau,\,r\theta_\alpha}) + (1-p_1)\big)^{C_1}\big(p_2(\psi^2_{(1-\tau),\,r\theta_\alpha} + \psi^2_{\tau,\,r\theta_\alpha}) + (1-p_2)\big)^{C_2}$$

Where

$$\psi^1_{(1-\tau),\,r\theta_\alpha} = (1-\tau_1)\big((1-\vartheta_1)s_1(\,1-\delta\kappa_1)^{n_1} + (1-\vartheta_1)(1-s_1)(\,1-\kappa_1)^{n_1} + \vartheta_1 s_1(\,1-(1-\varrho)\delta\kappa_1)^{n_1} + \vartheta_1(1-s_1)(\,1-(1-\varrho)\kappa_1)^{n_1}\big)$$

$$\psi^1_{\tau,\,r\theta_\alpha} = \tau_1\big((1-\vartheta_1)s_1(\,1-(1-\sigma)\delta\kappa_1)^{n_1} + (1-\vartheta_1)(1-s_1)(\,1-(1-\sigma)\kappa_1)^{n_1} + \vartheta_1 s_1(\,1-(1-\sigma)(1-\varrho)\delta\kappa_1)^{n_1} + \vartheta_1(1-s_1)(\,1-(1-\sigma)(1-\varrho)\kappa_1)^{n_1}\big)$$

$$\kappa_1 = \beta_f(1-r\theta_\alpha)(1-\varepsilon\gamma_1)$$

And

$$\psi^2_{(1-\tau),\,r\theta_\alpha} = (1-\tau_2)\big((1-\vartheta_2)s_2(\,1-\delta\kappa_2)^{n_2} + (1-\vartheta_2)(1-s_2)(\,1-\kappa_2)^{n_2} + \vartheta_2 s_2(\,1-(1-\varrho)\delta\kappa_2)^{n_2} + \vartheta_2(1-s_2)(\,1-(1-\varrho)\kappa_2)^{n_2}\big)$$

$$\psi^2_{\tau,\, r\theta_\alpha} = \tau_2\big((1-\vartheta_2)s_2(\,1-(1-\sigma)\delta\kappa_2)^{n_2} + (1-\vartheta_2)(1-s_2)(\,1-(1-\sigma)\kappa_2)^{n_2} + \vartheta_2 s_2(\,1-(1-\sigma)(1-\varrho)\delta\kappa_2)^{n_2} + \vartheta_2(1-s_2)(\,1-(1-\sigma)(1-\varrho)\kappa_2)^{n_2}\big)$$

$$\kappa_2 = \beta_f(1-r\theta_\alpha)(1-\varepsilon\gamma_2)$$

(S2.4)

All models were programmed in R version 3.3.2[9].

2.1 Country case studies

We apply the models to South Africa, Zimbabwe and Kenya, which are have generalised high prevalence HIV epidemics.[10–13] These countries were chosen as case studies as they span a range of HIV burden levels in the region, they have each have adopted a national PrEP strategy,[14,15,16] and been at the forefront of PrEP roll-out in sub-Saharan Africa[17].

In each country, we consider four groups of women at high risk of HIV through heterosexual transmission[2,10,11,12]: $j = \{$FSW, adolescent girls and young women aged 15-24 years (AGYW), women 25-34 years and women 35-49 years$\}$.

FSW are assumed to have partners drawn from two populations: regular partners and clients. AGYW are assumed to have partners drawn from their own age group and also the 25-34 years age group, given that 17% and 14% women 15-19 years report relationships with men at least 10 years older in Zimbabwe[18] and Kenya[19] respectively, and 36% South African women 15-19 years report relationships with men at least 5 years older.[10] Women 25-34 years and women 35-49 years are assumed to have partners drawn from their own age groups.

Data ranges to parameterise the models of HIV risk for each high-risk female group were drawn from the latest available in the literature and fitted to the latest national estimates of HIV incidence by group (see *Supplementary Materials: Methods: Table S2*) using Latin Hypercube Sampling (R PSE Package[20]) to yield at least 200 sets of parameter fits for each high-risk woman population modelled.

2.2 Assessment of cost-effectiveness of scaling-up PrEP

Given the significantly higher individual HIV risk faced by FSW,[2] a priority group for PrEP roll-out in these settings,[14,15,16] we assumed FSW as the benchmark for assessment of cost-effectiveness.

Let $\$Y_j$ be the unit cost per high risk woman from population $j \neq FSW$ retained in a PrEP program for population j, with 12-month retention level r_j, and $\$Y_{FSW}$ the equivalent unit cost for a FSW PrEP program per FSW retained with 12-month retention level r_{FSW}.

Then the program's cost to avert 1 infection per year due to PrEP in each population is $\frac{\$Y_j}{\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j})}$ and $\frac{\$Y_{FSW}}{\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}})}$ respectively.

A PrEP program for high risk population $j \neq FSW$ will then be equally as cost-effective per infection averted due to PrEP, as it is for FSW where

$$\frac{\$Y_j}{\$Y_{FSW}} = \frac{\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j})}{\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}})}$$

(S2.5)

To determine the coverage, ω_j, of PrEP in high-risk woman population $j \neq FSW$ needed to achieve the same risk reduction as coverage ω_{FSW} in FSW, we have:

$$\omega_j N_j(1-p_j)\left(\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j})\right) = \omega_{FSW}N_{FSW}(1-p_{FSW})\left(\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}})\right),$$

(S2.6)

when

$$\omega_j = \omega_{FSW}\frac{N_{FSW}(1-p_{FSW})\left(\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}})\right)}{N_j(1-p_j)\left(\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j})\right)}.$$

(S2.7)

These levels of coverage would be at a relative total cost given by

$$\frac{\$Y_j\omega_j N_j(1-p_j)}{\$Y_{FSW}\omega_{FSW}N_{FSW}(1-p_{FSW})}$$

(S2.8)

If PrEP were scaled up at equal coverage in both populations, then the relative number of infections averted per year in high-risk woman population $j \neq FSW$ with respect to the FSW population would be:

$$\frac{N_j(1-p_j)(\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j}))}{N_{FSW}(1-p_{FSW})(\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}}))}$$

(S2.9)

This is equivalent to the relative total maximum number of infections averted per year if PrEP programs were scaled up to all HIV negative women in each population.

For each $\$100k$ available for PrEP programming for each population, the estimated number of infections averted a year in each population would be:

In high-risk women $j \neq FSW$

$$\frac{\$100k}{\$Y_j}(\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j})),$$

and in FSW

$$\frac{\$100k}{\$Y_{FSW}}(\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}}))$$

(S2.10)

The proportion of the potential total number of infections that could be averted a year in each population with $\$100k$ is:

In high-risk women $j \neq FSW$

$$\frac{\$100k.(\Pi_j(0)-\Pi_j(r_j\theta_{\alpha_j}))}{\$Y_j.N_j(1-p_j).\Pi_j(0)},$$

and in FSW

$$\frac{\$100k.(\Pi_{FSW}(0)-\Pi_{FSW}(r_{FSW}\theta_{\alpha_{FSW}}))}{\$Y_{FSW}.N_{FSW}(1-p_{FSW}).\Pi_{FSW}(0)}$$

(S2.11)

Estimating costs of PrEP to each high-risk group of women

We estimated the costs of offering PrEP to each high-risk group of women. FSW were assumed to be offered PrEP through programmes with outreach and community mobilisation components. All other women were assumed to be offered PrEP through sexual and reproductive health services, with services for AGYW having larger counselling components. We reviewed cost data from demonstration projects and previous PrEP costing publications in Kenya[21,22] and South Africa.[3] We disaggregated cost estimates into service delivery and drug costs. For our calculations, we replaced reported drug costs by a range of USD57-80 per year. The lower bound is the internationally traded value of USD3.75 with a 25% top up of freight and distribution costs in country (15% shipping and handling charges, and 10% for drug distribution costs).[23] The high bound is the highest reported price for drugs in the demonstration projects - 30 days TDF/FTC at USD6.75. For Zimbabwe, in addition to drug costs, we transferred non-tradable components of South African estimates using purchasing power parities[24] following standard methods.[25] In each case, the costs per person retained at 12-months account for costs associated with drop out of individuals from the same population group enrolled but not retained in PrEP programs by month 12, consistent with previous studies.[3,21,22] We adjusted all previously published costs to USD 2017.[26] The amounts and detailed assumptions underpinning the estimated unit costs for each high-risk women group by country are set out in Table S1 below.

Table of Estimated Unit Costs for High-Risk Women Populations in South Africa, Zimbabwe and Kenya

Country	Population	Unit cost (min - max)	Service delivery excl. drugs	Drugs only (min - max)	Comments
South Africa	FSW	190 – 210	130	57 - 80	Unit costs measured during a demonstration project in Johannesburg and Pretoria via FSW clinics. Costs reported by Eakle et al[3] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment) and indirect costs (eg, management, utilities, and transportation). We allocated outreach, demand creation and HCT costs to a unit cost of per person-year on PrEP as these were reported separately.
South Africa	AGYW (15-24y)	149 – 169	89	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[27] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors' estimation of costs among female adolescents.
South Africa	Women (25-34y)	128 – 148	68	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[27] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors' estimation of costs among young women.
South Africa	Women (35-49y)	87 – 107	27	57 - 80	Unit costs estimated from local data and with input from several demonstration projects in South Africa. Costs reported by Meyer-Rath et al[27] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), indirect costs (eg, management, utilities, and transportation), and outreach, demand creation and HCT costs. These estimates reflect the authors estimation of costs among pregnant women - we assumed for this lowest risk population, the cost will be similar to those attending ANC.
Zimbabwe	FSW	293 – 317	237	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[28]
Zimbabwe	AGYW (15-24y)	219 – 243	163	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[28]

Zimbabwe	Women (25-34y)	181 - 204	124	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[28]
Zimbabwe	Women (35-49y)	106 - 130	50	57 - 80	Drug costs were kept constant and we adjusted service costs in South Africa using PPP index.[28]
Kenya	FSW	399 - 423	343	57 - 80	Unit costs measured in preparation for a demonstration project in Nairobi via SWOP clinics (for FSW). Costs reported by Cremin et al[21] included direct costs (eg, antiretrovirals, laboratory tests and consumables, labour and equipment), related costs (eg, outreach and demand creation), and indirect costs (eg, management, utilities, and transportation).
Kenya	AGYW (15-24y)	358 - 382	302	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[22] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs, laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among the highest risk subpopulation in the general population.
Kenya	Women (25-34y)	294 - 318	238	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[22] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs, laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among all women.
Kenya	Women (35-49y)	185 - 209	129	57 - 80	Unit costs measured as part of a demonstration project aiming to integrate PrEP into routine maternal and child health and family planning clinics in western Kenya. Costs reported by Roberts et al[22] included fixed (start-up costs, such as microplanning and training, capital, overheads (e.g. building costs, transportation, and airtime) and administrative and supervisory personnel) or variable (drugs, clinical personnel direct service costs, laboratory testing, and other supplies). These estimates reflect the authors measurement of costs among all women excluding screening costs.

Table S1: Table of Estimated Unit Costs for High-Risk Women Populations in South Africa, Zimbabwe and Kenya*. The estimated unit costs for FSW, AGYW, women 25-34 years and women 35-49 years are shown disaggregated by the portion that is service delivery costs and the portion that is drug costs. The costs were calculated in line with the methodology set out in Supplementary Materials: Methods. The far right hand side column of the table sets out addition comments about specific assumptions made in calculating the data.*

**For our calculations, we replaced reported drug costs by a range of USD57-80. The low bound is the internationally traded value of USD3.75 (https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf) plus 25% top up of freight and distribution costs in country (15% shipping and handling charges, and 10% for drug distribution costs). The high bound is the highest reported price for drugs in the demonstration projects - 30 days TDF/FTC at USD6.75.*

***transferability of costs between countries followed standard guidelines (https://pdfs.semanticscholar.org/36ab/74fd24fb883db703c475364c34ad574a3f35.pdf)*

**** Purchasing Power Parities (PPP)*

Model calibration

The data used in the parameterisation and fitting of the models for all 3 country case studies shown in Table S2.

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
Epidemic parameters							
FSW: HIV incidence, per 100 person years	i_{FSW}	3.9 (2.2-5.6)	Nairobi, 2011[29] Nairobi, 2008[30] Estimate is mid-point. For context, 2.6 Mombasa, 2006[31]	5.87 (5.55-6.21)	2017 estimates[32]. 95% confidence intervals (CIs) estimated assuming binomially distributed, based on population size and proportion HIV-	7.2 (4.5-9.8)	CAPRISSA 002 2008[33]
AGYW: HIV incidence, per 100 person years	i_{AGYW}	0.28 (0.137 – 0.490)	UNAIDS 2018 Estimates[34]	0.53 (0.13, 0.93)	2016 estimates[35]	1.51 (1.31-1.71)	National estimates, 2017[36]
Women 25-34 years: HIV incidence, per 100 person years	i_{W25-34}	0.25 (0.120 – 0.431)	UNAIDS 2018 Estimates[34]	1.11 (0.41, 1.80)	2016 estimates[35]	1.045 (0.87-1.22)	2017 estimates[37]. Low and High are min and max across all ages within range.
Women 35-49 years: HIV incidence, per 100 person years	i_{W35-49}	0.16 (0.078– 0.282)	UNAIDS 2018 Estimates[34]	0.42 (0.00, 0.92)	2016 estimates[35]	0.665 (0.49-0.84)	2017 estimates[37]. Low and High are min and max across all ages within range.
FSW: Population size, in 1,000s of women	N_{FSW}	134	2013 size estimation[38]	45	2017 estimates[32]	138	2013 size estimation[39]
AGYW: Population size, in 1,000s of women	N_{AGYW}	4,067	2009 census[40]	1,304	2012 census[41]	4,901	2018 mid-year estimates[42]
Women 25-34 years: Population size, in 1,000s of women	N_{W25-34}	2,935	2009 census[40]	1,089	2012 census[41]	5,366	2018 mid-year estimates[42]
Women 34-49 years: Population size, in 1,000s of women	N_{W35-49}	2,374	2009 census[40]	817	2012 census[41]	5,354	2018 mid-year estimates[42]
Clients of FSW: HIV prevalence	p_c	0.165 (0.135-0 .194)	Truck drivers, Kenya, 2005[43]	0.273 (0.248, 0.295)	Long distance truck drivers, 2005[44]	0.339 (0.275 – 0.410)	Non-residents (study proxy for migrant

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
			Maximum county male prevalence (Siaya, males, 15-49 years), 2017[12] Estimate is mid-point.				work), men, from KwaZulu-Natal, South Africa, 2004.[45]
Men in general population 15-49 years: HIV prevalence	sp_{M15-49}	0.045 (0.0448-0.0451)	0.045 Males 15-49, 2017[12]. 0.044 (0.036-0.052) males 15-64 years, KAIS, 2012[46]. Use KAIS estimates as consistent with estimates used for individual age ranges below. No CI for 2017 estimate, but fits within CI of KAIS	0.107 (0.1066-0.1074)	2016 estimates[35] 95% CI estimated assuming binomially distributed, based on population size[41]	0.148 (0.133 – 0.165)	National estimates, 2017[10]
Men 15-24 years: HIV prevalence	p_{M15-24}	0.011 (0.005-0 .018)	KAIS, 2012[46]	0.030 (0.0297-0.03030)	2016 estimates[35] 95% CI estimated assuming binomially distributed, based on population size[41]	0.039 (0.014 – 0.06)	AIDSInfo 2017[34]
Men 25-34 years: HIV prevalence	p_{M25-34}	0.054 (0.039-0 .068)	KAIS, 2012[46]	0.060 (0.0595-0.0605)	2016 estimates[35] 95% CI estimated assuming binomially distributed, based on population size[41]	0.124-0.184	Min and max of 5-year age categories (full national results not yet released). National estimates, 2017[36]
Men 35-49 years: HIV prevalence	p_{M35-49}	0.064 (0.051-0 .076)	35 years+, KAIS, 2012[46]	0.237 (0.236-0 .238)	2016 estimates[35] 95% CI estimated assuming binomially	0.224-0.248	Min and max of 5-year age categories (full national results not yet

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
					distributed, based on population size[41]		released). National estimates, 2017[36]
FSW: HIV prevalence	p_{FSW}	0.293 (0.290,0 .295)	2013 size estimation[38] 95% CI estimated assuming binomially distributed, based on population size	0.571 (0.566-0.576)	AIDSInfo 2017[34] 95% CI estimated assuming binomially distributed, based on population size[41]	0.689 (0.565-0.812)	FSW Johannesburg, South Africa, 2014.[47] Estimate is midpoint.0.10
AGYW: HIV prevalence	p_{AGYW}	0.03 (0.022-0. 038)	KAIS, 2012[46]	0.059 (0.0586-0.0594)	2016 estimates[35]	0.102 (0.046–0.148)	AIDSInfo 2017[34]
Women 25-34 years: HIV prevalence	p_{W25-34}	0.073 (0.06-0. 087)	KAIS, 2012[46]	0.182 (0.1813-0.1827)	2016 estimates[35]	0.275-0.347	Min and max of 5-year age categories (full national results not yet released). National estimates, 2017[36]
Women 35-49 years: HIV prevalence	p_{W35-49}	0.093 (0.083-0 .113)	35 years+, KAIS, 2012[46]	0.282 (0.281-0 .283)	2016 estimates[35]	0.303-0.394	Min and max of 5-year age categories (full national results not yet released). National estimates, 2017[36]
Behavioural parameters							
FSW: number of client partners/ year	C_{c_FSW}	320 (276-364)	Monthly liaisons x12, FSW at hotspots along Mombasa-Kampala highway, 2007[43] Median number in last 7 days x52 Nairobi, 2010[48] Estimate is midpoint.	360 (234-486)	Across studies[49,50] Estimate is midpoint.	424 (312 – 504)	Mean monthly reported number of clients per FSW, multiplied by 12.[51]
FSW: number of regular partners from male population 15-49 years/ year	C_{M15-49_FSW}	(1-4)	Nairobi, 2010[48]	2.0 (0.74-4.0)	Imputed from South Africa, due to lack of data. Number of	2.0 (0.74-4.0)	Number of main sexual partners per 6 months, multiplied by 2.[52]

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	**References**	**Estimate (Low-High)**	**References**	**Estimate (Low-High)**	**References**
			Point estimate not deducible as categorical data.		main sexual partners per 6 months, multiplied by 2.[52]		
FSW: number of sex acts per client/ year	n_{c_FSW}	1.59 (1-2.17)	FSW at hotspots along Mombasa-Kampala highway, 2007[43] Estimate is midpoint.	1 (1-1.2)	Imputed from South Africa, due to lack of data. Number of sexual encounters per client.[53]	1 (1-1.2)	Number of sexual encounters per client.[53]
FSW: number of sex acts with regular partners/ year	n_{M15-49_FSW}	96 (48-144)	Imputed from South Africa, due to lack of data.	96 (48-144)	Imputed from South Africa, due to lack of data.	96 (48-144)	Mean monthly frequency of sex acts in main partnerships, multiplied by 12.[51]
FSW: average condom consistency with clients	γ_{c_FSW}	0.773 (0.626-0.92)	Paying clients, FSW Nairobi, 2010[48] UNAIDS, 2017[34] Estimate is mid-point.	0.708 (0.455-0.961)	% reporting full adherence to condom use[54] 2017 estimates[32] Estimate is mid-point.	0.764 (0.609-0.902)	FSW Johannesburg, South Africa, 2014.[47]
FSW: average condom consistency with regular partners	γ_{M15-49_FSW}	0.463 (0.386-0.540)	Non-paying partner, Mombasa, 2007[55] Non-paying partner, Nairobi, 2010[48] Estimate is mid-point.	0.3375 (0.333-0.342)	Survey, 2011[56] Estimate is mid-point.	0.345 (0.173-0.548)	FSW Johannesburg, South Africa, with non-paying partner, 2014.[47]
FSW: probability at least 1 person in partnership has an STI – with clients	s_{c_FSW}	0.011 (0.004-0.021)	Prevalence of Neisseria gonorrhoea, FSW Nairobi, 2010[48]	0.019 (0.005-0.034)	Prevalence of Neisseria gonorrhoea, 2005[57]	0.21 (0.15-0.30)	Low: Prevalence of Chlamydia trachomatis & Neisseria gonorrhoea in Hillbrow FSW.[53] High: FSW STI prevalence, Durban.[33]

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
FSW: probability at least 1 person in partnership has an STI – with regular partners	s_{M15-49_FSW}	0.011 (0.004-0.021)	Prevalence of Neisseria gonorrhoea, FSW Nairobi, 2010[48]	0.019 (0.005-0.034)	Prevalence of Neisseria gonorrhoea, 2005[57]	0.21 (0.15-0.30)	Low: Prevalence of Chlamydia trachomatis & Neisseria gonorrhoea in Hillbrow FSW.[53] High: FSW STI prevalence, Durban.[33]
AGYW: number of male partners 15-24 years/ year	C_{M15-24_AGYW}	(0-4)	Estimated range, Women 15-24, 2014[19], accounting for the proportion who have never had sexual intercourse and mean lifetime partners. Point estimate not deducible as categorical data. A wider parameter range was considered in the fitting process (0-10).	(0-4)	Estimated range, Women 15-24, 2015[18], accounting for the proportion who have never had sexual intercourse and mean lifetime partners. Point estimate not deducible as categorical data. A wider parameter range was considered in the fitting process (0-10).	(0-4)	Estimated range, Women 15-24, 2016[58], accounting for the proportion who have never had sexual intercourse and mean lifetime partners. Point estimate not deducible as categorical data. A wider parameter range was considered in the fitting process (0-10).
AGYW: number of male partners 25-34 years/ year	C_{M25-34_AGYW}	(0-4)	Estimated range, Women 15-24, 2014[19], accounting for the proportion of age-discordant relationship. Point estimate not deducible as categorical data. A wider parameter range was	(0-4)	Estimated range, Women 15-24, 2015[18], accounting for the proportion of age-discordant relationship. Point estimate not deducible as categorical data. A wider parameter range was	(0-4)	Estimated range, Women 15-24, 2016[58], accounting for the proportion of age-discordant relationships. Point estimate not deducible as categorical data. A wider parameter range

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
			considered in the fitting process (0-10).		considered in the fitting process (0-10).		was considered in the fitting process (0-10).
AGYW: number of sex acts male partners 15-24 years/ year	n_{M15-24_AGYW}	182 (156-208)	Imputed based on South Africa, due to lack of data	82 (156-208)	Imputed based on South Africa, due to lack of data	182 (156-208)	3-4 a week x 52, youth, with regular partner, 2000[59] Estimate is mid-point.
AGYW: number of sex acts male partners 24-34 years / year	n_{M25-34_AGYW}	48 (36-60)	Imputed based on South Africa, due to lack of data	48 (36-60)	Imputed based on South Africa, due to lack of data	48 (36-60)	3 sex acts a month, youth, non-spousal partner, 2000[59] 5 sex acts a month x12, married 18-20 year old, average number sex acts per short term partner formation, 2016[60] Estimate is mid-point
AGYW: average condom consistency with male partners 15-24 years	γ_{M15-24_AGYW}	0.355 (0.11-0.60)	Condom use at last sexual encounter with partner of unknown status[61] Condom use at last sexual intercourse, Women 15-24, 2014[19] Estimate is mid-point.	0.406 (0.213-0.599)	% who had intercourse in the past 12 months with a non-marital, non-cohabiting partner[18] 1-[Trial control arm, did not use condom at last sex, females,18-22 year olds[62]] Estimate is mid-point.	0.588 (0.498 - 0.677)	0.498, 0.677. Females, males. 15-24 years, condom use at last sex, 2017. [10] Estimate is mid-point.
AGYW: average condom consistency with male partners 25-34 years	γ_{M25-34_AGYW}	0.292 (0.11-0.474)	Condom use at last sexual encounter with partner of unknown status[61] Condom use at last transactional sex,	0.299 (0.1-0.498)	Females aged <25, males aged 25+, 2005[64] Never married women, % who	0.504 (0.473-0.534)	0.473 females 15-24 years, condom use last sex, those with more than 1 partner in the last year, 2017.[10] Estimate is mid-point.

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
			Women 15-64 years, 2012[63] Estimate is mid-point.		used condom at last sexual intercourse[18] Estimate is mid-point.		
AGYW: probability at least 1 person in partnership has an STI – with male partners 15-24 years	s_{M15-24_AGYW}	0.018 (0.002 – 0.062)	Gonorrhoea prevalence 15-24 year olds (combined study with Tanzania), 2010[65]	0.018 (0.01 – 0.029)	Gonorrhoea prevalence 15-24 year olds, 2001[65]	0.018 (0.008–0.041)	Maximum of prevalence of gonorrhoea in 15-24 year old males and females
AGYW: probability at least 1 person in partnership has an STI – with male partners 25-34 years	s_{M25-34_AGYW}	0.009 (0.001 - 0.032)	Gonorrhoea prevalence 25-49 year olds (combined study with Tanzania), 2010[65]	0.025 (0.018 – 0.036)	Gonorrhoea prevalence 25-49 year olds, 2001[65]	0.05 (0.022-0.04)	Gonorrhoea prevalence 25-49 year olds, 2010[65] (greater than 15-24 years estimate above)
Women 25-34 years: number of male partners 25-34 years/ year	C_{M25-34_W25-3}	1.96 (0.92-3.0)	Lower bound as for Zimbabwe Estimated upper bound, Women 25-29, 30-39, accounting for mean lifetime partners, 2014[19] Estimate is mid-point. A wider parameter range was considered in the fitting process (0-10).	1.96 (0.92-3.0)	Total partnerships in last 12 months reported by adult women, 2005[66] Estimated upper bound, Women 25-29, 30-39, accounting for mean lifetime partners, 2015[18] Estimate is mid-point. A wider parameter range was considered in the fitting process (0-10).	2.02 (1.03–3.0)	Total partnerships in last 12 months reported by adult women, 2006[66] Estimated upper bound, Women 25-29 and 30-39, accounting for mean lifetime partners, 2016[58] Estimate is mid-point. A wider parameter range was considered in the fitting process (0-10).

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
Women 25-34 years: number of sex acts male partners 24-34 years / year	n_{M25-34_W25-3}	93 (54-132)	Average number of sex acts per partner per year, before intervention, 1998, Kenya[67] Upper bound imputed from South Africa due to lack of data Estimate is mid-point.	96 (60-132)	Imputed from South Africa due to lack of data	96 (60-132)	Mean 5 sex acts a month x 12, 18-40 year old women, KwaZulu-Natal, 2010[68] 2.54 mean sex acts a week x52, women, 2007[69] Estimate is mid-point.
Women 25-34 years: average condom consistency with male partners 25-34 years	γ_{M25-34_W25-3}	0.183 (0.038-0.328)	Women 15-64 years, Married/ Coinhabiting, 2012[63] Women 15-64 years, Casual/Other, 2012[63] Estimate is mid-point.	0.295 (0.07-0.520)	Females ages 25+, males aged 25+, 2005[64] Condom use during last sexual intercourse, women reporting 2+ partners in last 12 months, max(25-29 year olds, 30-39 year olds)[18] Estimate is mid-point.	0.344 (0.324–0.366)	Condom use at last sex, 25-49 years, 2012[70]
Women 25-34 years: probability at least 1 person in partnership has an STI – with male partners 25-34 years	s_{M25-34_W25-3}	0.009 (0.001 - 0.032)	Gonorrhoea prevalence 25-49 year olds (combined study with Tanzania), 2010[65]	0.025 (0.018 – 0.036)	Gonorrhoea prevalence 25-49 year olds, 2001[65]	0.05 (0.022-0.04)	Gonorrhoea prevalence 25-49 year olds, 2010[65]
For model structural sensitivity analysis: Women 25-34 years: number of male partners 35-49 years/ year	C_{M35-49_W25-3}	50% of C_{M35-49_W35-49}	As below	50% of C_{M35-49_W35-49}	As below	50% of C_{M35-49_W35-49}	As below

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
For model structural sensitivity analysis: Women 25-34 years: number of sex acts male partners 35-49 years / year	n_{M35-49_W25-3}	n_{M35-49_W35-49}	As below	n_{M35-49_W35-49}	As below	n_{M35-49_W35-49}	As below
For model structural sensitivity analysis: Women 25-34 years: average condom consistency with male partners 35-49 years	γ_{M35-49_W25-3}	γ_{M25-34_W25-34} (same parameter value as γ_{M35-49_W35-49})	As above	γ_{M25-34_W25-34} (minimum of this and parameter value of γ_{M35-49_W35-49})	As above	γ_{M25-34_W25-34} (same parameter value as γ_{M35-49_W35-49})	As above
For model structural sensitivity analysis: Women 25-34 years: probability at least 1 person in partnership has an STI – with male partners 35-49 years	s_{M35-49_W25-3}	s_{M25-34_W25-34} (same parameter value as s_{M35-49_W35-49})	As above	s_{M25-34_W25-34} (same parameter value as s_{M35-49_W35-49})	As above	s_{M25-34_W25-34}(same parameter value as s_{M35-49_W35-49})	As above
Women 35-49 years: number of male partners 35-49 years/ year	C_{M35-49_W35-4}	1.96 (0.92-3.0)	Lower bound as for Zimbabwe Estimated upper bound, Women 30-39, 40-49, accounting for mean lifetime partners, 2014[19] Estimate is mid-point. A wider parameter range was considered in the fitting process (0-10).	1.96 (0.92-3.0)	Total partnerships in last 12 months reported by adult women, 2005[66] (no data to calc 95% CI) Estimated upper bound for maximum women 30-30, 40-49, accounting for mean lifetime partners, 2015[18] Estimate is mid-point. A wider parameter range was considered in	2.02 (1.03–3.0)	Total partnerships in last 12 months reported by adult women, 2006[66] Estimated upper bound, Women 30-39, 40-49, accounting for mean lifetime partners, 2016[58] Estimate is mid-point. A wider parameter range was considered in the fitting process (0-10).

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	**References**	**Estimate (Low-High)**	**References**	**Estimate (Low-High)**	**References**
					the fitting process (0-10).		
Women 35-49 years: number of sex acts male partners 35-49 years / year	n_{M35-49_W35-4}	93 (54-132)	Average number of sex acts per partner per year, before intervention, 1998, Kenya[67] Upper bound imputed from South Africa due to lack of data Estimate is mid-point.	96 (60-132)	Imputed from South Africa due to lack of data	96 (60-132)	Mean 5 sex acts a month x 12, 18-40 year old women, KwaZulu-Natal, 2010[68] 2.54 mean sex acts a week x52, women, 2007[69] Estimate is mid-point.
Women 35-49 years: average condom consistency with male partners 35-49 years	γ_{M35-49_W35-4}	0.183 (0.038-0.328)	Women 15-64 years, Married/ Coinhabiting, 2012[63] Women 15-64 years, Casual/Other, 2012[63] Estimate is mid-point.	0.354 (0.07-0.638)	Females ages 25+, males aged 25+, 2005[64] Condom use during last sexual intercourse, women reporting 2+ partners in last 12 months, max(30-39year olds, 40-49) year olds[18] Estimate is mid-point.	0.344 (0.324–0.366)	Condom use at last sex, 25-49 years, 2012[70]
Women 35-49 years: probability at least 1 person in partnership has an STI – with male partners 35-49 years	s_{M35-49_W35-4}	0.009 (0.001 - 0.032)	Gonorrhoea prevalence 25-49 year olds (combined study with Tanzania), 2010[65]	0.025 (0.018 – 0.036)	Gonorrhoea prevalence 25-49 year olds, 2001[65]	0.05 (0.022-0.04)	Gonorrhoea prevalence 25-49 year olds, 2010[65]

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
Clients of FSW: proportion of HIV+ individuals virally supressed	ϑ_c	0.358 (0.3222-0.3938)	All ages, not disaggregated by sex (only data available), 2017[71]. Low and high values not reliably calculable binomially, as calculated based on ART cascade with unknown range at higher cascade levels, so taking low and high to be +/-10% of point estimate Same for below viral suppression data.	0.489 (0.4401-0.5379)	2016 estimates[35]. Low and high values not reliably calculable binomially, as calculated based on ART cascade with unknown range at higher cascade levels, so taking low and high to be +/-10% of point estimate Same for below viral suppression data.	0.508 (0.451 – 0.564)	Prevalence of viral load suppression, 15-49 years, 2017.[10] Estimate is mid-point
Men in general population 15-49 years: proportion of HIV+ individuals virally supressed	ϑ_{M15-49}	0.358 (0.3222-0.3938)	All ages, not disaggregated by sex (only data available), 2017[71]	0.489 (0.4401-0.5379)	2016 estimates[35]	0.508 (0.451 – 0.564)	Prevalence of viral load suppression, 2017.[10] Estimate is mid-point
Men 15-24 years: proportion of HIV+ individuals virally supressed	ϑ_{M15-24}	0.358 (0.3222-0.3938)	All ages, not disaggregated by sex (only data available), 2017[71]	0.401 (0.3609-0.4411)	2016 estimates[35]	0.491 (0.4419-0.5401)	Prevalence of viral load suppression, 2017.[10] Low and high values not reliably calculable binomially, as calculated based on ART cascade with unknown range at higher cascade levels, so taking low and high to be +/-10% of point estimate.

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
							Same for below viral suppression data.
Men 25-34 years: proportion of HIV+ individuals virally supressed	ϑ_{M25-34}	0.358 (0.3222-0.3938)	All ages, not disaggregated by sex (only data available), 2017[71]	0.365 (0.3285-0.4015)	2016 estimates[35]	0.415 (0.3735-0.4565)	Prevalence of viral load suppression, 2017.[10]
Men 35-49 years: proportion of HIV+ individuals virally supressed	ϑ_{M35-49}	0.358 (0.3222-0.3938)	All ages, not disaggregated by sex (only data available), 2017[71]	0.562 (0.5058-0.6182)	2016 estimates[35]	0.522 (0.4698-0.5742)	Prevalence of viral load suppression, 35-44 years, 2017.[10]
Clients of FSW: proportion circumcised	τ_c	0.962 (0.9618-0.9621)	Males 15-49, 2014[19] 95% CI estimated assuming binomially distributed, based on population size[40]	0.143 (0.1426-0.1434)	Males 15-49, 2015[18] 95% CI estimated assuming binomially distributed, based on population size[41]	0.138 (0.1378-0.1382)	15-64 years, 2017.[10] 95% CI estimated assuming binomially distributed, based on population size[42]
Men in general population 15-49 years: proportion circumcised	τ_{M15-49}	0.962 (0.9618-0.9621)	Males 15-49, 2014[19] 95% CI estimated assuming binomially distributed, based on population size[40]	0.143 (0.1426-0.1434)	Males 15-49, 2015[18]	0.138 (0.1378-0.1382)	15-64 years, 2017.[10] 95% CI estimated assuming binomially distributed, based on population size[42]
Men 15-24 years: proportion circumcised	τ_{M15-49}	0.914 (0.9136-0.9144)	Males 15-24, 2014[19] 95% CI estimated assuming binomially distributed, based on population size[40]	0.188 (0.1873-0.18878)	Males 15-24, 2015[18]	0.702 (0.7014-0.7026)	2017.[10] 95% CI estimated assuming binomially distributed, based on population size[42]
Men 25-34 years: proportion circumcised	τ_{M25-34}	0.939 (0.934-0.946)	Males 25-29 and Males 30-39, 2014[19]	0.107 (0.10-0.116)	Males 25-29 and Males 30-39, 2015[18]	0.628 (0.6280-0.6284)	2017.[10] 95% CI estimated assuming binomially

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
			Estimate is weighted average		Estimate is weighted average		distributed, based on population size[42]
Men 35-49 years: proportion circumcised	τ_{M35-49}	0.931 (0.919-0.94)	Males 30-39 and Males 40-49, 2014[19] Estimate is weighted average	0.111 (0.104-0.116)	Males 30-39 and Males 40-49, 2015[18]	0.626 (0.6255-0.6265)	35-44 years, 2017.[10] 95% CI estimated assuming binomially distributed, based on population size[42]
PrEP parameters							
FSW: average 12-month PrEP program retention	r_{FSW}					22%	TAPS[3]
FSW: average self-reported adherence	α_{FSW}					70-85%	TAPS[3]
FSW: HIV prevention-effective PrEP adherence	θ_{FSW}	Risk reduction of 0.79–0.99 ≥4 out 7 (≥ 57%) reported daily doses of PrEP a week Risk reduction of 0.73–1.06 ≥6 out 7 (≥ 86%) reported daily doses of PrEP a week For self-reported adherence of 70-85%, assume risk reduction range spanning range of both risk reduction estimates: 0.73-0.99			Partners Demonstration Project prevention-effective adherence analysis - females[8]		
Transmission Probabilities							
Per sex act probability of HIV transmission from a chronically infected female to a male partner	β_f	0.00085 (0.0006 - 0.0011)	Per-act HIV-1 transmission probability, male to female[5] Estimate is mid-point	As stated			
Average reduction in probability HIV transmission on ART	ϱ	0.945 (0.9 – 0.99)	Minimum and maximum across studies[72] Estimate is mid-point				
HIV risk-reduction efficacy of condoms	ε	0.85 (0.8 - 0.9)	With consistent use[73] and with consistent use[74]				

Parameter	Symbol	Kenya		Zimbabwe		South Africa	
		Estimate (Low-High)	References	Estimate (Low-High)	References	Estimate (Low-High)	References
			Estimate is mid-point				
Multiplicative increase in per sex act probability of HIV transmission in the presence of an STI	δ	4 (2-6)	Combined study effectiveness estimate across STDs, and range spanning individual STD combined study effect estimates[75] Estimate is mid-point				
Average reduction in probability of HIV transmission to women, when the male partner has been circumcised	σ_f	0.1 (0–0.2)	Male circumcision; estimates of HIV infection in women.[76] Estimate is mid-point				

Table S2: Parameters and data sources used in the parameterisation and fitting of the models. *Point estimates are stated first with lower and upper bounds used in the latin hypercube fitting in brackets.*

Supplementary Materials: Supplementary Results

Model calibration

The model fits to HIV incidence for each country and high-risk women population are shown in Figures S1-3.

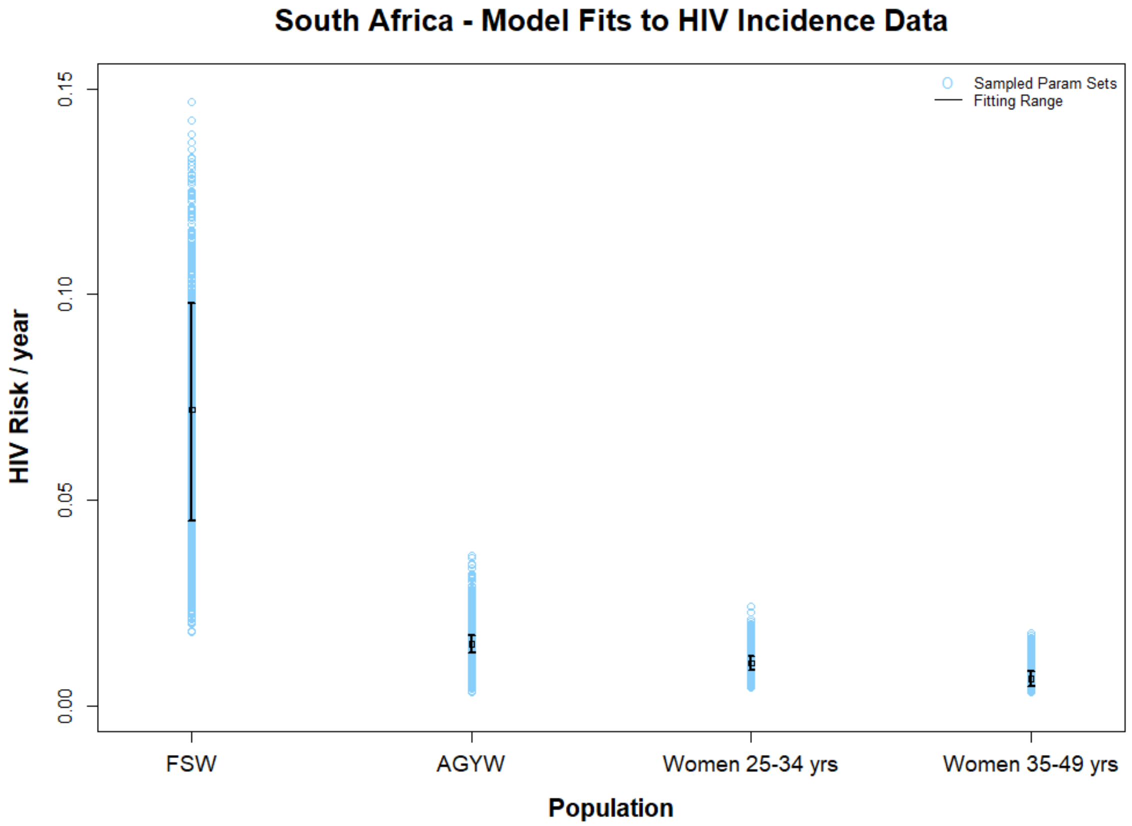

Figure S1: Model Fits to HIV Incidence Data for South Africa. *The model outcomes across the parameter ranges simulated through latin hypercube sampling are show in blue. The black book-ended lines show the 95% confidence intervals around national HIV incidence estimates (HIV risk per year), and the model outcomes that fit within this range are considered to be fits to data. The model outcomes and fitting ranges are shown distinctly for the four high-risk women populations: female sex workers (FSW), adolescent girls and young women aged 15-24 years (AGYW), women aged 25-34 years and women aged 35-49 years.*

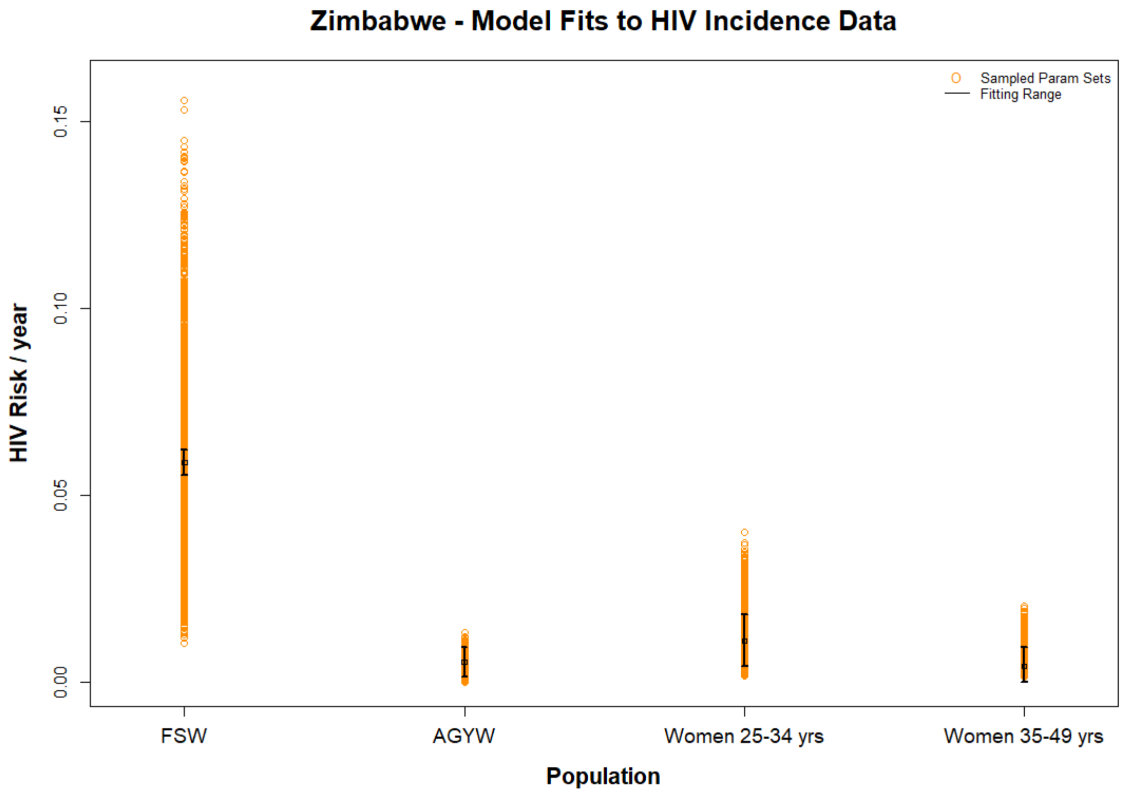

Figure S2: Model Fits to HIV Incidence Data for Zimbabwe. *The model outcomes across the parameter ranges simulated through latin hypercube sampling are show in orange. The black book-ended lines show the 95% confidence intervals around national HIV incidence estimates (HIV risk per year), and the model outcomes that fit within this range are considered to be fits to data. The model outcomes and fitting ranges are shown distinctly for the four high-risk women populations: female sex workers (FSW), adolescent girls and young women aged 15-24 years (AGYW), women aged 25-34 years and women aged 35-49 years.*

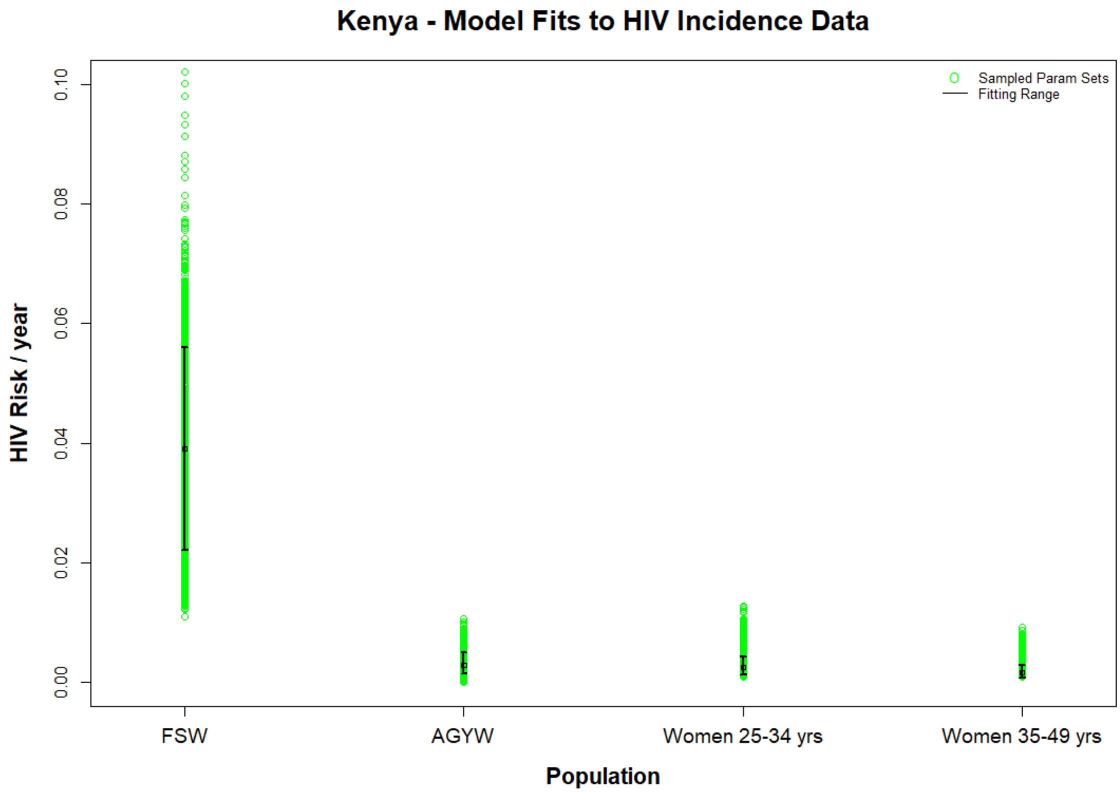

Figure S3: Model Fits to HIV Incidence Data for Kenya. *The model outcomes across the parameter ranges simulated through latin hypercube sampling are show in green. The black book-ended lines show the 95% confidence intervals around national HIV incidence estimates (HIV risk per year), and the model outcomes that fit within this range are considered to be fits to data. The model outcomes and fitting ranges are shown distinctly for the four high-risk women populations: female sex workers (FSW), adolescent girls and young women aged 15-24 years (AGYW), women aged 25-34 years and women aged 35-49 years.*

Supplementary Results

Figure S4 illustrates the relative cost at which PrEP will be equally as cost-effective to scale-up in a lower-risk group as it will be in a high-risk group, in the case that HIV prevalence in the higher-risk women partner population is 20%. It is demonstrated in four scenarios: underlying HIV prevalence in the lower-risk women's partner population of 5%, 10%, 15% and 20%. This figure corresponds to *Figure 2* in the main text, which demonstrates that case that HIV prevalence in the higher-risk women's partner population is 40%.

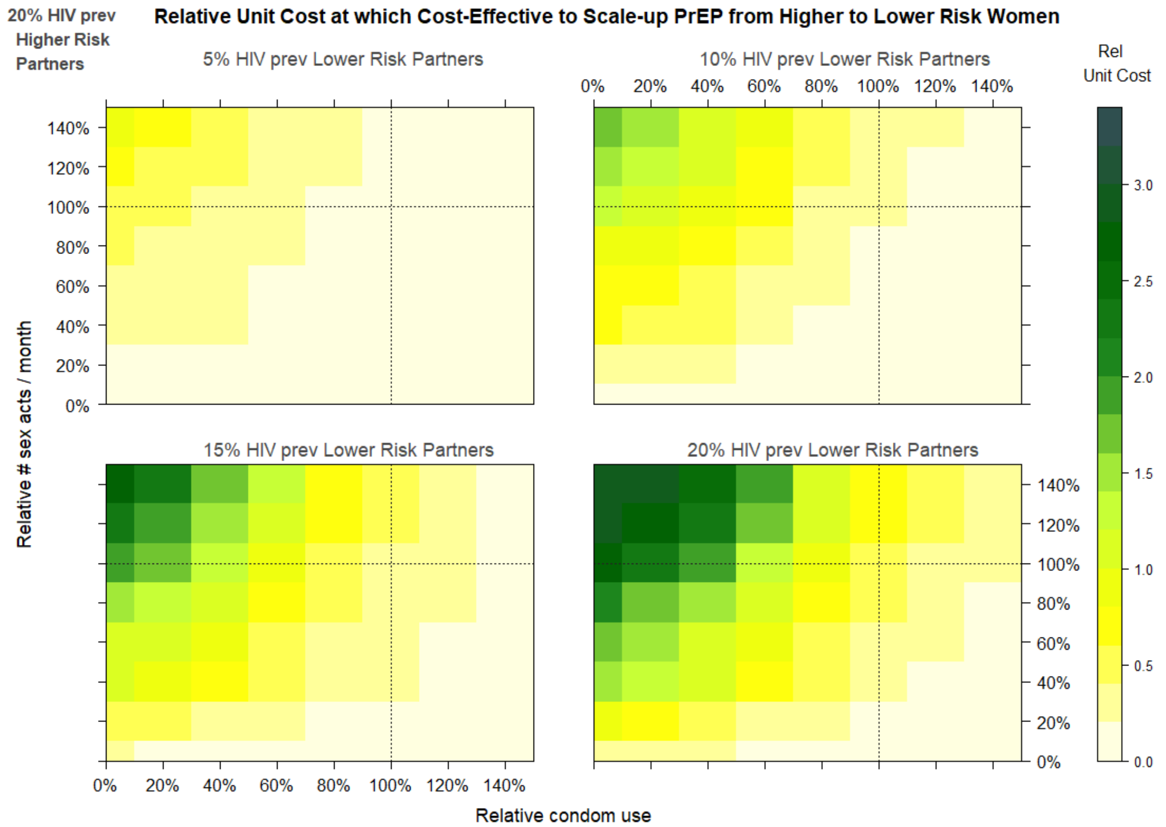

Figure S4: Relative unit cost at which it is cost-effective to scale-up PrEP from a higher- to lower-risk women group. *The heatmaps show the relative unit cost at which it is cost-effective to scale-up PrEP from a higher- to a lower-risk group. The relative unit cost at which PrEP is cost-effective is shown by the relative average condom use in the lower-risk group compared to the higher-risk group (x-axis), and the relative number of sex acts a month for women in the lower-risk group compared to the higher-risk group (y-axis). The unit cost of PrEP in the lower-risk group relative to the higher-risk group at which PrEP is equally cost-effective between the two groups is shown by colour, according to the colour key on the right-hand side of the graph. A colour within the yellow spectrum denotes that the relative unit cost of PrEP in the lower-risk group relative to the higher-risk group has to be less than 1 for it to be equally as cost cost-effective. A colour within the green spectrum denotes that the relative unit cost of PrEP in the lower-risk group relative to the higher-risk group will be greater than 1 for it to be equally as cost cost-effective. The 4 heatmaps correspond respectively (left to right, top to bottom) to underlying partner HIV prevalence of 5%, 10%, 15% and 20% in the lower-risk group's partner population and all of them corresponding to 20% HIV prevalence in the higher-risk women's partner population. The heatmaps are calculated using equation (S1.5) from the Supplementary Materials: Methods, assuming that women's partners are drawn from a single population each. The higher-risk group are assumed to have 12-month PrEP program retention levels of 22%[3] and adherence levels of 70-85% (corresponding to a risk reduction of 73-99%[8]). The PrEP program retention levels for the lower-risk group were simulated between +/- 25% the retention of the higher-risk group.[4] For those lower-risk women retained in the PrEP program, it was assumed that PrEP adherence was the same as the higher-risk group.*

Comparison of the Maximum Unit Costs of PrEP in Lower-Risk Groups Relative to Unit Costs FSW to be Equally as Cost-Effective, with Estimates of Current Relative Unit Costs

		High Risk Women Population		
Country	**Unit Cost Relative to FSWs**	**AGYW**	**Women 25-34 years**	**Women 35-49 years**
South Africa	Maximum Relative Unit Cost to be Cost-Effective	23.3 % (13.3 % , 36.8 %)	16.2 % (9.1 % , 26 %)	10.5 % (5.7 % , 18 %)
	Estimated Current Relative Unit Cost	79.6 % (72.4 % , 86.7 %)	68.7 % (62.7 % , 75.8 %)	48.3 % (42.4 % , 54.7 %)
	Difference (relative to FSW Unit Cost)	-56.2 % (-69.2 % , -40.4 %)	-52.2 % (-62.5 % , -41.4 %)	-37.6 % (-45.8 % , -28.7 %)
	Difference (relative to own Unit Cost)	-70.8 % (-83.4 % , -53.2 %)	-76.2 % (-87.0 % , -62.6 %)	-78.4 % (-88.1 % , -61.8 %)
Zimbabwe	Maximum Relative Unit Cost to be Cost-Effective	7.1 % (2.7 % , 14.9 %)	17.7 % (7.1 % , 31.2 %)	11 % (5.5 % , 17.2 %)
	Estimated Current Relative Unit Cost	75.6 % (70.8 % , 80.8 %)	63 % (58 % , 67.7 %)	38.8 % (34.1 % , 42.7 %)
	Difference (relative to FSW Unit Cost)	-67.7 % (-75.1 % , -60.1 %)	-44.6 % (-58.3 % , -31.1 %)	-28.1 % (-35.3 % , -18.7 %)
	Difference (relative to own Unit Cost)	-90.4 % (-96.5 % , -80.6 %)	-71.8 % (-88.9 % , -50.8 %)	-72 % (-86.1 % , -53.6 %)
Kenya	Maximum Relative Unit Cost to be Cost-Effective	8.1 % (3.9 % , 18.5 %)	9.1 % (3.6 % , 17.7 %)	6.4 % (3.1 % , 11.6 %)
	Estimated Current Relative Unit Cost	90.3 % (86.2 % , 94.8 %)	74.9 % (71.1 % , 78.4 %)	48.1 % (45.1 % , 51.6 %)
	Difference (relative to FSW Unit Cost)	-81.5 % (-89 % , -71 %)	-66 % (-73.4 % , -57.5 %)	-41.7 % (-46.4 % , -36.2 %)
	Difference (relative to own Unit Cost)	-91 % (-95.7 % , -79.6 %)	-88 % (-95.3 % , -76.6 %)	-86.7 % (-93.7 % , -75.4 %)

Table S3: Comparison of the Maximum Unit Costs of PrEP in Lower-Risk Groups Relative to Unit Costs FSW to be Equally as Cost-Effective, with Estimates of Current Relative Unit Costs. *The table shows the maximum relative unit costs of PrEP in AGYW, women 25-34 years and women 35-49 years relative to the unit costs of PrEP for FSW, for PrEP to be equally as cost-effective (calculated using equation S1.5 in Supplementary Materials: Methods). It compares this to the estimated current relative unit costs between the populations, calculated using the data set out in Table S2. The table shows the difference between these two estimates (relative to the FSW unit cost of PrEP). It also shows what this difference represents relative to the group's (i.e. AGYW, women 25-34 years or women 35-49 years) own unit cost, which is equivalent to the % the unit cost would have to drop for PrEP to be equally as cost-effective as for FSW. The comparisons are shown separately for South Africa, Zimbabwe and Kenya. The values shown in the table outside the brackets are the median values, and the values shown in the brackets are the 95% credible intervals (CrIs).*

	Median relative Cost of Equal Coverage of PrEP between stated female population group and FSW		
Country	AGYW	Women 25-34 years	Women 35-49 years
South Africa	28.3	26.7	18.7
Zimbabwe	21.9	15.2	7
Kenya	27.4	16.4	8.5

Table S4a: Median relative cost of equal coverage of PrEP between stated female population group and FSW. *The table shows the median cost of equal coverage of PrEP between FSW, AGYW, women 25-34 years or women 35-49 years and FSW. It is calculated as (population size of female group*unit cost of PrEP for female group)/ (population size of FSW*unit cost of PrEP for FSW). The unit costs of PrEP for each high-risk woman group are as stated in Table S2. AGYW is used as shorthand for adolescent girls and young women 15-24 years.*

Table S4 sets out the estimated number of infections that could be averted a year due to PrEP in each high-risk women population group, in each country, for every $100,000 available for PrEP programming, at the PrEP unit costs stated in Table S2. These data correspond to Figure 4 in the main text.

For each $100k available for PrEP programming a year,
the number of HIV infections that could be averted due to PrEP

	High Risk Women Population			
Country	FSW	AGYW	Women 25-34 years	Women 35-49 years
South Africa	5.7 (3.8 , 8.8)	1.7 (1.1 , 2.4)	1.3 (0.9 , 2)	1.2 (0.8 , 2)
Zimbabwe	3.4 (2.9 , 4.1)	0.3 (0.1 , 0.7)	1 (0.4 , 1.8)	0.9 (0.5 , 1.6)
Kenya	1.5 (0.9 , 2.4)	0.1 (0.1 , 0.3)	0.2 (0.1 , 0.3)	0.2 (0.1 , 0.3)

Table S5: Median and 95% credible intervals (95% CrIs) of the relative number of infections that could be averted a year due to PrEP for each $100k available for PrEP programming. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the number of HIV infections that could be averted a year due to PrEP, for each $100k available for PrEP programming, for FSW, AGYW, women 25-34 years or women 35-49 years. The relative number of infections that could be averted is calculated using equation S2.10 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] The unit costs of PrEP for each high-risk woman group are as stated in Table S2. AGYW is used as shorthand for adolescent girls and young women 15-24 years.*

In South Africa, $100,000 could avert a median 5.7 infections a year or 0.2% (95% CrI: 0.1%, 0.4%) of the total infections a year due to PrEP in FSW; median 1.7 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of the total infections a year in AGYW; mediaan 1.3 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of total infections a year in women 25-34 years; and median 1.2 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of total infections a year in women 35-49 years. This highlights, that to maximise cost-effectiveness on an individual basis, PrEP would be scaled-up first in FSW, then AGYW, then women 35-49 years, then women 25-34 years.

In Zimbabwe, $100,000 could avert a median 3.4 infections a year or 0.3% (95% CrI: 0.3%, 0.4%) of the total infections a year due to PrEP in FSW; median 0.3 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of the total infections a year in AGYW; median 1.0 infections a year or <0.1% (95%

CrI: <0.1%, <0.1%) of total infections a year in women 25-34 years; and median 0.9 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of total infections a year in women 35-49 years. This highlights, that to maximise cost-effectiveness on an individual basis, PrEP would be scaled-up first in FSW, then women 25-34 years, then women 35-49 years, then AGYW.

In Kenya, $100,000 could avert a median 1.5 infections a year or <0.1% (95% CrI: <0.1%, 0.1%) of the total infections a year due to PrEP in FSW; median 0.1 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of the total infections a year in AGYW; median 0.2 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of total infections a year in women 25-34 years; and median 0.2 infections a year or <0.1% (95% CrI: <0.1%, <0.1%) of total infections a year in women 35-49 years. This highlights, that to maximise cost-effectiveness on an individual basis, PrEP would be scaled-up first in FSW, then women 25-34 years and women 35-49 years, and then AGYW.

Figure S5 shows, the proportion of the total number of HIV infections that could be averted a year for each $100k available for PrEP programming.. The corresponding data to the figure are set out in Table S5 below.

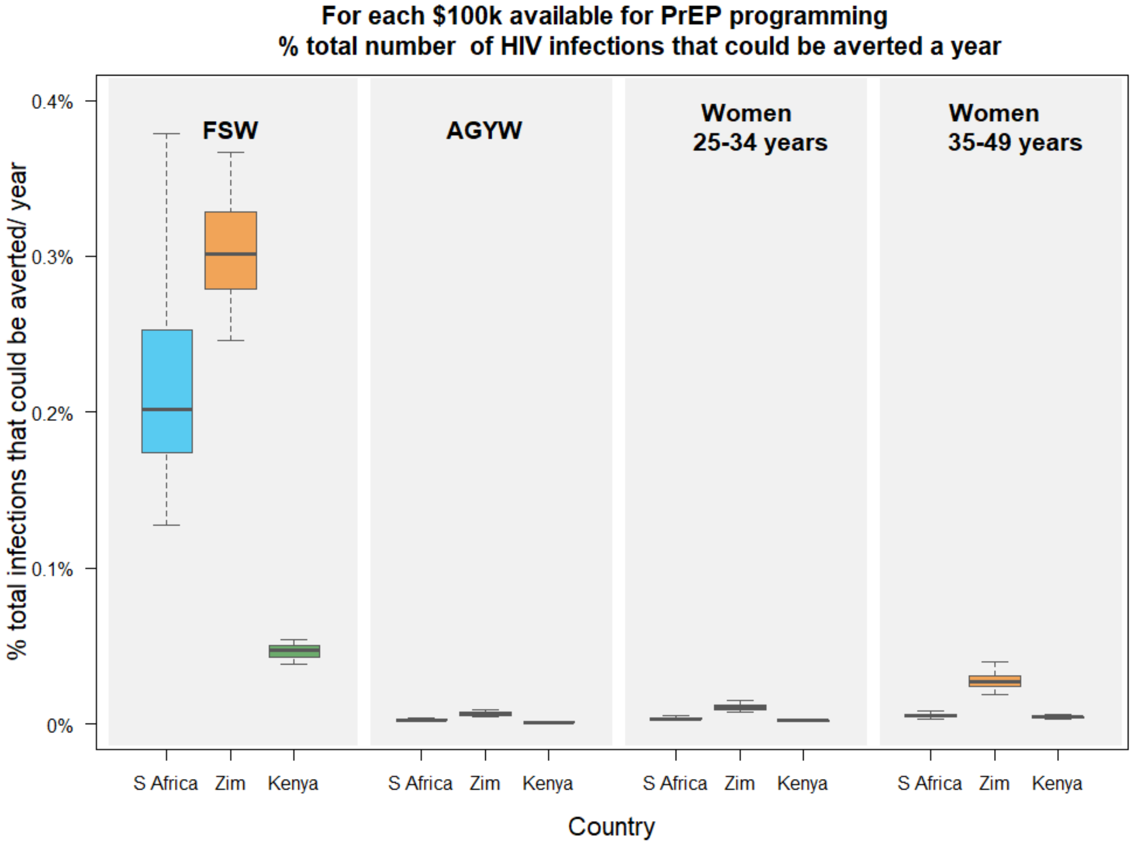

Figure S5: Boxplot showing for each $100k available for PrEP programming, the proportion of the total number of HIV infections that could be averted a year with these funds. *The boxplot shows for each $100k available for PrEP programming, the proportion of infections that could be averted a year with these funds for each of HIV negative FSW, AGYW, women 25-34 years or women 35-49 years. The proportion of total infections that could be averted a year are shown, grouped left to right, for FSW, AGYW, women 25-34 years and women 35-49 years. Within each age grouping, the results are show by country, left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in blue). The proportion of total infections that could be averted a year are calculated using equation S2.11 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.*[3] *The abbreviations used in the graph are as follows: AGYW denotes adolescent girls and young women 15-24 years, S Africa denotes South Africa and Zim denotes Zimbabwe.*

For each $100k available for PrEP programming,

the proportion of HIV infections that could be averted a year

	High Risk Women Population			
Country	FSW	AGYW	Women 25-34 years	Women 35-49 years
South Africa	0.2 % (0.1 % , 0.4 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)
Zimbabwe	0.3 % (0.3 % , 0.4 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)
Kenya	0 % (0 % , 0.1 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)	0 % (0 % , 0 %)

Table S6: Median and 95% credible intervals (95% CrIs) of the proportion of the total number of HIV infections that could be averted a year with each $100k available for PrEP programming. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the proportion of the total number of HIV infections that could be averted a year with each $100k available for PrEP programming for FSW, AGYW, women 25-34 years or women 35-49 years. The proportion of the total number of HIV infections that could be averted is calculated using equation S2.11 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] The unit costs of PrEP for each high-risk woman group are as stated in Table S2. AGYW is used as shorthand for adolescent girls and young women 15-24 years.*

Figure S6 sets out the number of HIV negative individuals in each high-risk woman population that would need to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW. The corresponding data to the figure are set out in Table S6.

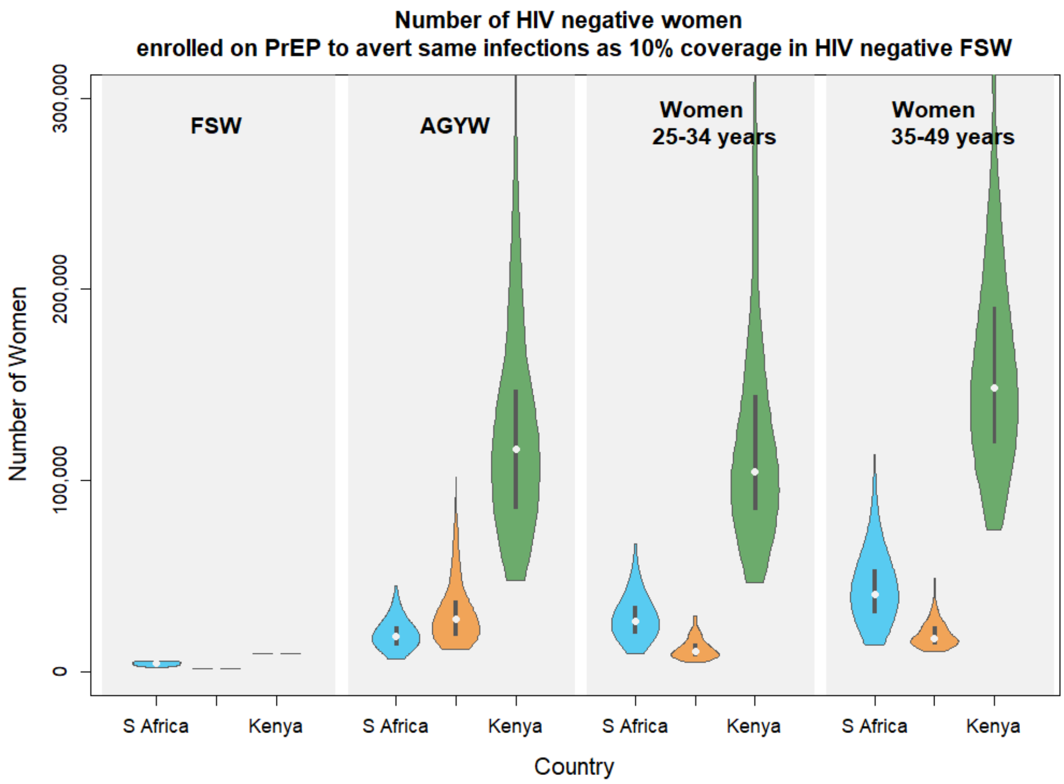

Figure S6: Number of HIV negative women needed to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW. *The violin plot shows number of HIV negative AGYW, women 25-34 years or women 35-49 years in the population that would have to be enrolled in a PrEP program in order to achieve the same number of infections averted over 12 months as with 10% of the HIV negative FSW population enrolled in a PrEP program. As a comparison, the number of women represented by 10% of HIV negative FSW is shown in the far left hand side block of the figure. The number of HIV negative women needed to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW is then grouped left to right, for AGYW, women 25-34 years or women 35-49 years. Within each age grouping, the results are show by country, left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in blue). In the violin plots, the white dots represent the median values, the thick* *black vertical lines represent the interquartile range, the vertical length of the violin represents the range of values and the width of the violin represents the frequency with which those values occur. Where two horizontal grey lines are shown instead of a violin, it indicates that the range of values is limited in variation. The number of HIV negative women needed to be enrolled on PrEP to avert the same number of infections averted as 10% PrEP program coverage in HIV negative FSW is calculated using equation S2.7 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] The abbreviations used in the graph are as follows: AGYW denotes adolescent girls and young women 15-24 years, S Africa denotes South Africa and Zim denotes Zimbabwe.*

Number of HIV negative women needed to be enrolled on PrEP
to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW

	High Risk Women Population			
Country	FSW (comparator)	AGYW	Women 25-34 years	Women 35-49 years
South Africa	4359 (2774, 5914)	18531 (9594, 37052)	31798 (16411, 65199)	52240 (26287 , 111053)
Zimbabwe	1933 (1910, 1953)	27496 (12962, 72904)	14933 (8535, 37453)	36978 (23578, 73838)
Kenya	9477 (9449, 9513)	116565 (51258, 246376)	151830 (78163, 380590)	274531 (149378, 567706)

Table S7: Median and 95% credible interval (CrIs) of the number of HIV negative women needed to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the number of HIV negative AGYW, women 25-34 years or women 35-49 years in the population that would have to be enrolled in a PrEP program in order to achieve the same number of infections averted over 12 months as with 10% of the HIV negative FSW population enrolled in a PrEP program. As a comparison, the median and 95% CrIs of the numbers of women represented by 10% of HIV negative FSW is shown in the far left column of the table. The median and 95% CrIs of the numbers of HIV negative women needed to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW is then grouped left to right in the 2nd to 4th columns of the table, for AGYW, women 25-34 years or women 35-49 years respectively. Within each age grouping, the results are show by country, for South Africa, Zimbabwe and Kenya in rows 1 to 3 respectively. The number of HIV negative women needed to be enrolled on PrEP to avert the same number of infections averted as 10% PrEP program coverage in HIV negative FSW is calculated using equation S2.7 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3]*

Figure S7 shows PrEP program coverage in HIV negative individuals in each high-risk woman population that would need to be enrolled on PrEP to avert the same number of infections as 10% PrEP program coverage in HIV negative FSW. The corresponding data are shown in Table S7 below.

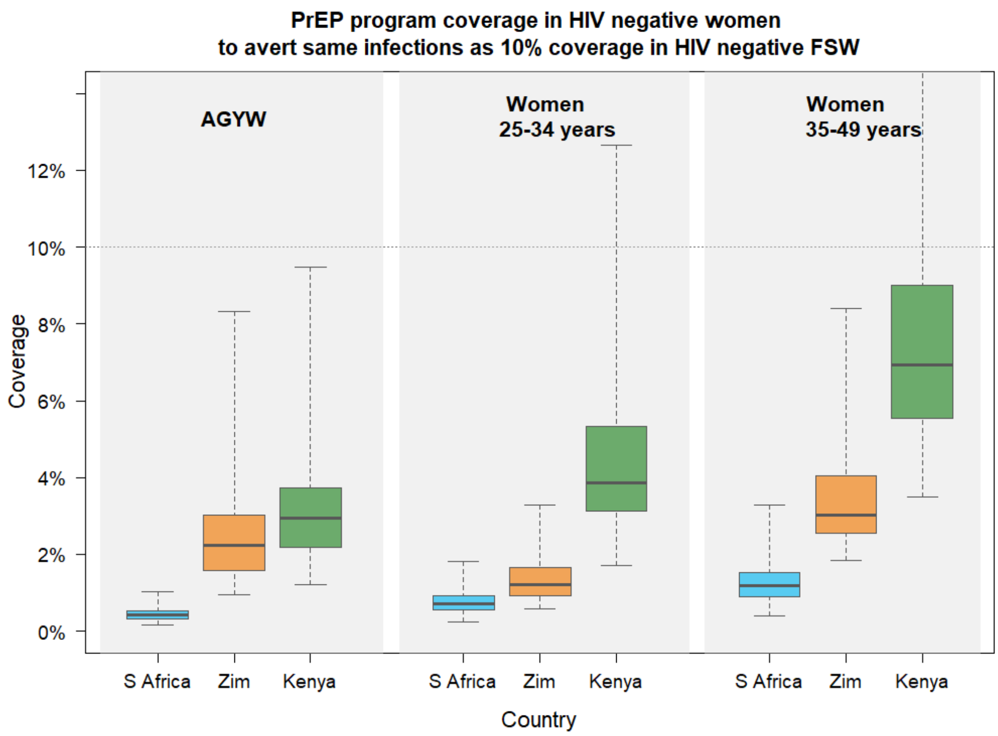

Figure S7: Boxplot of the PrEP program coverage in HIV negative women needed to avert the same number of HIV infections as 10% coverage in HIV negative FSW. *The boxplot shows the PrEP program coverage in HIV negative AGYW, women 25-34 years or women 35-49 years to avert the same number of infections as 10% program coverage in HIV negative FSW. The PrEP program coverage levels are shown, grouped left to right, for AGYW, women 25-34 years or women 35-49 years. Within each age grouping, the results are show by country, left to right, for South Africa (in blue), Zimbabwe (in orange) and Kenya (in blue). The coverage levels are calculated using equation S2.7 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] The abbreviations used in the graph are as follows: AGYW denotes adolescent girls and young women 15-24 years, S Africa denotes South Africa and Zim denotes Zimbabwe.*

PrEP program coverage in HIV negative women to avert the same number of infections as 10% coverage in HIV negative FSW

	High Risk Women Population		
Country	AGYW	Women 25-34	Women 35-49 years
South Africa	0.4 % (0.2 % , 0.8 %)	0.7 % (0.4 % , 1.4 %)	1.2 % (0.6 % , 2.5 %)
Zimbabwe	2.2 % (1.1 % , 5.9 %)	1.2 % (0.7 % , 3.1 %)	3 % (1.9 % , 6 %)
Kenya	2.9 % (1.3 % , 6.3 %)	3.8 % (2 % , 9.7 %)	6.9 % (3.8 % , 14.4 %)

Table S8: Median and 95% credible intervals (95% CrIs) of the PrEP program coverage in HIV negative women to avert the same number of infections as with 10% PrEP program coverage in HIV negative FSW. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the PrEP program coverage in AGYW, women 25-34 years or women 35-49 years to achieve the same number of infections a year as 10% PrEP program coverage in HIV negative FSW. The PrEP program coverage is calculated using equation S2.7 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] AGYW is used as shorthand for adolescent girls and young women 15-24 years.*

Table S8 shows the relative number of infections that could be averted a year with PrEP at equal coverage levels in AGYW, women 25-34 years and women 35-49 years as in FSW. These data correspond to Figure 5 in the main text.

Relative number of infections that could be averted a year on PrEP with equal program coverage as in FSW

	High Risk Women Population		
Country	AGYW	Women 25-34 years	Women 35-49 years
South Africa	24 (12 , 45)	14 (7 , 27)	8 (4 , 17)
Zimbabwe	4 (2 , 9)	8 (3 , 14)	3 (2 , 5)
Kenya	3 (2 , 8)	3 (1 , 5)	1 (1 , 3)

Table S9: Median and 95% credible intervals (95% CrIs) of the relative number of infections that could be averted a year on PrEP with equal program coverage as in FSW. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the relative number of infections that could be averted a year on PrEP in AGYW, women 25-34 years or women 35-49 years relative to the number that could be averted in FSW with equal PrEP program coverage. The relative number of infections that could be averted is calculated using equation S2.9 from Supplementary Materials and assumes that 12-month PrEP program retention in AGYW, women 25-34 years or women 35-49 years is within +/-25% of retention levels for FSW, taken to be 22%, in line with the results of the TAPS demonstration project.[3] AGYW is used as shorthand for adolescent girls and young women 15-24 years.*

Sensitivity analysis

25% less PrEP-adherence-related HIV risk reduction across all women groups

Table S9 shows the percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all women groups. These results are a comparison of the results set out in Table S3 (top row for each country) with what the results would be if the same analysis were repeated with 25% less PrEP-adherence-related HIV risk reduction across all women groups.

% Change in Maximum Unit Cost at which PrEP is equally as Cost-Effective as for FSW, with 25% reduced HIV risk-reduction across all Groups

	High Risk Women Population		
Country	AGYW	Women 25-34	Women 35-49 years
South Africa	0.001% (0.000%, 0.003%)	-0.002% (-0.002%, 0.000%)	0.000% (-0.002%, 0.000%)
Zimbabwe	0.001% (-0.002%, 0.002%)	-0.002% (-0.001%, 0.001%)	-0.001% (-0.002%, -0.001%)
Kenya	0.000% (0.000%, 0.001%)	0.001% (0.000%, 0.002%)	0.000% (0.000%, 0.000%)

Table S10: Percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all women groups. *The table shows the percentage change in the maximum relative unit costs of PrEP in AGYW, women 25-34 years and women 35-49 years relative to the unit costs of PrEP for FSW, for PrEP to be equally as cost-effective (calculated using equation S1.5 in Supplementary Materials: Methods), if the PrEP-adherence-associated HIV risk reduction were reduced by 25% compared to the baseline analysis presented in Table S3 (top row for each country). The comparisons are shown separately for South Africa, Zimbabwe and Kenya. AGYW is used as shorthand for adolescent girls and young women 15-24 years. The values shown in the table outside the brackets are the median values, and the values shown in the brackets are the 95% credible intervals (CrIs). All values are shown rounded to the nearest 3 decimal places.*

Table S10 sets out the percentage change in the in the relative number of infections averted a year on PrEP with equal coverage as with FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all women groups. These results are a comparison of the results set out in Table S8 with what the results would be if the same analysis were repeated with 25% less PrEP-adherence-related HIV risk reduction across all women groups.

	% Change in Relative Number of Infections Averted a Year on PrEP with equal coverage as with FSW, with 25% reduced PrEP-adherence-related HIV-risk reduction across Groups		
	High Risk Women Population		
Country	AGYW	Women 25-34 years	Women 35-49 years
South Africa	0.000 % (-0.001% , 0.000 %)	-0.001 % (-0.001% , -0.001%)	-0.001 % (-0.001 % , 0.000 %)
Zimbabwe	0.000% (-0.001 % , 0.002 %)	-0.002% (-0.001 % , 0.001%)	-0.001% (-0.002 % , -0.001 %)
Kenya	0.000% (0.000% , 0.001 %)	0.001% (0.000% , 0.002%)	0.000% (0.000 % , 0.000 %)

Table S11: Percentage change in the relative number of infections averted a year on PrEP with equal coverage as with FSW, with 25% reduced PrEP-adherence-related HIV-risk reduction across groups. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the percentage change in the relative number of infections that could be averted a year on PrEP in AGYW, women 25-34 years or women 35-49 years relative to the number that could be averted in FSW with equal PrEP program coverage, if the PrEP-adherence-associated HIV risk reduction were reduced by 25% compared to the baseline analysis presented in Table S8. For the underlying analyses, the relative number of infections that could be averted is calculated using equation S2.9 from Supplementary Materials. AGYW is used as shorthand for adolescent girls and young women 15-24 years. All values are shown rounded to the nearest 3 decimal places.*

<u>25% less PrEP-adherence-related HIV risk reduction across all non-FSW women groups</u>

Table S11 sets out the percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all non-FSW women groups (i.e. AGYW, women 25-34 years and women 35-49 years). These results are a comparison of the results set out in Table S3 (top row for each country) with what the results would be if the same analysis were repeated with 25% less PrEP-adherence-related HIV risk reduction across all non-FSW women groups.

	% Change in Maximum Unit Cost at which PrEP is equally as Cost-Effective as for FSW, with 25% reduced HIV risk-reduction across all non-FSW women groups		
	High Risk Women Population		
Country	AGYW	Women 25-34	Women 35-49 years
South Africa	0.253 % (0.252 %, 0.252 %)	0.253 % (0.252 %, 0.252%)	0.252 % (0.251%, 0.251%)
Zimbabwe	0.254 % (0.253 %, 0.253 %)	0.253 % (0.253% ,0.254%)	0.252 % (0.252%,0.252%)
Kenya	0.258 % (0.260 %, 0.256 %)	0.257 % (0.257%,0.258%)	0.256 % (0.255%,0.258%)

Table S12: Percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all non-FSW women groups (i.e. AGYW, women 25-34 years and women 35-49 years). *The table shows the percentage change in the maximum relative unit costs of PrEP in AGYW, women 25-34 years and women 35-49 years relative to the unit costs of PrEP for FSW, for PrEP to be equally as cost-effective (calculated using equation S1.5 in Supplementary Materials: Methods), if the PrEP-adherence-associated HIV risk reduction were reduced by 25% for all non-FSW women groups compared to the baseline analysis presented in Table S3 (top row for each country). The comparisons are shown separately for South Africa, Zimbabwe and Kenya. AGYW is used as shorthand for adolescent girls and young women 15-24 years. The values shown in the table outside the brackets are the median values, and the values shown in the brackets are the 95% credible intervals (CrIs). All values are shown rounded to the nearest 3 decimal places.*

Table S12 sets out the percentage change in the in the relative number of infections averted a year on PrEP with equal coverage as with FSW, if 25% less PrEP-adherence-related HIV risk reduction were assumed across all non-FSW women groups (i.e. AGYW, women 25-34 years and women 35-49 years). These results are a comparison of the results set out in Table S8 with what the results would be if the same analysis were repeated with 25% less PrEP-adherence-related HIV risk reduction across all non-FSW women groups.

	% Change in Relative Number of Infections Averted a Year on PrEP with equal coverage as with FSW, with 25% reduced PrEP-adherence-related HIV-risk reduction across all non-FSW women groups		
	High Risk Women Population		
Country	AGYW	Women 25-34 years	Women 35-49 years
South Africa	0.252 % (0.250 % , 0.252 %)	0.251 % (0.252 % , 0.252 %)	0.252 % (0.251 % , 0.251 %)
Zimbabwe	0.253 % (0.254 % , 0.254 %)	0.253 % (0.253 % , 0.254 %)	0.252 % (0.252 % , 0.253 %)
Kenya	0.257 % (0.260 % , 0.256 %)	0.26 % (0.257 % , 0.258 %)	0.256 % (0.255 % , 0.258 %)

Table S13: Percentage change in the relative number of infections averted a year on PrEP with equal coverage as with FSW, with 25% reduced PrEP-adherence-related HIV-risk reduction across all non-FSW women groups (i.e. AGYW, women 25-34 years and women 35-49 years). *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the percentage change in the relative number of infections that could be averted a year on PrEP in AGYW, women 25-34 years or women 35-49 years relative to the number that could be averted in FSW with equal PrEP program coverage, if the PrEP-adherence-associated HIV risk reduction were reduced by 25% for all non-FSW women groups compared to the baseline analysis presented in Table S8. For the underlying analyses, the relative number of infections that could be averted is calculated using equation S2.9 from Supplementary Materials. AGYW is used as shorthand for adolescent girls and young women 15-24 years. All values are shown rounded to the nearest 3 decimal places.*

Structural sensitivity analysis: women 25-34 years have partners from males 35-49 years, in addition to 25-34 years

Table S13 sets out the percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, under the structural sensitivity analysis exploring the case that women 25-34 years draw partners from males 35-49 years, in addition to 25-34 years. These results are a comparison of the results set out in Table S3 (top row for each country) with what the results would be if the same analysis were repeated with women 25-34 years drawing partners from males 35-49 years, in addition to 25-34 years (assumed to be the only partner population, in Table S3). Whilst the structural sensitivity analysis directly affects the model outcomes for women 25-34 years, it also indirectly affects the mean and 95% CrI outcomes for FSW, AGYW and women 35-49 year through changes to the number of underlying fitted parameter sets across all women groups.

	% Change in Maximum Unit Cost at which PrEP is equally as Cost-Effective as for FSW, with women 25-34 years having partners drawn from 2 populations		
	High Risk Women Population		
Country	AGYW	Women 25-34	Women 35-49 years
South Africa	-0.017 % (-0.063%, 0.017%)	-0.091% (-0.157%, -0.089%)	0.016% (-0.009%, 0.060%)
Zimbabwe	0.003% (0.015%, 0.018%)	-0.299% (-0.476%, -0.081%)	0.075% (-0.015%, 0.128%)
Kenya	0.020% (-0.004%, 0.000%)	-0.205% (-0.596%, 0.023%)	0.038% (0.030%, 0.059%)

Table S14: Percentage change in the maximum unit cost at which PrEP will be equally cost-effective in other high-risk women groups (AGYW, women 25-34 years and women 35-49 years) as in FSW, under the structural sensitivity analysis exploring the case that women 25-34 years draw partners from males 35-49 years, in addition to 25-34 years. *The table shows the percentage change in the maximum relative unit costs of PrEP in AGYW, women 25-34 years and women 35-49 years relative to the unit costs of PrEP for FSW, for PrEP to be equally as cost-effective (calculated using equation S1.5 in Supplementary Materials: Methods), if women 25-34 years are assumed to draw partners from males 35-49 years, in addition to 25-34 years, compared to the baseline analysis presented in Table S3 (top row for each country). The comparisons are shown separately for South Africa, Zimbabwe and Kenya. AGYW is used as shorthand for adolescent girls and young women 15-24 years. The values shown in the table outside the brackets are the median values, and the values shown in the brackets are the 95% credible intervals (CrIs). All values are shown rounded to the nearest 3 decimal places.*

Table S14 sets out the percentage change in the in the relative number of infections averted a year on PrEP with equal coverage as with FSW, if women 25-34 years are assumed to draw partners from males 35-49 years, in addition to 25-34 years. These results are a comparison of the results set out in Table S8 with what the results would be if the same analysis were repeated with women 25-34 years drawing partners from males 35-49 years, in addition to 25-34 years (assumed to be the only partner population, in Table S8). Whilst the structural sensitivity analysis directly affects the model outcomes for women 25-34 years, it also indirectly affects the mean and 95% CrI outcomes for FSW, AGYW and women 35-49 year through changes to the number of underlying fitted parameter sets across all women groups.

	% Change in Relative Number of Infections Averted a Year on PrEP with equal coverage as with FSW, with women 25-34 years having partners drawn from 2 populations		
	High Risk Women Population		
Country	AGYW	Women 25-34 years	Women 35-49 years
South Africa	0.044 % (-0.091 %, -0.03 %)	-0.024 % (-0.176 % , -0.12 %)	0.039 % (-0.054 %, 0.061 %)
Zimbabwe	0.001 % (0.008 %, 0.015 %)	-0.297 % (-0.483 %, -0.087 %)	0.064 % (-0.018 %, 0.125 %)
Kenya	0.023 % (-0.004 %, -0.002 %)	-0.223 % (-0.593 %, 0.023 %)	0.048 % (0.042 % , 0.074 %)

Table S15: Percentage change in the relative number of infections averted a year on PrEP with equal coverage as with FSW, under the structural sensitivity analysis exploring the case that women 25-34 years draw partners from males 35-49 years, in addition to 25-34 years. *The table shows the median (value outside the brackets) and 95% CrIs (inside the brackets) of the percentage change in the relative number of infections that could be averted a year on PrEP in AGYW, women 25-34 years or women 35-49 years relative to the number that could be averted in FSW with equal PrEP program coverage, if women 25-34 years are assumed to draw partners from males 35-49 years, in addition to 25-34 years, compared to the baseline analysis presented in Table S8. For the underlying analyses, the relative number of infections that could be averted is calculated using equation S2.9 from Supplementary Materials. AGYW is used as shorthand for adolescent girls and young women 15-24 years. All values are shown rounded to the nearest 3 decimal places.*

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