Title: Intersections of risk and intervention heterogeneity: a modelling study on the prevention impacts of antiretroviral therapy in eSwatini

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Abstract

* under construction *

1 Introduction

Despite sustained efforts and advances in HIV prevention, 2021 saw an estimated 1.5 million new HIV infections globally [1]. A core pillar of HIV prevention remains treatment via antiretroviral therapy (ART). Since 2016, WHO has recommended universal ART eligibility [2], and efforts to scale-up ART coverage around the world continue [1]. Such efforts are often measured through the ART cascade, as reflected in the UNAIDS 90-90-90 [3] and 95-95-95 [4] targets, corresponding to the percentage of people living with HIV who know their status, of whom, the percentage who are on ART, of whom, the percentage who have undetectable viral load.

Numerous modelling studies have sought to estimate the prevention impacts of ART scale-up in Sub-Saharan Africa, usually quantified as incidence reduction or cumulative infections averted in scenarios with higher cascade attainment versus scenarios with lower attainment [5–7]. Such studies often stratify modelled populations by risk, including key populations like female sex workers and their clients, to capture important epidemic dynamics related to risk heterogeneity [7, 8]. These studies almost always assume that cascade attainment, or rates of cascade progression — rates of diagnosis, treatment initiation, and treatment failure/discontinuation — are equal across modelled risk groups [7].

Yet, there is growing evidence of differential ART cascade across population strata [9, 10]. These differences can be driven by unique barriers to engagement in care faced by vulnerable populations, which intersect with drivers of HIV risk [11–13]. These intersections of risk and cascade heterogeneity could potentially undercut the prevention impacts of ART scale-up anticipated from model-based evidence [14]. Therefore, we sought to examine the following questions in an illustrative modelling analysis:

1. How are projections of ART prevention impacts influenced by differences in ART cascade across risk groups?
2. Under which epidemic conditions do such differences have the largest influence?

We examined these questions using a deterministic compartmental model of heterosexual HIV transmission in eSwatini [15], focusing on differential risk related to sex work. eSwatini has the highest national HIV prevalence in the world [16], but has recently achieved outstanding cascade gains — surpassing 95-95-95 — through multiple interventions led by the MaxART Consortium [1, 17]. As such, we use observed ART scale-up in eSwatini as a gold-standard base case for what is possible, and explore counterfactual scenarios in which scale-up is slower, and specific risk groups may be left behind.

2 Methods

We constructed a deterministic compartmental model of heterosexual HIV transmission, stratified by sex, sexual activity, HIV natural history, and ART cascade of care. The model includes 8 risk groups, including higher and lower risk female sex workers (FSW), and higher and lower risk clients of FSW, and 4 partnership types, including regular and occasional sex work (Figure A.1). We calibrated the model to reflect the HIV epidemic and ART scale-up in eSwatini (base case). We then explored counterfactual scenarios in which ART cascade was reduced among various combinations of risk groups, and quantified ART prevention impacts by comparing base case and counterfactual scenarios.

2.1 Model Parameterization & Calibration

Complete model details are given in Appendix A, and all code is available online.[1]

HIV: Our model of HIV natural history included acute infection and stages defined by CD4-count. We modelled relative rates of infectiousness by stage as an approximation of viral load [18–20], as well as rates of HIV-attributable mortality by stage [21–23].

Risk heterogeneity: We captured risk heterogeneity through risk-group-level factors, including group size, average duration in group, STI symptom prevalence, and numbers / types of partnerships per year; and partnership-level factors, including assortative mixing, partnership duration, frequency of vaginal / anal sex, and levels of condom use. Table 1 summarizes key parameter values and sampling distributions related to risk heterogeneity. We assumed that only condom use varied (increased) over time (Figure A.6). To parameterize higher versus lower risk FSW, we conducted exploratory analysis of survey data from Swazi FSW in 2011 [24] and 2014 [25] (Appendix **??**). We parameterized the remaining risk groups using reported data from national studies in 2006 [26], 2011 [27], and 2016 [28]. We modelled expansion of voluntary medical male circumcision [28], but did not model other interventions (e.g. ongoing pre-exposure prophylaxis scale-up [29]) nor non-heterosexual HIV transmission.

ART cascade: We modelled rates of HIV diagnosis among people living with HIV as monotonically increasing over time. We defined a base rate for low/medium activity women, and constant relative rates for low/medium activity men (< 1), clients (< 1), and FSW (> 1), reflecting increased access to HIV testing via antenatal care among women versus men, and enhanced screening among FSW [24]. We modelled ART initiation similarly except: the relative rate for ART initiation among FSW was < 1, reflecting unique barriers to uptake and engagement in care [30]; and we defined an additional relative rate by CD4 count (≤ 1) to reflect historical ART eligibility criteria [31]. We modelled viral suppression using a fixed rate for all groups, corresponding to an average of 4 months on ART [32]. We modelled treatment failure / discontinuation with a single monotonically decreasing rate applied to all risk groups in the base case, reflecting improving treatment success / retention over time [33]. Individuals with treatment failure / discontinuation could re-initiate ART at a fixed rate, reflecting re-engagement in care or detection of treatment failure and initiation of alternative regimens. We modelled rapid CD4 recovery during the first 4 months of ART, followed by slower recovery while virally suppressed [34–36]. We modelled reduced HIV-attributable mortality among individuals on ART, in addition to mortality benefits of CD4 recovery.

Calibration: We calibrated the model to reflect available data from eSwatini on HIV prevalence, HIV incidence, and ART cascade of care, stratified by risk groups (Appendix A.3) [24–28]. To reflect

[1] github.com/mishra-lab/hiv-fsw-art

Table 1: Model parameters related to risk heterogeneity (* under construction *)

Parameter	Stratification	Prior			Ref. *
		Mean	(95% CI)	Distrib.	
Population size	FSW of women overall	2.8	(0.6, 6.5)	Beta	
(% of total)	Clients of men overall	30	(6.0, 70)	—	See XX
	HR FSW of FSW overall	20	—	—	Assumed
	HR clients of clients overall	20	—	—	Assumed
Duration in group	HR FSW	3.6	(1.9, 5.8)	Gamma	See XX
(mean years)	LR FSW	10	(9.0, 11)	Gamma	See XX
	All clients	10	(6.0, 15)	Gamma	
Relative infectiousness	Acute infection	5.3	(1.0, 13)	Gamma	
	Any GUD p12m	2.9	(1.0, 5.7)	Gamma	
Relative susceptibility	Receptive vaginal sex	1.45	(1.0, 2.0)	Gamma	
	Receptive anal sex	10	—	—	
	Any GUD p12m: women	5.3	(1.5, 12)	Gamma	
	Any GUD p12m: men	7.7	(2.0, 18)	Gamma	
Any GUD p12m	LR FSW	16	(7, 28)	Beta	
prevalence (%)	HR FSW	47	(19, 89)	—	
	HR clients	12	(7, 22)	—	
	Everybody else	7	—	—	
Sex acts per	Main/spousal	78	(27, 156)	Gamma	
partnership-year	Casual	30	(4.4, 82)	—	See XX
	Occasional sex work	12	—	—	Assumed
	Regular sex work	31	(18, 48)	Gamma	
Partnership anal sex	Main/spousal & casual	5.9	(0.6, 17)	Beta	
(% of acts)	Occasional & regular sex work	9.7	(0.6, 29)	Beta	
Condom use in 2020	Main/spousal	42	(31, 54)	Beta	See XX
(% of acts protected)	Casual	69	(65, 74)	Beta	See XX
	Occasional sex work	88	(78, 97)	Beta	See XX
	Regular sex work	79	(64, 90)	Beta	See XX
	Anal vs vaginal sex	77	(50, 95)	Beta	
Partnerships per year	LR FSW, occasional sex work	49	(30, 72)	Gamma	
	HR FSW, occasional sex work	98	(58, 153)	—	
	LR FSW, regular sex work	101	(73, 133)	Gamma	
	HR FSW, regular sex work	151	(107, 205)	—	
Sex work visits	LR clients	26	(11, 50)	Gamma	
per year	HR clients	89	(34, 174)	Gamma	

Notation — FSW: female sex workers; Clients: of FSW; HR: higher risk; LR: lower risk; p12m: past 12 months.

uncertainty in model inputs, we sampled 100,000 sets of parameter values from specified prior distributions (e.g. Table 1). We used Latin hypercube sampling [37] to obtain good coverage of parameter space, except parameters with relational constraints (e.g. condom use in casual partnerships must be higher than in main/spousal partnerships), which were sampled randomly due to challenges of incorporating such constraints in Latin hypercube sampling. We computed the likelihood of each parameter set by comparing model projections to calibration targets, each target having an uncertainty distribution (Appendix A.3). We then selected the top 1% (1000) of parameter sets by likelihood ("model fits") for all subsequent analyses.

2.2 Scenarios & Analysis

2.2.1 Objective 1: Influence of differences in cascade between risk groups

For Objective 1, we used calibrated model fits as the *base case* scenario, reflecting observed ART cascade scale-up in eSwatini [26–28], following WHO guidelines and reaching approximately 95-95-95 overall by 2020 [1]. We also assumed that FSW specifically achieved 95-95-95 by 2020, reflecting trends in available data [24, 25], although the true FSW cascade in 2020 may have been lower.

Next, we defined 4 *counterfactual* scenarios in which the overall population reached 80-80-80 by 2020, reflecting approximate trends in SSA cascades prior to universal ART. In these counterfactual scenarios, we reduced cascade progression among specific risk groups: FSW, clients, and/or the remaining population ("lower risk"). We reduced cascade progression by calibrating and applying a constant relative scaling factor R to group-specific rates of: diagnosis ($R_d \in [0, 1]$), treatment initiation ($R_t \in [0, 1]$), and treatment failure / discontinuation ($R_f \in [1, 25]$). When FSW and/or clients had reduced cascade, we calibrated their Rs so that they achieved approximately 60-40-80 by 2020. By contrast, we calibrated Rs for the lower risk population so that the population *overall* achieved 80-80-80 in all counterfactual scenarios, thus ensuring that a consistent proportion of the overall population experienced reduced cascade. Table 2 summarizes these scenarios, and Figure B.5 plots the modelled cascades over time. When cascade rates among FSW and/or clients were unchanged from the base case, the cascade they achieved by 2020 could be lower than 95-95-95 due risk group turnover and higher incidence. All cascades continued to increase beyond 2020 due to fixed rates of diagnosis, treatment initiation, and treatment failure / discontinuation thereafter.

Table 2: Modelling scenarios for Objective 1 defined by 2020 calibration targets

	ART cascade in 2020 [a]			Re-scaled cascade rates [b]		
Scenario	FSW	Clients	Overall	FSW	Clients	LR
Base Case	95-95-95	—	95-95-95	—	—	—
Leave Behind: FSW	60-40-80	—	80-80-80	✓	✗	✓
Leave Behind: Clients	—	60-40-80	80-80-80	✗	✓	✓
Leave Behind: FSW & Clients	60-40-80	60-40-80	80-80-80	✓	✓	✓
Leave Behind: Neither	—	—	80-80-80	✗	✗	✓

[a] Cascade: % diagnosed among HIV+; % on ART among diagnosed; % virally suppressed among on ART; [b] Rates of: diagnosis; ART initiation; treatment failure. Notation — FSW: female sex workers; Clients: of FSW; LR: lower risk. Figure B.5 plots the resulting cascades over time.

We quantified ART prevention impacts via cumulative additional infections (CAI) and additional incidence (AI) in the counterfactual scenarios versus the base case. Differences (CAI and AI) were defined relative to the base case, and computed over multiple time horizons up to 2040. For each scenario, we computed ART prevention impacts for each model fit, and reported median (95% CI) values across model fits, reflecting uncertainty.

2.2.2 Objective 2: Conditions under which cascade differences matter most

* under construction * For Objective 2, we aimed to estimate the effects of lower ART cascades among certain risk groups on relative CAI and AI, and potential effect modification by epidemic conditions. For this analysis, we explored a wider range of counterfactual scenarios by randomly sampling $R_d, R_t \sim \text{Beta}(\alpha = 1.8, \beta = 1.2)$, and $R_f \sim \text{Gamma}(\alpha = 1.33, \beta = 3)$ for each of: FSW, clients, and the remaining lower risk population (9 total values). Sampling distributions were chosen to obtain cascades in 2020 spanning approximately 75-80-95 through 95-95-95 (Figure B.9). We sampled $N_k = 10$ sets of R for each model fit using Latin hypercube sampling.

For each R sample k and model fit (10,000 total parameter sets), we computed the relative CAI and AI versus the base case, as in Objective 1, and the proportion virally unsuppressed (U) among people living with HIV by 2020, as a summary measure of ART cascade gaps. Then, we defined $D_k = U_k - U_0$ as the difference in proportion virally unsuppressed for the population *overall* in sample $k \in [1, 10]$ versus the base case $k = 0$, and likewise $d_{ki} = U_{ki} - U_{k0}$ for *risk group* i (FSW and clients) — reflecting disproportionate unsuppression.

Next, we defined the following key measures of epidemic conditions (C) related to sex work: FSW and client population sizes (% of population overall); average duration (years) selling sex (FSW) and buying sex (clients); and HIV prevalence ratios in 2010 among FSW vs other women, and among clients vs other men. For these measures, we combined higher and lower risk FSW, and likewise higher and lower risk clients. We used HIV prevalence ratios to reflect summary measures of risk heterogeneity, whereas including all modelled risk factors for HIV acquisition and transmission (Table 1) in the analysis could lead to overfitting and improper inference due to effect mediation.

Using these variables, we conceptualized a general linear model for each outcome $y = \{CAI, AI\}$:

$$y = \beta_0 + \beta_1 D + \sum_i \beta_i d_i + \sum_{ij} \beta_{ij} d_i C_j \quad (1)$$

Using this model, we calculated the partial rank correlation coefficients [38] for each term D, d_i, and $d_i C_j$. Such coefficients are defined as the residual correlation between each term and the outcome y, after adjusting for all other terms; thus, these coefficients reflect the relative contribution of each term to explaining the overall variance in outcomes *CAI* and *AI*. We used generalized estimating equations for adjustment to control for repeated use of each model fit [39].

3 Results

Early epidemic emergence was driven by regular sex work partnerships (Figures B.1 and B.3). However, casual partnerships contributed the majority of infections by 1994, including 60% (median) of new infections in 2020 in the base case. By 2020, clients of FSW had transmitted the most infections (Figure B.2a) and lower risk women had acquired the most infections (Figure B.2b). Overall HIV prevalence in 2020 was median (95% confidence interval): 25.6 (21.1, 31.9)% (Figure A.2), and overall incidence was 7 (4, 13) per 1000 person-years (Figure A.3). The prevalence ratio among FSW versus lower risk women was 2.01 (1.37, 2.59), and among clients of FSW versus lower risk men it was 1.66 (1.19, 2.27) (Figure A.4). Due to turnover and higher HIV incidence among FSW, achieving similar rates of diagnosis among FSW versus other women (Figure A.5a) required 2.46 (1.08, 4.87) times the rate of testing. Sex work contributed a growing proportion of infections over 2020–2040: from 23% to 28% (Figure B.1).

3.1 Influence of differences in cascade between risk groups

Figure 1 illustrates cumulative additional infections in each counterfactual scenario (80-80-80 overall by 2020) versus the base case (95-95-95 overall by 2020); Figure B.7 illustrates additional incidence. Leaving behind both FSW and clients resulted the most additional infections: 40.1 (23.3, 69.4)% more than the base case by 2040. By contrast, leaving behind neither FSW nor clients resulted in the fewest additional infections: 19.8 (9.6, 39.7)% more than the base case by 2040 — a 49.9 (22.3, 71.7)% reduction. Leaving behind either FSW or clients resulted in a similar number of additional infections: 28.3 (15.3, 51.4)% and 31.5 (17.8, 52.8)%, respectively. However, who acquired these additional infections differed (Figure B.8c), with more additional infections among clients when FSW were left behind, versus among lower risk risk women when clients were left behind. The majority of additional infections were transmitted via casual partnerships in all scenarios (Figure B.8a).

3.2 Conditions under which cascade differences matter most

* under construction * Figure 2 illustrates the standardized effects of disproportionate viral unsuppression among FSW and clients versus the population overall (d) on cumulative additional infections versus the base case by 2040, controlling for population-overall unsuppression (effect not shown). Trends were consistent across multiple time horizons (Figure B.11) and for additional incidence in 2030 (Figure B.10). However, when stratifying cumulative additional infections by subpopulation (FSW, clients, and everybody else), some effect trends differed (Figure B.12). Consistent with Objective 1 results, disproportionate viral unsuppression among FSW and clients versus the population overall was associated with more additional infections.

Disproportionate unsuppression among FSW was associated with more infections in the context of: larger FSW and client population sizes; and larger HIV prevalence ratio among FSW versus lower risk women; and larger HIV prevalence ratio among clients versus lower risk men. Disproportionate unsuppression among clients was associated with more infections in the context of: larger client population size; larger HIV prevalence ratio among among clients versus lower risk men; smaller HIV prevalence ratio among FSW versus lower risk women; and shorter duration buying sex.

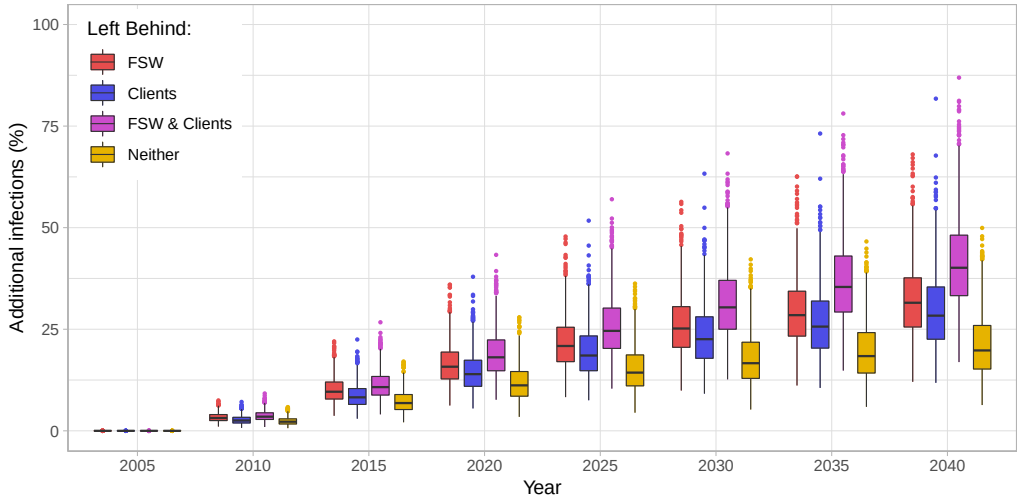

Figure 1: Cumulative additional HIV infections (%) in counterfactual scenarios (80-80-80 overall by 2020) vs the base case scenario (95-95-95 by 2020). Scenarios explore reduced cascades (60-40-80 by 2020) among FSW, clients of FSW, both, or neither as part of reduced cascade overall.

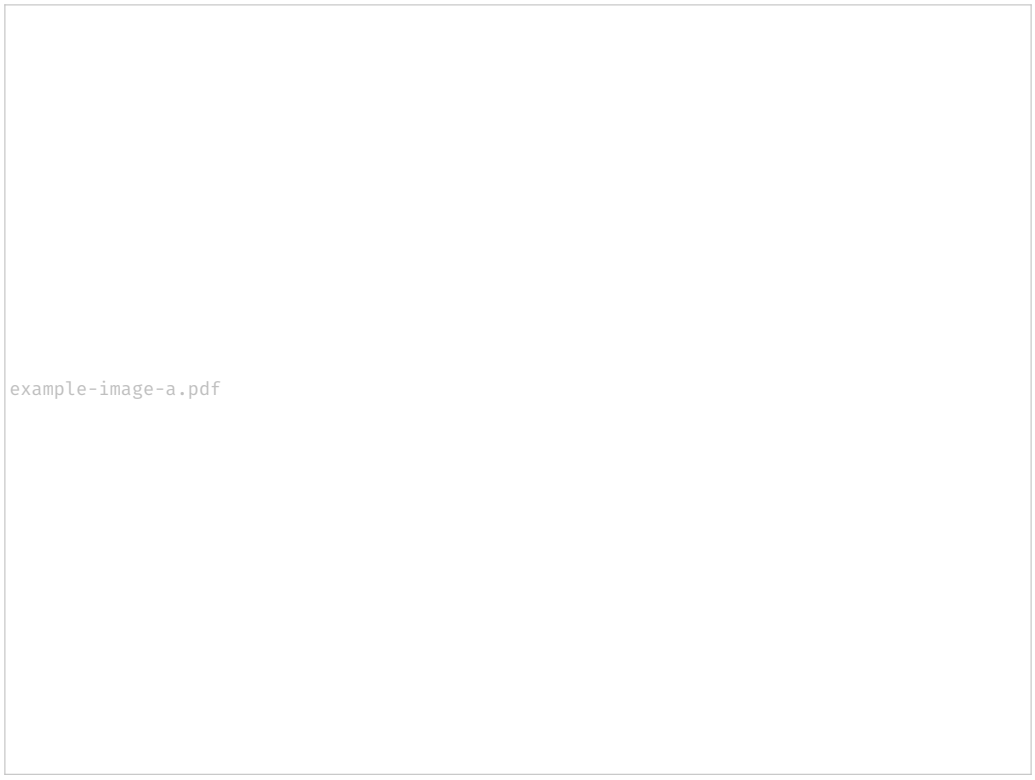

Figure 2: Partial rank correlation coefficients reduced viral suppression (d) among FSW and clients on cumulative additional infections by 2040, plus effect modification by epidemic conditions, controlling for population-overall viral suppression

Points and lines show the mean and 95% confidence interval for β terms from Eq. (1). d X: absolute difference in viral suppression among group X versus the population overall; FSW: female sex workers; Clients: of FSW; LR: lower risk; Duration: average time spent in the risk group; % Pop: relative population size; HIV PR: HIV prevalence ratio. All model variables were standardized like $\hat{x}_k = (x_k - \mu_{x_k})/\sigma_{x_k}$ to reflect the relative influence of variables.

4 Discussion

We sought to explore how intersections of risk heterogeneity and differential ART coverage may influence model-estimated prevention impacts of ART. We showed that ART scale-up that "leaves behind" higher risk groups, such as female sex workers (FSW) and their clients, can result in substantially more HIV infections, even for the same population-overall coverage. We also found that the transmission impact of leaving behind higher risk groups generally increased with: risk group size, prevalence ratio, and turnover.

Although our analysis only considered eSwatini, our findings are likely generalizeable to other epidemic contexts. In fact, HIV prevalence ratios between key populations and the population overall are relatively low in eSwatini versus elsewhere [40, 41]; thus, the transmission impact of cascade gaps among key populations in other contexts would likely be even greater than we found for eSwatini. Moreover, as HIV incidence declines in many settings, epidemics may become re-concentrated among key populations [42, 43], further magnifying the transmission impact of cascade disparities.

To our knowledge, our study is the first to explore the transmission impact of heterogeneity in ART coverage across risk groups, within consistent population-overall coverage. In a previous review of mathematical modelling of ART scale-up in Sub-Saharan Africa, we found that few studies have considered any cascade differences by risk group, but that such differences likely mediate ART prevention impacts [7]. Cascade gaps have been observed among men versus women [10, 44], younger versus older populations [10, 45], key populations versus the population overall [9], and within key populations themselves [46, 47]. Moreover, unmeasured cascades — such as among populations who have not been reached by programs and interventions — are likely lowest [9, 48]. Consistent integration of these data going forward could improve the quality of model-based evidence for HIV resource prioritization.

Global ART scale-up undoubtedly has many benefits, including for individual-level health outcomes [36, 49], prevention in serodiscordant relationships [50], and contributing to population-level incidence declines [51]. However, efforts to maximize cascade coverage should not overlook populations that may be harder to reach, where barriers to engagement in HIV care often intersect with drivers of HIV risk [11–14]. Such populations can be reached effectively through tailored services to meet their unique needs [52], services which can be designed and refined with ongoing community engagement [53–55]. As we have shown, an equity-focused approach to ART scale-up can maximize prevention impacts, and accelerate the end of the HIV epidemic.

Our study has three major strengths. First, drawing on our conceptual framework for risk heterogeneity [7, Table 1] and multiple sources of context-specific data [24–27, 56], we captured several dimensions of risk heterogeneity, including: heterosexual anal sex, four types of sexual partnerships, sub-stratification of FSW and clients into higher and lower risk, and risk group turnover. Second, whereas most modelling studies of ART scale-up project hypothetical future scenarios which may not be achievable, our base case scenario reflects observed scale-up in eSwatini. Finally, our analytic approach to objective 2, in which epidemic conditions are conceptualized as potential effect modifiers, represents a unique methodological contribution to the HIV modelling literature.

Our study has four main limitations. First, we only considered heterosexual HIV transmission in eSwatini, and mainly explored risk heterogeneity related to sex work. However, our findings would likely generalize to other transmission networks and determinants of risk heterogeneity, including risk groups not classically recognized as key populations, such as mobile populations and young women [57, 58]. Second, we did not consider transmitted drug resistance. Drug resistance is more

likely to emerge in the context of barriers to viral suppression [59]; thus, cascade gaps among those at higher risk would likely accelerate emergence of transmitted drug resistance, and amplify impacts of such gaps. Third, even among the top 1% of model fits, substantial uncertainty remained in the values of inferred parameters, yielding wide confidence intervals in the outputs of interest (additional infections and incidence). In the absence of additional data, such intervals reflect our true uncertainty in the magnitude of these outputs, but not the trends across scenarios. Finally, our statistical analysis

In summary, …* under construction *

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APPENDIX

Title: Intersections of risk and intervention heterogeneity: a modelling study on the prevention impacts of antiretroviral therapy in eSwatini

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[*] *in memory of*

Date: September 29, 2022

A Model

A.1 Structure & Notation

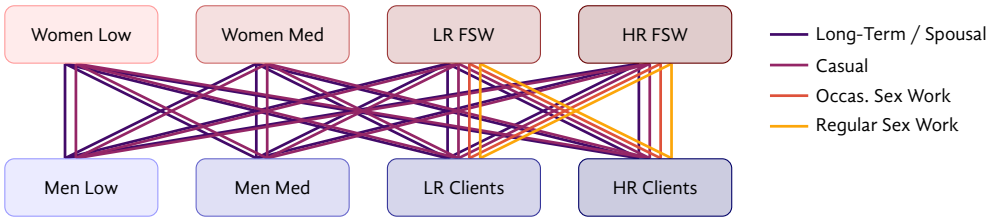
Table A.1 summarizes the modelled population stratifications, including 2 sex × 4 activity × (5 HIV × 5 cascade + 1 susceptible) = 208 total possible states. Figure A.1 summarizes the model structure and state transitions with respect to (a) risk groups and partnership types; (b) HIV status; and (c) ART cascade.

Table A.1: Modelled stratifications: population (top) and partnership-level dimensions (bottom)

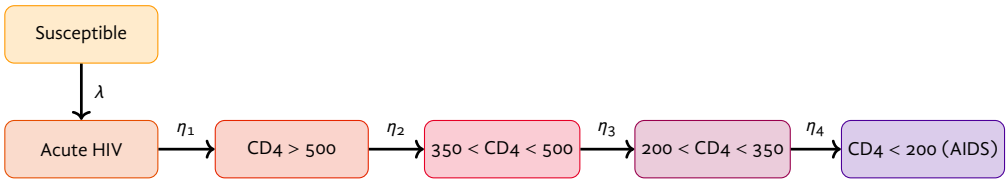
Stratification	Index		Strata
Sex	s	1	Heterosexual Women
		2	Heterosexual Men
Activity group	i	1	Lower Activity
		2	Medium Activity
		3	Lower Risk Sex Work
		4	Higher Risk Sex Work
HIV status	h	1	Susceptible
		2	Acute HIV
		3	CD4 > 500
		4	350 < CD4 < 500
		5	200 < CD4 < 350
		6	CD4 < 200 (AIDS)
ART cascade	c	1	Undiagnosed
		2	Diagnosed & Linked
		3	Diagnosed & Unlinked
		4	On ART
		5	Virally Suppressed
Partnership types	p	1	Main / Spousal
		2	Casual
		3	Occasional Sex Work
		4	Regular Sex Work
Sex act types	a	1	Vaginal
		2	Anal

A.2 Parameterization

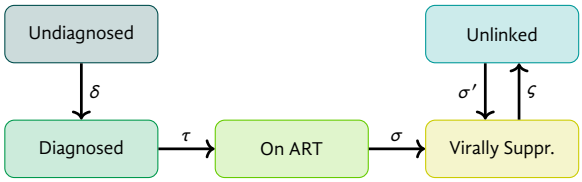
* under construction *



(a) Risk groups and partnership types



(b) HIV states



(c) ART cascade states

Figure A.1: Model structure and transitions

Notation — Low/LR: lower risk; Med: medium risk; HR: higher risk; FSW: female sex workers; Clients: of FSW; CD4: CD4+ T-cell count per mm^3; Not shown: turnover amongst risk groups in (a).

A.3 Calibration

Figures A.2 and A.3 illustrate HIV prevalence and incidence in the base case scenario, and the associated calibration targets. Figure A.4 similarly shows prevalence ratios between selected risk groups.

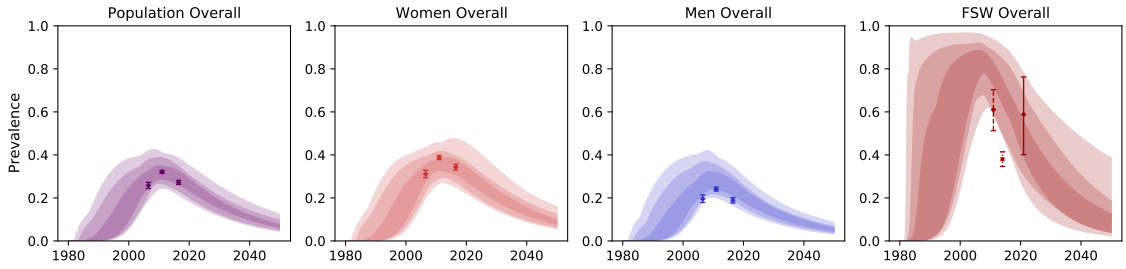


Figure A.2: HIV prevalence in the base case scenario and associated calibration targets

Three ribbons illustrate range of 100%, top 20%, and top 4% of model fits by likelihood for all base case calibration targets; points and error bars illustrate the mean and 95% CI for each calibration target.

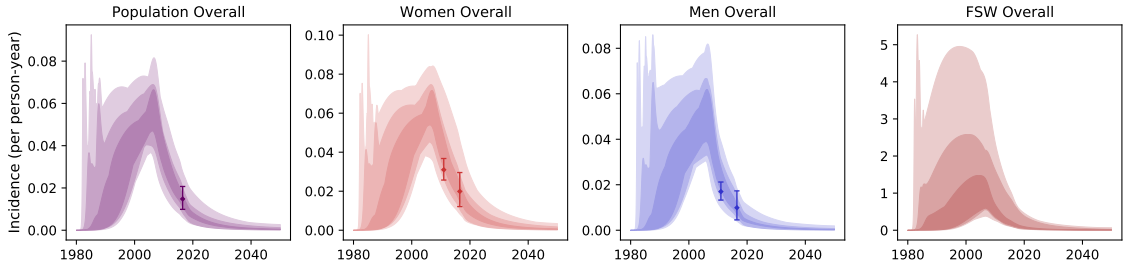


Figure A.3: HIV incidence in the base case scenario and associated calibration targets

Three ribbons illustrate range of 100%, top 20%, and top 4% of model fits by likelihood for all base case calibration targets; points and error bars illustrate the mean and 95% CI for each calibration target.

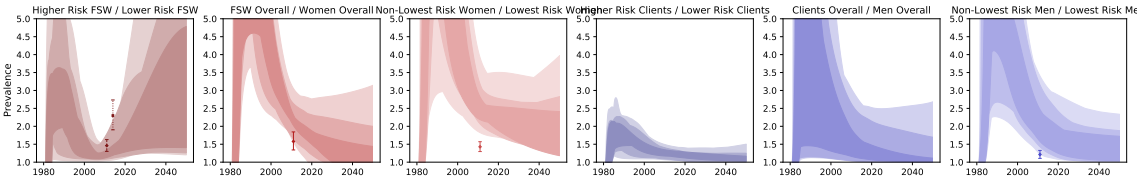
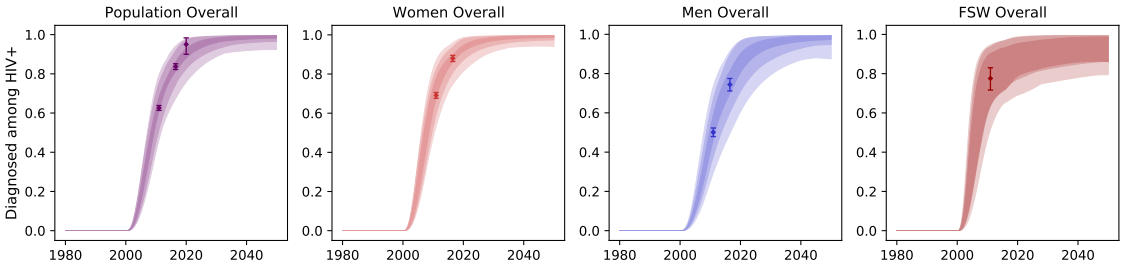
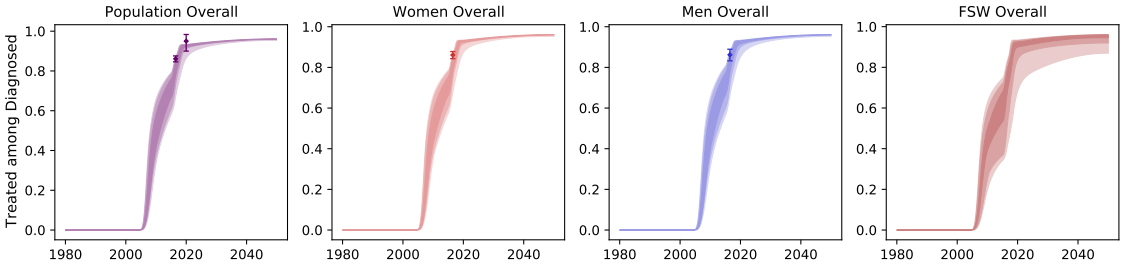


Figure A.4: HIV prevalence ratios in the base case scenario and associated calibration targets

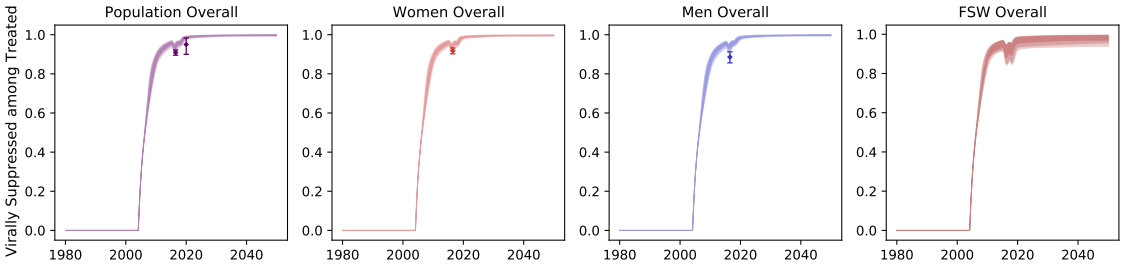
Three ribbons illustrate range of 100%, top 20%, and top 4% of model fits by likelihood for all base case calibration targets; points and error bars illustrate the mean and 95% CI for each calibration target.



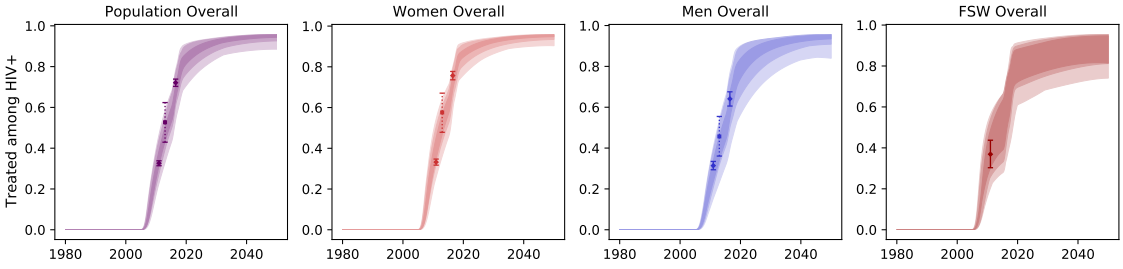
(a) % Diagnosed among HIV+



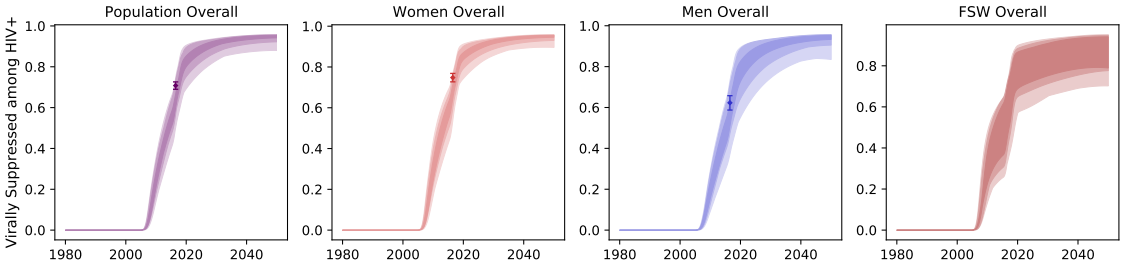
(b) % On ART among diagnosed



(c) % Virally suppressed among on ART



(d) % On ART among HIV+



(e) % Virally suppressed HIV+

Figure A.5: ART cascade in the base case scenario and associated calibration targets

Three ribbons illustrate range of 100%, top 20%, and top 4% of model fits by likelihood for all base case calibration targets; points and error bars illustrate the mean and 95% CI for each calibration target.

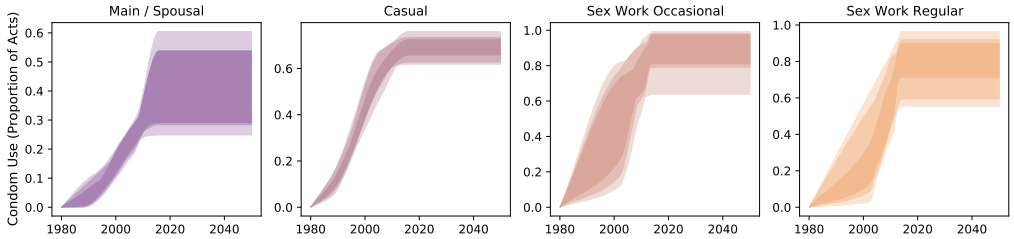


Figure A.6: Condom use by partnership type in the base case scenario and associated calibration targets

Three ribbons illustrate range of 100%, top 20%, and top 4% of model fits by likelihood for all base case calibration targets

B Supplemental Results

B.1 Base Case

B.1.1 Distribution of Infections

The following figures explore the numbers and proportions of infections transmitted between risk groups, stratified by partnership type throughout the epidemic. For each stratification (from, to, partnership type, and year), we use the median numbers of infections across all model fits. Figure B.1 illustrates infections transmitted via the modelled partnership types over time in the base case, while Figure B.2 illustrates the risk groups transmitting (a) and acquiring (b) infections. Figure B.3 illustrates the distribution of infections stratified by all three factors every 10 years using an alluvial diagram. Figure B.4 illustrates the ratio of infections transmitted from vs acquired among individuals in each risk group, which could be interpreted as a measure related to the group-specific reproductive number.

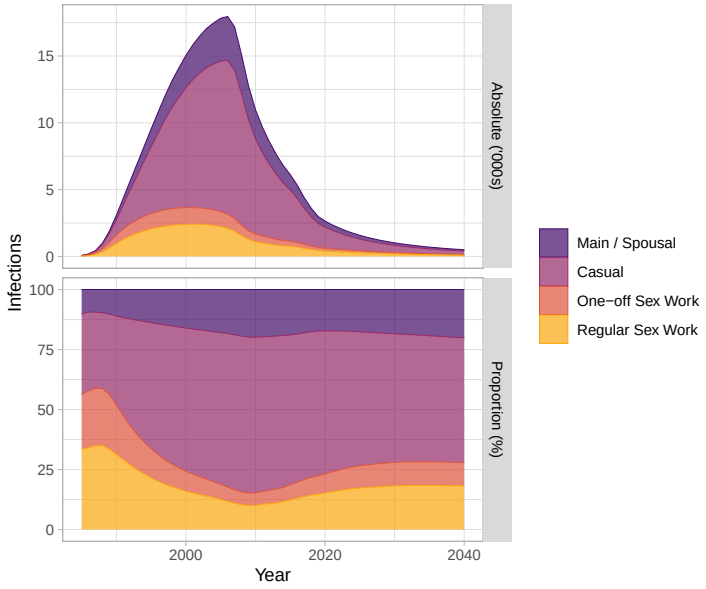
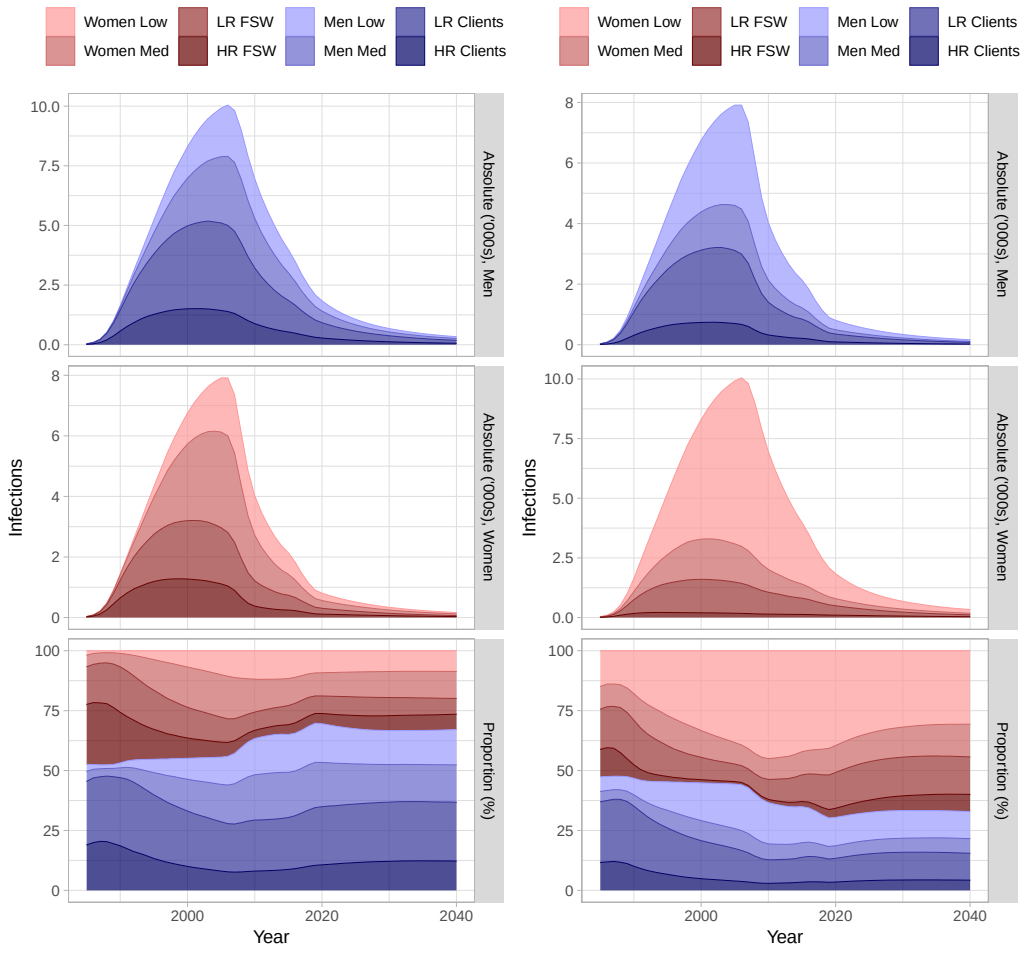


Figure B.1: Absolute numbers and proportions of infections transmitted via different modelled partnership types in the base case scenario

Median numbers of infections across all model fits are shown.



(a) Transmitted from

(b) Acquired among

Figure B.2: Absolute numbers and proportions of infections (a) transmitted from and (b) acquired among modelled risk groups in the base case scenario

Notation — Low/LR: lower risk; Med: medium risk; HR: higher risk; FSW: female sex workers; Clients: of FSW. Median numbers of infections across all model fits are shown.

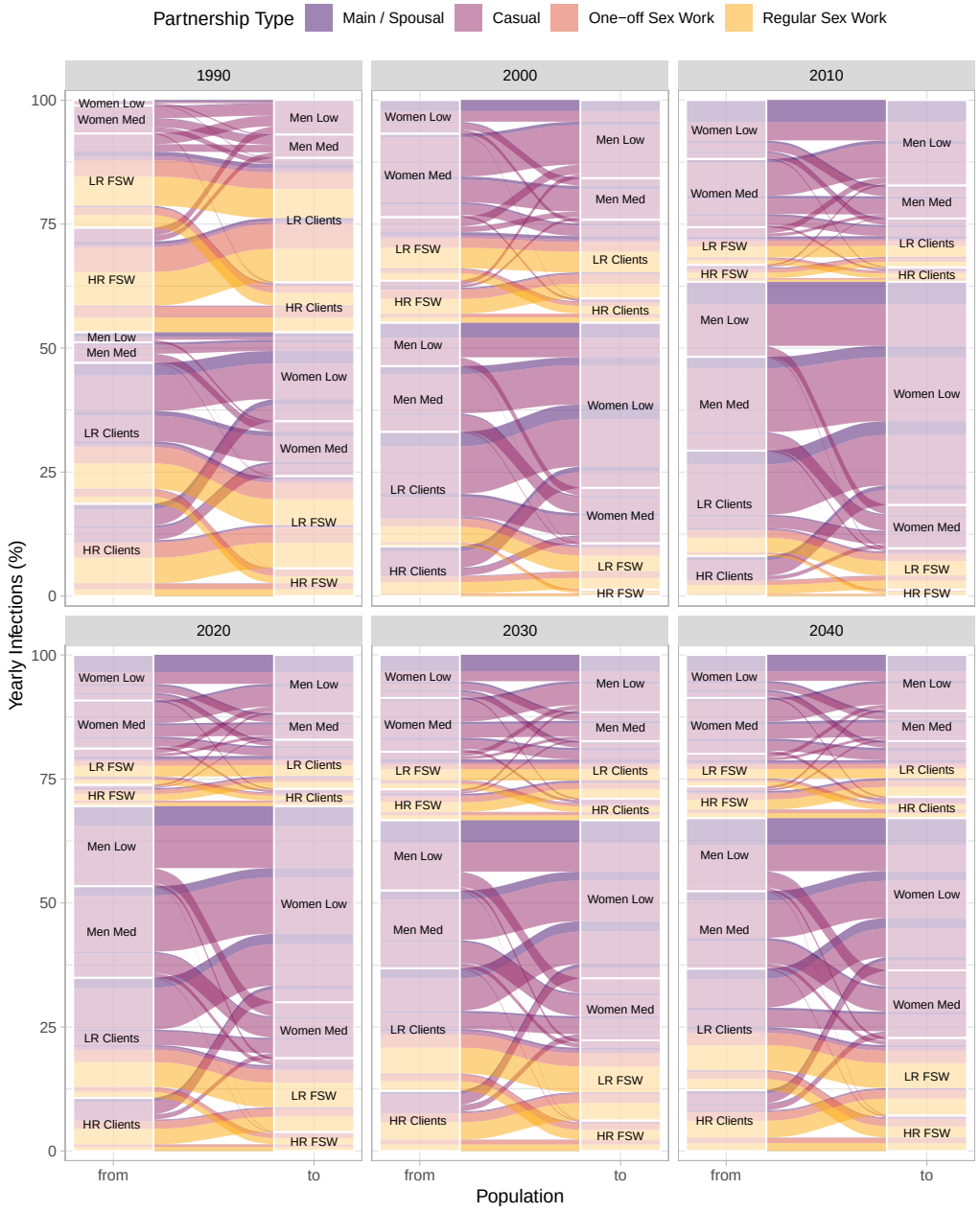


Figure B.3: Alluvial diagram showing proportions of all yearly infections (flows) transmitted from (left) to (right) modelled risk groups, stratified by partnership type (color) and year (facets), in the base case scenario

Median numbers of infections across all model fits are shown. An animated version of this figure is available online at github.com/mishra-lab/hiv-fsw-art

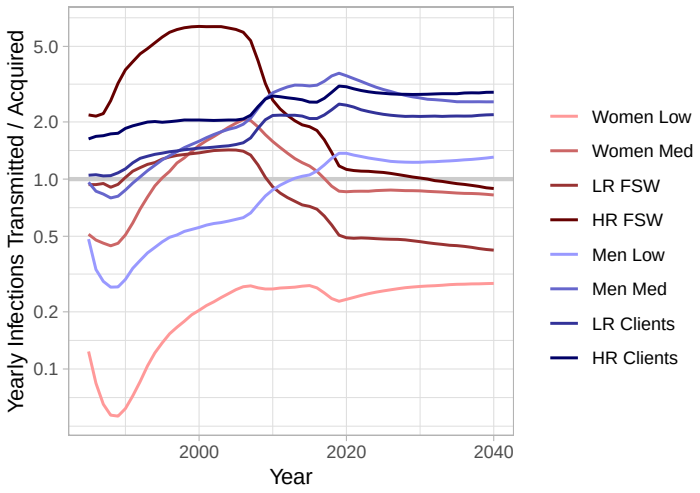


Figure B.4: Ratio of yearly infections transmitted from vs acquired among modelled risk groups in the base case scenario

Median numbers of infections across all model fits are shown.

B.2 Objective 1

* under construction *

B.2.1 Scenario Cascades

Figure B.5 illustrates …

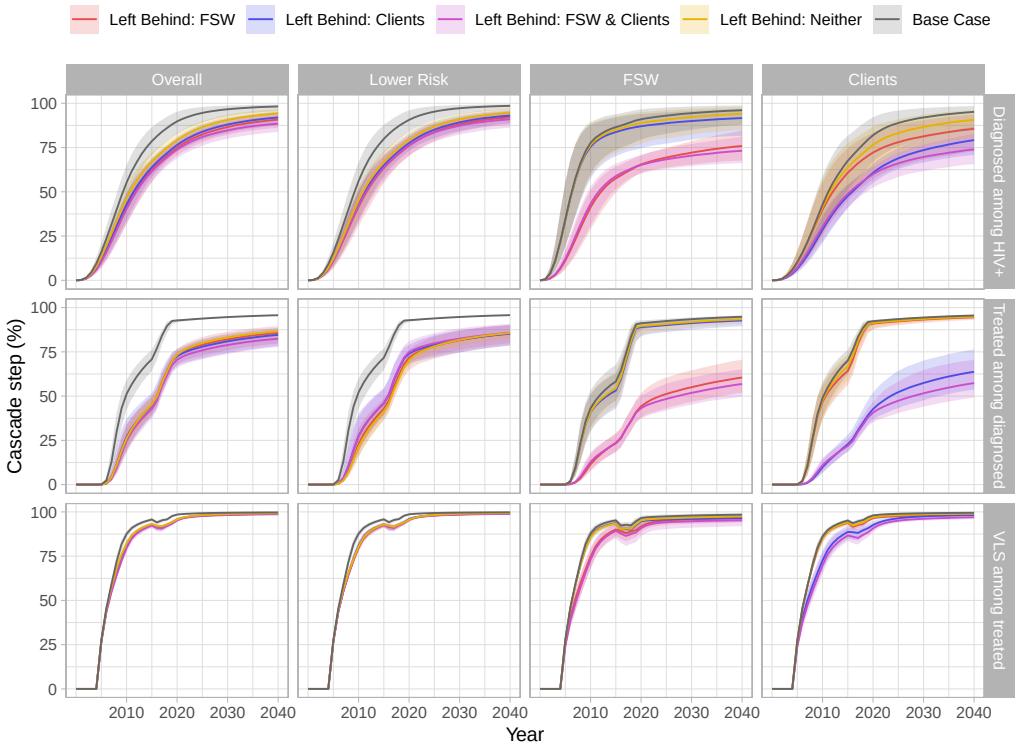


Figure B.5: Cascade attainment over time in counterfactual scenarios (80-80-80 overall by 2020) vs the base case scenario (95-95-95 by 2020). Scenarios explore reduced cascades (60-40-80 by 2020) among FSW, clients of FSW, both, or neither as part of reduced cascade overall.

Lines and ribbons illustrate the median and 90% CI, respectively, for each output.

B.2.2 Additional Incidence

Figure B.6 illustrates …

Figure B.7 illustrates …

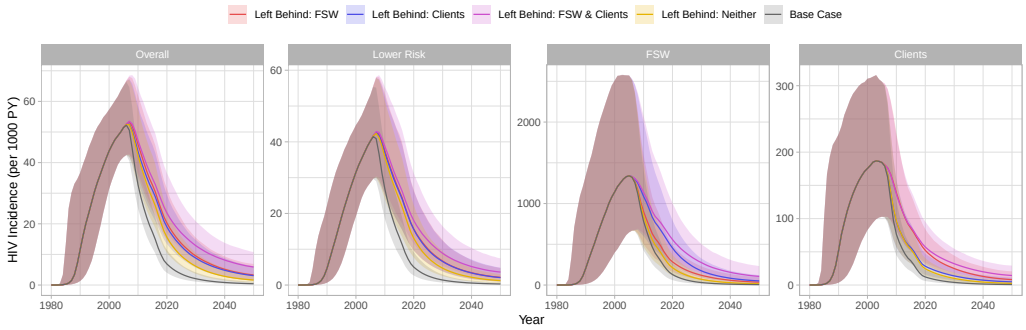


Figure B.6: HIV Incidence in the base case and counterfactual scenarios

Lines and ribbons illustrate the median and 90% CI, respectively, for each output.

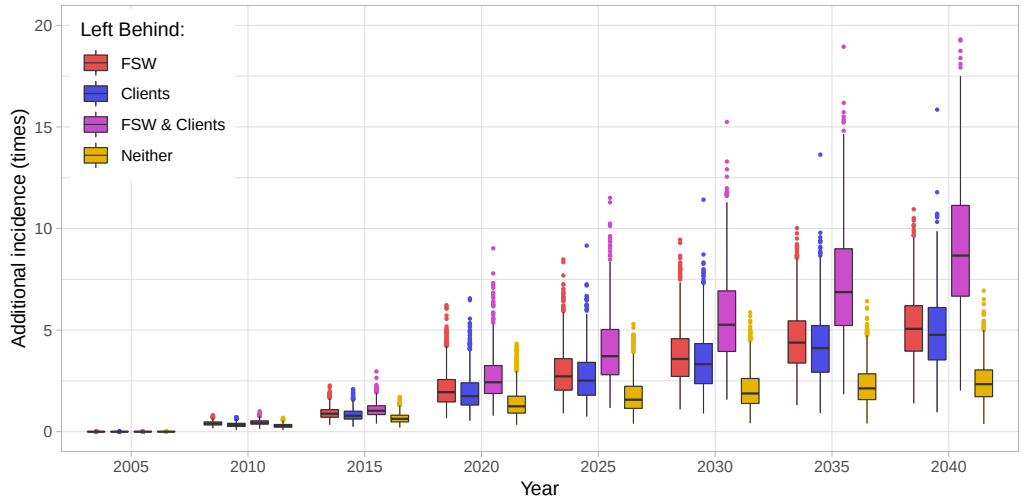
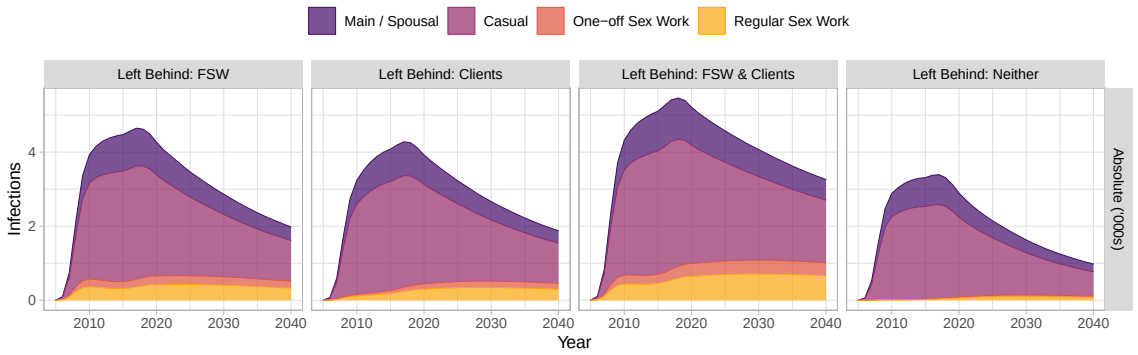


Figure B.7: Additional HIV incidence (times) in counterfactual scenarios (80-80-80 overall by 2020) vs the base case scenario (95-95-95 by 2020). Scenarios explore reduced cascades (60-40-80 by 2020) among FSW, clients of FSW, both, or neither as part of reduced cascade overall.

B.2.3 Distribution of Infections

As in § B.1.1, Figure B.8 illustrates …



(a) Partnership type

(b) Transmitted from

(c) Acquired among

Figure B.8: Numbers of additional infections in each counterfactual scenario vs the base case, stratified by: (a) partnership type, (b) transmitting group, and (c) acquiring group

Notation — Low/LR: lower risk; Med: medium risk; HR: higher risk; FSW: female sex workers; Clients: of FSW. Median numbers of infections across all model fits are shown.

B.3 Objective 2

Figure B.9 illustrates the distribution of HIV treatment cascade attainment by 2020 in randomly sampled scenarios for Objective 2, stratified by sub-population. Median (95% CI) viral suppression (*VS*) among HIV+ were: 43 (15, 72)% among overall, 44 (13, 76)% among lower risk, 45 (18, 72)% among FSW, and 33 (9, 65)% among clients.

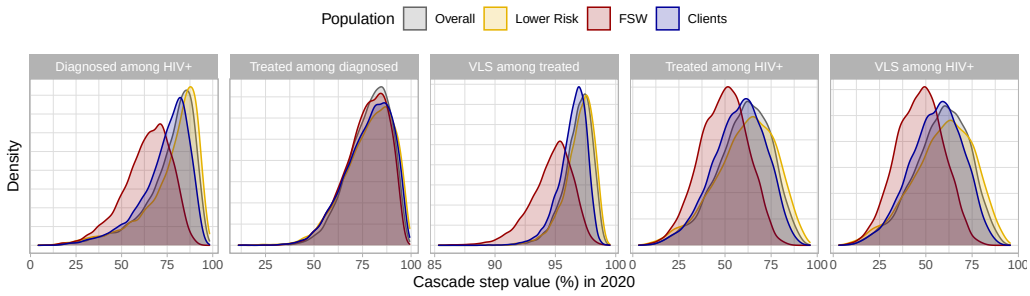


Figure B.9: Distribution of HIV treatment cascade attainment by 2020 in randomly sampled scenarios, stratified by sub-population

Figure B.10 illustrates effects on additional incidence by 2040, rather than cumulative additional infections. Figure B.11 expands on Figure 2 by illustrating effects over multiple time horizons (2020, 2030, 2040). Figure B.12 expands on Figure 2 by illustrating effects for cumulative additional infections among different risk groups.

Figure B.10: Standardized effects of reduced viral suppression (d) among FSW and clients on *additional incidence* by 2040, plus effect modification by epidemic conditions, controlling for population-overall viral suppression

Points and lines show the mean and 95% confidence interval for β terms from Eq. (1). d X: absolute difference in viral suppression among group X versus the population overall; FSW: female sex workers; Clients: of FSW; LR: lower risk; Duration: average time spent in the risk group; % Pop: relative population size; HIV PR: HIV prevalence ratio. All model variables were standardized like $\hat{x}_k = (x_k - \mu_{x_k})/\sigma_{x_k}$ to reflect the relative influence of variables.

Figure B.11: Standardized effects of reduced viral suppression (d) among FSW and clients on cumulative additional infections *by 2020, 2030, and 2040*, plus effect modification by epidemic conditions, controlling for population-overall viral suppression

Points and lines show the mean and 95% confidence interval for β terms from Eq. (1). d X: absolute difference in viral suppression among group X versus the population overall; FSW: female sex workers; Clients: of FSW; LR: lower risk; Duration: average time spent in the risk group; % Pop: relative population size; HIV PR: HIV prevalence ratio. All model variables were standardized like $\hat{x}_k = (x_k - \mu_{x_k})/\sigma_{x_k}$ to reflect the relative influence of variables.

Figure B.12: Standardized effects of reduced viral suppression (d) among FSW and clients on cumulative additional infections *among different risk groups*, plus effect modification by epidemic conditions, controlling for population-overall viral suppression

Points and lines show the mean and 95% confidence interval for β terms from Eq. (1). d X: absolute difference in viral suppression among group X versus the population overall; FSW: female sex workers; Clients: of FSW; LR: lower risk; Duration: average time spent in the risk group; % Pop: relative population size; HIV PR: HIV prevalence ratio. All model variables were standardized like $\hat{x}_k = (x_k - \mu_{x_k})/\sigma_{x_k}$ to reflect the relative influence of variables.