

Chapter 3

Model Structure, Parameterization, & Calibration

Drawing on the insights from Chapter ??, this chapter details the development of a compartmental model of heterosexual HIV transmission in Eswatini. The model aims to capture key determinants of heterosexual transmission dynamics, including sex work, numbers of sexual partners, levels of condom use, anal sex, and ART scale-up.

The model was implemented in Python v3.8.10 with Numpy v1.22.2, and solved numerically using 4th order Runge-Kutta [1] using a timestep of 0.05 years. Post-hoc analysis was conducted in R v3.6.3. All code and selected results are available on GitHub.¹

3.1 Model Structure

The model aims to capture heterosexual HIV transmission among the Swati population aged 15–49. The model stratifies the modelled population along four dimensions: two sexes (s), four activity groups (i), six HIV states (h), and five cascade states (c), summarized in Table 3.1 and Figure 3.1. In total, $2 \times 4 \times (1 + 5 \times 5) = 208$ states are modelled. Two additional “dimensions” help organize: four partnership types (p), and two types of sex acts (a).

Sexual activity groups were defined to reflect persistent differences in HIV incidence and prevalence [2, 3, 4, 5] — reflecting acquisition and/or onward transmission risk — as well as common stratifications in the available data, and epidemiologically relevant sub-populations. The lowest sexual activity group ($i = 1$) comprises individuals who had 0–1 sexual partners in the past 12 months (p12m), but did not engage in sex work. The medium activity group ($i = 2$) similarly comprises individuals who had 2+ sexual partners in p12m but did not engage in formal sex work. The highest two activity groups among women ($i = 3, 4$) comprise lower and higher risk FSW (see § 3.2.1 for more details), and the highest two activity groups among men ($i = 3, 4$) likewise comprise lower and higher risk clients of FSW.

¹ github.com/mishra-lab/hiv-fsw-art

Table 3.1: Overview of model dimensions and stratifications

Dimension	Index	Strata
Sex	(s)	1 Heterosexual Women
		2 Heterosexual Men
Activity group	(i)	1 Lowest 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
		3 On ART
		4 Virally Suppressed
		5 Virally Un-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

See footnote 4 regarding indices in the code.

Four types of sexual partnerships are modelled, with different levels of condom use and expected durations: long-term/spousal partnerships ($p = 1$, lowest condom use, 14–19 years); short-term partnerships ($p = 2$, medium condom use, 3–18 months); one-off new/occasional sex work partnerships ($p = 3$, highest condom use, 1 sex act); and regular sex work partnerships ($p = 4$, medium condom use, 2–24 months). Figure 3.1a illustrates the modelled activity groups and possible partnership types between them.

HIV infection is stratified into acute-HIV and stages defined by CD4 count (Figure 3.1b) to reflect changes in mortality [6], historical ART eligibility [7, 8, 9, 10], and, with CD4 as a proxy for viral load, infectiousness [11]. The modelled ART cascade (Figure 3.1c) includes the major steps associated with the “90-90-90” targets, plus a generic “virally un-suppressed” state reflecting any combination of treatment failure, discontinuation, or loss to follow-up after achieving viral suppression. Loss to follow-up prior to viral suppression is not explicitly modelled, but subsumed into the rates of ART initiation and viral suppression.

3.1.1 Initialization & Solving

The first cases of HIV and AIDS in Eswatini were diagnosed in 1986 and 1987, respectively [12], although HIV may have been present several years earlier [13]. As such, I initialize the model in 1980 with no

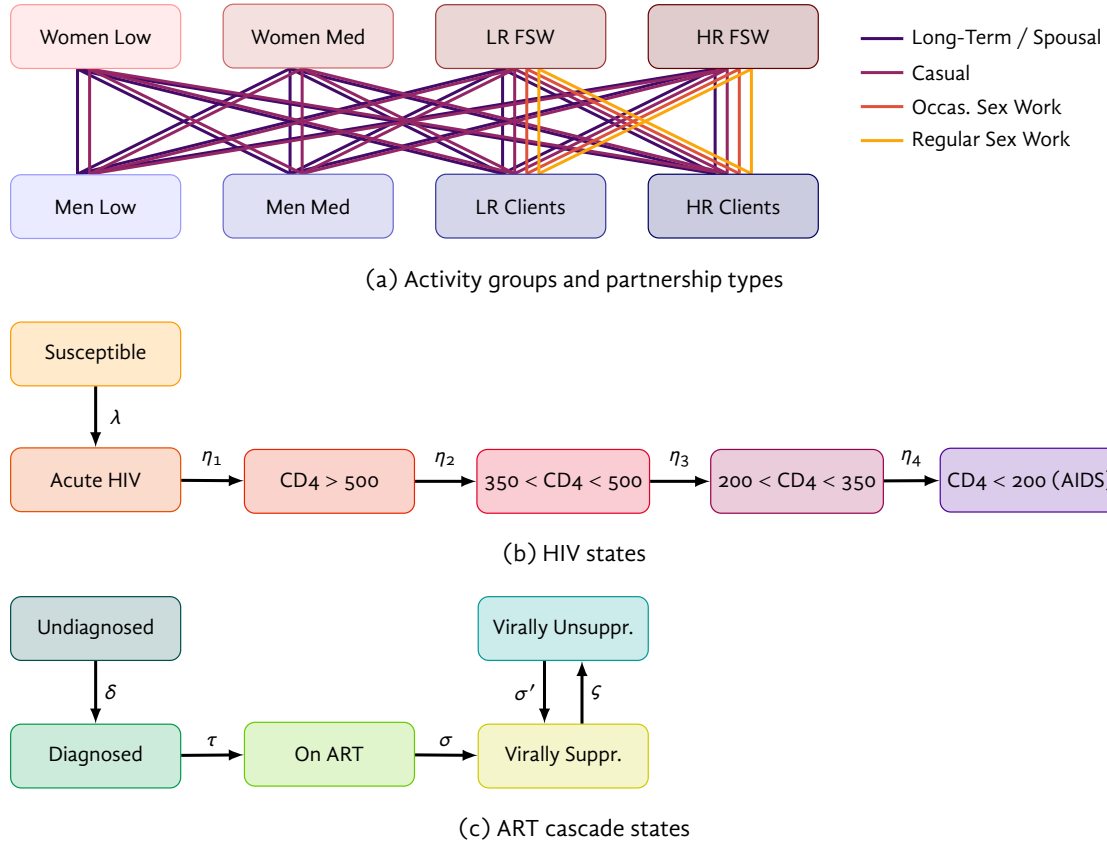


Figure 3.1: Model structure and transitions

Low: lowest activity; Med: medium activity; LR/HR: lower/higher risk; FSW: female sex workers; Clients: of FSW; CD4: CD4+ T-cell count per mm³; Not shown: turnover amongst activity groups in (a).

HIV, and simulate introduction of HIV at a random year between 1980 and 1985 (uniform prior). HIV introduction is modelled as exogenous infection of 0.01% (~ 24) individuals in the model,² distributed across activity groups in proportion to their size, comprising: 5% acute HIV ($h = 2$), 65% with $CD4 > 500$ ($h = 3$) and 30% with $350 < CD4 < 500$ ($h = 4$), all undiagnosed ($c = 1$).³ The population size of EmaSwati aged 15–49 in 1980 was defined as 243,000 from [14].

3.2 Parameterization

As described in § ??, model parameterization involves specification of model parameter values, such as proportions, probabilities, rates, and ratios, including stratified values to reflect heterogeneity, and sampling distributions to reflect uncertainty. Proportions and probabilities were generally modelled using a beta approximation of the binomial distribution (BAB, see § A.1.2), while rates and ratios were generally modelled using a gamma, skewnormal, or inverse gaussian distribution.

² No further import/export of HIV to/from Eswatini is considered thereafter in the model. HIV transmission between Eswatini and neighbouring countries, including South Africa and Mozambique, has likely continued throughout the epidemic due to labour migration and other factors [13]. However, I assume that such transmissions have low overall influence on epidemic dynamics.

³ In compartmental models, the numbers of individuals in each state (compartment) need not be whole numbers.

Notation. If X is a parameter stratified by dimensions a, b, c , then $X_{ab_1c_{23}}$ denotes the values of X for a particular but *unspecified* stratum of a , the *specific* stratum $b = 1$, and the *aggregated* strata $c = 2, 3$ (the aggregating operation is context-dependent, e.g., sum for probabilities). Additionally, the indices $sihc$ from Table 3.1 denote “self” strata, whereas $s'i'h'c'$ denote “other” strata — i.e., individuals’ partners.⁴ Finally, I re-use several dummy variables throughout the chapter: p for proportions, λ for rates, T for time periods, and f for constants.

3.2.1 Risk Heterogeneity Among FSW

HIV transmission models which include FSW rarely sub-stratify this population, such as to reflect differential HIV risk or distinct typologies of sex work [15, 16]; yet such heterogeneities likely influence transmission dynamics. Among the studies identified in Chapter ??, only three sub-stratified FSW by risk-related factors: Cremin et al. [17] defined three levels of risk via regression analysis, Low et al. [18] distinguished between occasional and full-time FSW, while Shannon et al. [19] sub-stratified FSW by work environment, violence exposure, and context-specific structural factors. Seven other studies, reflecting two unique models [20, 21], employed age stratification of all activity groups, including FSW; these models had several risk-related parameters which varied by age.

The model structure here (Figure 3.1a) was designed to capture *within*-FSW risk heterogeneity. The objective of the following analysis was therefore to parameterize lower versus higher risk FSW. I sought to define these groups based on biobehavioural and/or contextual factors which are demonstrably associated with HIV risk, and which can be mechanistically incorporated into a transmission model — i.e., through the force of infection equation. Later, the parameterization of these groups was validated through model fitting to relative differences in HIV prevalence § 3.3.2.1.

Many cross-sectional studies of HIV among FSW quantify the association of risk factors with HIV serostatus [22, 23, 16, 24]. However, serostatus reflects cumulative risk exposure, whereas sexual risk behaviour is dynamic [25, 26], as is use of prevention resources [27]. For example, while HIV prevalence often increases with age, HIV incidence among women can peak shortly after sexual debut [28]. Thus, risk factors associated with HIV serostatus are not necessarily mechanistically related to HIV acquisition. Indeed, FSW may reduce risk behaviours in response to seroconversion [29]. Cohort studies that measure incidence can help identify risk factors for HIV acquisition [30, 31], but large sample sizes are often required to accurately estimate overall incidence rate, let alone risk factors [32].

3.2.1.1 FSW Survey Data

Three surveys, in 2011 [33] ($N = 325$), 2014 [34] ($N = 781$), and 2021 [35] ($N = 676$) provide HIV and biobehavioural data on FSW in Eswatini. The 2011 survey employed respondent driven sampling (RDS, details in [36]), as did the 2021 survey. The 2014 survey employed venue-based snowball sampling, based on the Priorities for Local AIDS Control Efforts (PLACE) methodology, which aims to identify areas of higher incidence [37]. I analyzed the individual-level data from 2011 and 2014 (data from 2021 not yet

⁴ In the code: R uses one-based indexing, which match the notation here directly, while Python uses zero-based indexing, which therefore appear as $i \rightarrow i - 1$ in the code. Also, the model code reorders states in the ART Cascade dimension for computational efficiency, with $c = 1$: Undiagnosed; 2: Diagnosed; 3: Virally Un-suppressed; 4: On ART; 5: Virally Suppressed.

available) to explore the potential association of biobehavioural factors with HIV risk, so that such factors could then be used to distinguish between lower risk versus higher risk FSW.

3.2.1.2 HIV Status

Only the 2011 and 2021 studies included serologic testing for HIV. Among those tested in 2011 ($N = 317$, 98%), 70% were HIV+, yielding RDS-adjusted prevalence estimate of 61% (CI: 51–71%) [33]. Among serologically HIV–, 11% self-reported HIV+ status (false positive), and among serologically HIV+, 26% self-reported HIV– status (false negative or undiagnosed). Overall, self-reported HIV status underestimated HIV prevalence in 2011 by a factor of approximately 0.78 (55 vs 70%). Unadjusted HIV prevalence in 2021 was 58.8%, with 88% (363/411) reporting previous awareness of HIV+ status.

In 2014, self-reported HIV prevalence was 38% among respondents who reported (85%). This 38% is surprisingly low considering that the PLACE methodology explicitly aimed to sample venues with higher HIV incidence [37], and 2014 versus 2011 respondents were older (median 27 vs. 25 years), had been selling sex longer (median 5 vs. 4 years), and tested more frequently (87 vs. 75% tested at least once in the past year, 82 vs. 63% among self-reported HIV–). Perhaps the differences are attributable to the sampling methodology. Among respondents who self-reported HIV+ status, the 2014 survey also asked for age of HIV diagnosis (6% missing). Age of HIV diagnosis supports crude time-to-event analysis (next section), which can account for confounding by age and censoring, as compared to logistic regression on HIV status, keeping in mind the limitations of self-reported HIV status.

3.2.1.3 Risk Factors

Next, I explored the potential association of risk factors with HIV via the following three models:⁵

1. Logistic regression on serologic HIV status (2011 data)
2. Logistic regression on self-reported HIV status (2014 data)
3. Cox proportional hazards for interval-censored time to HIV infection, with interval from self-reported sex work debut to either self-reported time of HIV diagnosis or survey date (2014 data); Figure 3.2 illustrates the four potential censoring cases in this framework.

An important limitation to all models is that risk factors reported by FSW at the time of survey are assumed to be fixed characteristics of the respondents, rather than dynamic characteristics that vary over time. Additionally, respondents with any missing variables for each individual model were excluded from that model.

Risk factors were selected based on prior knowledge of plausible mechanistic influence on HIV incidence and/or prevalence. The risk factors explored are summarized in Table 3.2, including univariate and multivariate association under each model. Variable selection for multivariate models was performed using backward selection as described by Lawless and Singhal [38], using a $p \leq 0.1$ (per variable) threshold for stepwise variable retention. Estimated conditional effects of variables retained in the multivariate logistic regression models are illustrated in Figure 3.3.

⁵ Logistic regression models were implemented using `lrm` from: cran.r-project.org/package=rms.

Cox proportional hazards models were implemented using `coxalen` from: cran.r-project.org/package=coxinterval.

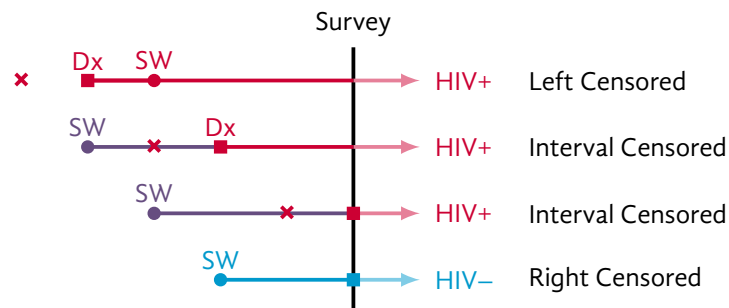


Figure 3.2: Illustration of time-to-event analysis framework for cross-sectional FSW survey data

x: HIV infection; SW: time of sex work debut; Dx: time of HIV diagnosis.

Table 3.2: Risk factors explored for association with HIV+ status among FSW in Eswatini

Factor	2011 LR				2014 LR				2014 CPH			
	Univar		Multivar		Univar		Multivar		Univar		Multivar	
	OR	p	OR	p	OR	p	OR	p	HR	p	HR	p
Age ^a	1.11	<0.001*	—	—	1.14	<0.001*	1.15	<0.001*	1.09	<0.001*	1.09	<0.001*
Years selling sex ^a	1.13	<0.001*	1.13	<0.001*	1.12	<0.001*	—	—	1.08	<0.001*	—	—
Monthly sex work income ^b	0.98	0.155	—	—	0.98	0.097	0.97	0.084	0.98	0.019*	0.97	0.001*
Non-paying partners ^c	0.88	0.307	—	—	1.07	0.233	—	—	1.05	0.312	—	—
Monthly new clients ^c	1.01	0.412	—	—	1.05	<0.001*	1.07	<0.001*	1.04	<0.001*	1.04	<0.001*
Monthly regular clients ^c	1.01	0.351	—	—	1.03	0.002	—	—	1.02	<0.001*	1.02	0.034*
Non-paying condom use ^d	0.90	0.703	—	—	0.90	0.673	—	—	0.92	0.677	—	—
New client condom use ^d	0.60	0.100	—	—	0.48	0.006*	1.25	0.599	0.56	0.004*	—	—
Regular client condom use ^d	0.58	0.110	—	—	0.39	<0.001*	0.35	0.004*	0.49	<0.001*	0.50	<0.001*
Any anal sex past month	0.97	0.896	—	—	1.89	0.015*	—	—	1.57	0.015*	1.27	0.260
Any STI symptoms past year	2.29	<0.001*	2.41	<0.001*	2.75	<0.001*	2.80	<0.001*	2.17	<0.001*	2.05	<0.001*

^a OR per year; ^b OR per Swati lilangeni per month; ^c OR per partner; ^d 2011: always vs. not always, 2014: at last sex. — indicates variable was not selected in the multivariate model. LR: logistic regression on HIV+/- status; CPH: Cox proportional hazards on time to self-reported HIV seroconversion. OR: odds ratio; HR: hazard ratio; p: p-value. 2011 data based on serologic HIV test; 2014 data based on self-reported HIV status, age of sex work debut, and age of HIV diagnosis.

Following variable selection, each multivariate model was used to predict the total HIV+ status odds ratio (logistic) or HIV incidence hazard ratio (Cox) for each respondent in the respective survey — i.e., $e^{X_i\beta}$ for respondent i — representing an overall “risk score” under each model. Respondents were then stratified into the top 20% and bottom 80% by these risk scores. The values of each variable were compared between these two strata using a test for the ratio of the means [39] to support model parameterization; these ratios are summarized in Table 3.3, and the distributions of variable values are illustrated in Figures C.1 and C.2.

3.2.1.4 Discussion

TODO

3.2 PARAMETERIZATION

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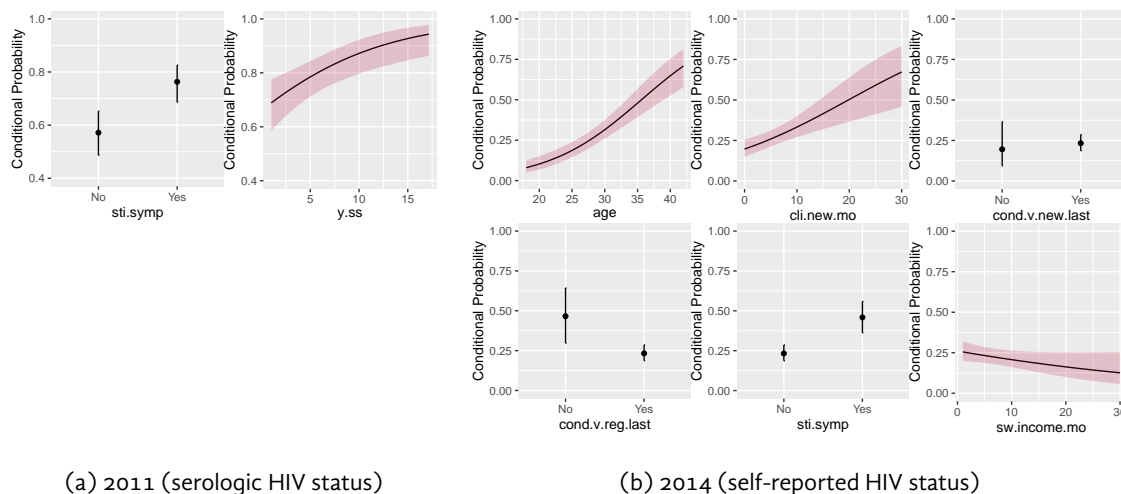


Figure 3.3: Predicted conditional effects (probability) of significant variables in multivariate logistic regression models from 2011 and 2014 surveys

sti.symp: any STI symptoms past year; y.ss: years selling sex; cli.new.mo: monthly new clients; sw.income.mo: monthly sex work income. Conditional probabilities shown for fixed covariates at arbitrary values.

Table 3.3: Ratios of HIV risk factor variables among higher vs. lower risk FSW in Eswatini

Factor	2011 LR		2014 LR		2014 CPH	
	High / Low	Ratio (95% CI)	High / Low	Ratio (95% CI)	High / Low	Ratio (95% CI)
Age	31.8 / 24.7	1.29 (1.22, 1.36)*	32.6 / 26.2	1.24 (1.20, 1.28)*	33.5 / 26.6	1.26 (1.21, 1.31)*
Years selling sex	11.3 / 4.03	2.81 (2.41, 3.25)*	10.0 / 5.47	1.83 (1.64, 2.03)*	10.2 / 5.83	1.75 (1.54, 1.98)*
Monthly sex work income ^a	15.1 / 15.2	1.00 (0.86, 1.15)	6.77 / 7.06	0.96 (0.82, 1.11)	6.32 / 7.28	0.87 (0.73, 1.02)
Non-paying partners	1.42 / 1.43	0.99 (0.81, 1.19)	1.56 / 1.11	1.40 (1.11, 1.72)*	1.53 / 1.19	1.29 (0.98, 1.62)
Monthly new clients	5.50 / 6.98	0.79 (0.49, 1.15)	8.39 / 4.15	2.02 (1.63, 2.44)*	8.36 / 4.41	1.90 (1.43, 2.39)*
Monthly regular clients	9.35 / 9.05	1.03 (0.69, 1.42)	11.1 / 8.25	1.35 (1.13, 1.57)*	12.4 / 8.61	1.44 (1.18, 1.71)*
Non-paying condom use ^{bc}	0.26 / 0.35	0.73 (0.40, 1.11)	0.77 / 0.81	0.95 (0.84, 1.06)	0.76 / 0.81	0.95 (0.81, 1.08)
New client condom use ^{bc}	0.68 / 0.76	0.89 (0.73, 1.06)	0.79 / 0.91	0.86 (0.79, 0.94)*	0.74 / 0.94	0.79 (0.69, 0.88)*
Regular client condom use ^{bc}	0.38 / 0.46	0.83 (0.45, 1.28)	0.67 / 0.91	0.74 (0.65, 0.82)*	0.60 / 0.92	0.65 (0.55, 0.75)*
Any anal sex past month	0.59 / 0.41	1.41 (1.06, 1.84)*	0.17 / 0.07	2.43 (1.47, 3.85)*	0.23 / 0.07	3.24 (1.95, 5.34)*
Any STI symptoms past year ^c	0.79 / 0.43	1.86 (1.54, 2.25)*	0.59 / 0.15	3.94 (3.15, 5.03)*	0.61 / 0.17	3.67 (2.87, 4.79)*
HIV prevalence ^d	0.94 / 0.64	1.46 (1.30, 1.63)*	0.66 / 0.29	2.29 (1.92, 2.75)*	0.71 / 0.31	2.32 (1.94, 2.80)*

High / Low: mean variable value among higher / lower risk groups, as defined by the top 20% / bottom 80% in multivariate model-predicted risk score; odds ratio from logistic regression (LR); hazards ratio from Cox proportional hazards (CPH). ^a Swati lilangeni per month; ^b 2011: always vs. not always, 2014: did use condom at last sex; ^c proportion of respondents; ^d 2011: serologic HIV status; 2014: self-reported HIV status; * statistically significant, $p < 0.05$.

3.2.2 Probability of HIV Transmission

I parameterized the overall probability of transmission per sex act β as the product of a base rate β_0 , and independent relative effects corresponding to multiple factors. Such factors (indexed f) included: sex act type a , condom use, prevalence of circumcision among susceptible men, partner HIV infection stage h' and viral suppression via ART c' , as well as prevalence of STI co-infection/symptoms among both partners. Thus, β was defined as:

$$\beta_{asis'i'h'c'} = \beta_0 R_{\beta,f_1} \dots R_{\beta,f_N} \quad (3.1)$$

The impact of each factor (except ART) on the probability of HIV transmission is described in the following subsections, while the prevalence of each factor is given in § 3.2.3. The impact of ART on transmission is described in § 3.2.5.1.

3.2.2.1 HIV Infection Stage

Boily et al. [11] synthesized per-act transmission probability in the absence of ART from 43 studies in 25 populations. Among 7 studies reporting stage of HIV infection (early, asymptomatic, late), infection stage explained 95% of variance in per-act probability of transmission in [11]. Such differences in transmission are most likely due to differences in viral load, which is associated with HIV stage [40, 41]. The probability of transmission during the middle asymptomatic period, was reported as mean (95% CI) 0.072 (0.053, 0.097)% per act, reflecting β_0 . To improve model fit (see § 3.3), the 95% CI was increased to (0.053, 0.15)%, which was used to define a gamma prior distribution for β_0 . This probability was assumed to apply to vaginal intercourse, based on the studies considered.

For early infection ($h = 2$), Boily et al. [11] estimated the relative infectiousness of the first 5 months of infection as 9.2 (4.5, 18.8) times higher than the asymptomatic period. However, both the duration and infectiousness of the acute phase have been long debated [42, 43, 44]. In a recent reanalysis of the Rakai cohort data, Bellan et al. [45] estimate a much smaller contribution of the acute phase to overall infection, summarized as 8.4 (0, 63) “excess hazard-months” (EHM). This excess risk represents the joint uncertainty and collinearity in the estimated duration of 1.7 (.55, 6.8) months and relative infectiousness of 5.3 (.79, 57). Thus, I sampled the duration $\delta_{h=2}$ from a gamma prior with mean (95% CI) 1.7 (.55, 6) months, and relative infectiousness $R_{\beta,h=2}$ from a gamma prior with 5.3 (1, 15) times the asymptomatic period (confidence intervals were adjusted to fit the gamma distributions, and to ensure $1 < \text{EHM} < 63$).

For late-stage disease, defined as 6–15 months before death in [11], Boily et al. estimated the relative rate of transmission as 7.3 (4.5, 11.9). However, I defined later HIV stages by CD4 count, including $200 < \text{CD4} < 350$ ($h = 5$) and $\text{CD4} < 200$ ($h = 6$, AIDS), which reflects closer to 50 and 18 months before death in the absence of ART, respectively. Therefore, I combined estimates from several sources [46, 11, 41] to define two gamma prior distributions with mean (95 CI%) 1.6 (1.3, 1.9) and 8.3 (4.5, 13), for the relative rate of HIV transmission in these two stages ($h = 5, 6$), respectively. For $\text{CD4} > 350$ ($h = 3, 4$), I assumed no change from the baseline probability β_0 .

3.2.2.2 Sex Act Types

The model considers vaginal and anal intercourse, further stratified by sex (male-to-female/insertive vs. female-to-male/receptive). For vaginal intercourse, evidence for differential risk by sex is mixed, with some studies reporting no difference [46, 47], and others reporting up to 2-times higher male-to-female ($s' = 2, s = 1$) transmission vs. female-to-male ($s' = 1, s = 2$) [48, 11]. To reflect this uncertainty, I sampled the relative rate of male-to-female vs. female-to-male transmission from $\text{Unif}[1, 2]$; in applying this relative rate, both male-to-female and female-to-male transmission probabilities were adjusted such that the overall mean was preserved.

Baggaley et al. [49] synthesized the per-act transmission probability for anal intercourse, with most data from MSM studies. Analyses in [49] were not stratified by HIV stage, so I assumed the same relative rates derived in § 3.2.1 applied equally to vaginal and anal intercourse. Overall female-to-male (insertive) per-act transmission probabilities were similar for anal intercourse [50] (without ART): 0.14 (0.04, 0.29)% vs. vaginal intercourse [11] (without commercial sex exposure): 0.164 (0.056, 0.481)%; thus I assumed that female-to-male (insertive) transmission probabilities for anal vs. vaginal intercourse were equal. By contrast, male-to-female (receptive) per-act transmission probabilities were approximately 10 higher in anal intercourse [49] (without ART): 1.67 (0.44, 3.67)% vs. vaginal intercourse [11] (without commercial sex exposure): 0.143 (0.088, 0.233)%; thus I assumed a fixed 10-fold increase in male-to-female transmission probability for anal vs. vaginal intercourse. See § 3.2.10 for sex act frequency within each partnership type.

3.2.2.3 Circumcision

Relative risk in per-act HIV female-to-male transmission for circumcised vs. uncircumcised men via vaginal intercourse has consistently been estimated as approximately 0.50, with 95% CI spanning (0.29, 0.96) [11, 47, 51]. Since circumcision status is unrelated to the research question, I fixed this effect at 50% relative risk. For anal intercourse, Wiysonge et al. [52] estimated that circumcision resulted in .27 (.17, .44) the odds of HIV acquisition for the insertive partner. It can be shown that relative reduction in incidence represents a lower bound on relative reduction in per-act transmission probability.⁶ Thus, for anal intercourse, I similarly fixed the per-act effect at 27%. Finally, there is inconclusive evidence to suggest that circumcision status affects male-to-female/receptive transmission [53, 52], so I assumed no effect. See § 3.2.3.1 for prevalence of circumcision in Eswatini over time.

3.2.2.4 Condoms

The most recent meta-analysis of condom effectiveness in heterosexual couples by Giannou et al. [54] estimated a relative risk of approximately 0.26 (0.13, 0.43). No significant differences were noted between female-to-male vs. male-to-female transmission. A recent study among men who have sex with men found a similar effect for anal sex [55]. Thus, condom effectiveness was fixed at 74%. See § 3.2.3.2 for levels of condom use in Eswatini over time.

⁶ See § 3.2.1 for more discussion.

3.2.2.5 Genital Ulcer Disease

Genital ulcer disease (GUD) is another established risk factor for HIV transmission [56, 57]. Some, but not all GUD is associated with sexually transmitted infections (STIs), and some, but not all STIs can cause GUD [57]. GUD is thought to increase both HIV susceptibility and infectiousness through a variety of mechanisms [57, 58, 59], but HIV may also facilitate transmission of various STIs through immunosuppression [60]. The meta-analysis by Boily et al. [11] found that presence of STI alone was not associated with increased HIV transmission: RR 1.11 (0.30, 4.14), but GUD was: RR 5.29 (1.43, 19.6), with most studies examining GUD among the HIV-susceptible partner. One study [61] estimated RR 2.58 (1.03, 5.69) of transmission for GUD among the HIV-positive partner. Most studies defined GUD status as any experience of symptoms during the study period (e.g., past 12 months, p12m), since precise delineation of GUD episodes is challenging. Moreover, individuals may take action to reduce onward STI transmission, such as accessing treatment, having less sex, and using condoms [2]. Thus, the true effect of GUD on HIV transmission via unprotected sex during active GUD episodes may be larger. However, if estimates of GUD prevalence and GUD effect (on HIV transmission) use consistent definitions (e.g., any GUD in p12m), then the time-averaged effect can be applied without need to estimate GUD episode duration. On the other hand, association of GUD and HIV transmission may not reflect *causation*, but rather *confounding* by uncontrolled exposure risk. As such, I applied factors for increased susceptibility and infectiousness due to GUD in accordance with group-specific p12m GUD prevalence (see § 3.2.3.3), with median 95% CI (1.2, 7.0) and (1.2, 3.4) (gamma priors), respectively.

3.2.3 Prevalence of Transmission Modifiers

3.2.3.1 Circumcision

Traditional (non-medical) circumcision in Eswatini is rare, reported as approximately 0.7% of men aged 15–49 in 2016 [5]. Voluntary medical male circumcision (VMMC) increased circumcision coverage to 8.2% by 2007, following demand for mainly hygienic reasons [2]. In 2007, the government further increased scale-up of VMMC services as part of HIV prevention efforts [2], leading to 17.1% coverage in 2011 [62], 30.0% in 2017 [5], and 37% in 2021 [63]. Since VMMC continues to be a key element of Eswatini’s HIV response [63], I assumed that coverage could reach and plateau at 50–90% (95% CI) by 2050. There is minimal evidence of differential condom use by circumcision status [62], so I assumed no differences. Similarly, while circumcision differed by union status in [5] (e.g., 22.1% circumcised among men in a union vs. 31.7% among men not in a union), differences did not persist after re-stratifying these men into groups with 0–1 vs. 2+ partners per year, as described in § 3.2.8. In Zambia, circumcision status was not associated with paying for sex [64].

3.2.3.2 Condom Use

Condom use is typically reported as either categorical for a recent period, usually 30 days, e.g., “*never, rarely, sometimes, often, always*”; or binary for the most recent sex act. Both report types may be subject to reporting bias, but the “last sex” more directly translates into a proportion of sex acts. The direction of reporting bias may vary with social context, with [65] suggesting over-reporting of condom use, and [66]

Table 3.4: Estimates of condom use in Eswatini

Partnership Type	Year	Population	Type	%	(95% CI)	Ref	Notes
Main	2006	Women	last sex	23.5	(23.2, 23.9)	[2]	a
		Men	last sex	23.1	(19.4, 26.9)	[2]	a
	2016	Women	last sex	52.7	(52.5, 52.9)	[5]	a
		Men	last sex	33.7	(30.8, 36.7)	[5]	a
Main or Casual	1988	Women	currently	0.6	(0.4, 1.3)	[67]	b
		Men	currently	7.3	(5.9, 12.1)	[67]	b
	2002	FSW	last sex	60	—	[68]	cd
			always	45.8	—	[68]	cd
	2006	Women	last sex	36.5	—	[2]	
		Men	last sex	47.2	—	[2]	
	2011	Women	always	30	—	[2]	
		Men	always	34	—	[2]	
		FSW	last sex	51.1	(41.8, 60.4)	[33]	de
			always	20.8	(14.7, 26.9)	[33]	de
	2014	FSW	last sex	80.6	(64.7, 89.6)	[34]	g
	2016	Women	last sex	58.3	—	[5]	
		Men	last sex	53.1	—	[5]	
Casual	2006	Women	last sex	53.5	—	[2]	
		Men	last sex	66.0	—	[2]	
	2016	Women	last sex	64.9	—	[5]	
		Men	last sex	73.7	—	[5]	
Sex Work Unspecified	2002	FSW	last sex	90	—	[68]	d
			always	74.4	—	[68]	d
	2020	FSW	always	50	—	[35]	
New Sex Work	2011	FSW	last sex	84.8	(57.9, 92.4)	[33]	ef
			always	56.7	(47.8, 65.6)	[33]	d
	2014	FSW	last sex	88.5	(54.9, 95.9)	[34]	g
Regular Sex Work	2011	FSW	last sex	82.9	(56.8, 90.0)	[33]	ef
			always	38.6	(29.5, 47.7)	[33]	e
	2014	FSW	last sex	85.6	(47.9, 95.0)	[34]	g

^a Back-calculated as described in § 3.2.3.2; ^b 95% CI from urban & rural data; ^c Described as “non-paying partners” in the survey;

^d Two major cities only (Manzini & Mbambane); ^e RDS-adjusted; ^f 95% CI lower bound reduced by 25% due to possible reporting bias; ^g 95% CI bounds from regions with lowest and highest reported condom use.

suggesting under-reporting of condom use. As such, I made no systemic adjustments to the available condom use data. Table 3.4 summarizes the available condom use data for Eswatini.

Main/Spousal & Casual. No direct estimates of condom use in main/spousal partnerships are available; condom use at last sex (with a non-paying partner) was either reported overall or for casual partners only.⁷ However, the proportions of individuals with various relationship statuses (e.g., polygynous union, non-polygynous union, not in a union, see § 3.2.8) can be used to back-calculate condom use in main/spousal partnerships for both 2006 [2] and 2016 [5]. To do so, I assumed whether “last sex” among individuals in unions with 2+ partners was with their main/spousal partner or with a casual partner; or more generally, what proportion of most recent sex acts was with a casual partner. I repeated the back-calculation assuming 5% and 95%, yielding the confidence intervals shown in Table 3.4. Estimates of condom use in

⁷ “Higher risk” partners were defined in [2] as: “Sexual intercourse with a partner who was neither a spouse nor lived with the respondent”, effectively matching the model definition of “casual” partnerships.

non-paying partners were lower among FSW vs. the wider population in 2011 (20.8% vs ~ 32% “always”), but higher in 2014–16 (80.1% vs ~ 55.7% “last sex”). Therefore, I assumed no differences in condom use among FSW vs. the wider population for main/spousal or casual partnerships.

Sex Work. All data on sex work partnerships in Eswatini is from FSW (i.e., not their clients). A 2001 study in Ghana [69] suggested that FSW were more likely than their clients to report having used a condom. As such, I adjusted the lower bound of 95% CI for condom use in sex work partnerships ($p = 3, 4$) as either 75% of the reported lower bound, or the lowest reported region-specific estimate. Estimates for 2002 [68] were obtained from two major cities only (Manzini and Mbambane); since early condom availability was mainly urban, treated these estimates as 95% CI upper-bounds, and defined the lower bound as 20% of the reported values.

Anal Sex. Owen et al. [70] estimate that among FSW globally, condom use in anal sex is approximately 79 (66, 94)% that of condom use in vaginal sex.⁸ In Eswatini [33, 34], relative condom use in anal sex vs. vaginal sex ranged from 44% among new clients in 2011 to 88% among regular clients in 2014. So, I sampled relative condom use in anal vs. vaginal sex from a BAB prior distribution with 95% CI: (50, 95)%.

Sampling & Trends. While levels of condom use reported by men and women do not always agree, the levels should agree in simulated partnerships. To reflect uncertainty due to the discrepancy, I sampled condom use for each year and partnership type from BAB prior distributions having 95% CI that spans the range of estimates from men and women (where applicable), including the widest points of all confidence intervals. I further expanded the confidence intervals in some cases by enforcing a maximum value of $N = 100$ for the BAB distribution. I assume that condom use was effectively zero in 1980 [67]. I also assume and enforce two conditions that: condom use must be monotonic increasing over time; and condom use must be highest in new sex work partnerships, and lowest in main partnerships, for all sampled parameter values. For each available year, I simultaneously sample condom use for all partnership types, and samples failing the condition are discarded. As illustrated in § A.1.3, this sampling strategy minimizes differences between the prior and sampled-with-constraint distributions. For each partnership type, I then smoothly interpolate between sampled levels of condom use over the available years using monotone piecewise cubic interpolation [71].

3.2.3.3 Genital Ulcer Disease

Self-reported prevalence of GUD in p12m among sexually active women and men aged 15–49 was approximately 7% in 2006 [2, Table 13.14]; this prevalence was not stratified by numbers of partners, so I assumed it was equal across sexually active individuals in lowest and medium activity groups. However, approximately 19 and 32% of the lowest activity women and men were not sexually active during p12m (see § 3.2.8); thus I reduced GUD prevalence by 19 and 32%, respectively, among these groups.

The 2011 and 2014 FSW surveys did not ask respondents about GUD specifically, but about any STI symptoms in p12m.⁹ In the wider population [2], approximately 60% of women self-reporting any STI symptoms specifically reported GUD in p12m; thus, self-reported STI symptoms among FSW may overestimate p12m GUD prevalence. Approximately 50% and 25% of FSW reported STI symptoms in

⁸ I integrated the reported confidence intervals using the delta method after assuming binomial-distributed proportions.

⁹ The survey question about STI symptoms was: “In the last 12 months, have you had symptoms of a sexually transmitted infection including discharge from your vagina or sores on or around your vagina or anus”.

2011 and 2014, respectively. Reflecting uncertainty related to self-reported estimates, STI vs. GUD, and sampling bias, I sampled p12m GUD prevalence among lower risk FSW from a BAB distribution with 95% CI (10, 40)%. Per analysis in § 3.2.1, I assumed that STI (and thus GUD) prevalence was approximately 3 (1.5, 5) times higher among higher risk FSW (gamma prior), with an upper bound of 100%. FSW data also suggest declining STI prevalence between 2011 and 2014. However, STI prevalence among Swati youth in 2017–18 remained high [72]. Thus, to reflect uncertainty in STI/GUD prevalence trends, I sampled a relative reduction in GUD prevalence for all populations between 2020 and 2050 from a uniform distribution spanning [0.2, 1].

Finally, no Eswatini-specific data are available for clients of FSW, but studies in Zimbabwe [73], Senegal [74] and Zambia [64] have found 2.5–3.7 (95% CI span 1.4–5.0) the odds of STI symptoms during the past 6–12 months among clients vs. non-clients. Yet, I assumed that even higher risk clients could not have greater GUD prevalence than lower risk FSW. Thus, I sampled higher risk client GUD prevalence uniformly between 7% and that of lower risk FSW, and sampled lower risk client GUD prevalence uniformly between 7% and that of higher risk clients.

3.2.4 HIV Progression & Mortality

3.2.4.1 HIV Progression

The length of time spent in each HIV stage is related to rates of progression between stages η_h , rates of additional HIV-attributable mortality by stage $\mu_{HIV,h}$, and treatment via antiretroviral therapy (ART). Lodi et al. [75] estimate median times from seroconversion to CD4 < 500, < 350, and < 200 cells/mm³, while Mangal [6] directly estimate the rates of progression between CD4 states η_h in a simple compartmental model. Based on these data, I modelled mean durations ($1/\eta_h$) of:¹⁰ 0.142 years in acute infection ($h = 2$, from § 3.2.2.1); 3.35 years in CD4 > 500 ($h = 3$); 3.74 years in 350 < CD4 < 500 ($h = 4$); and 5.26 years in 200 < CD4 < 350 ($h = 5$); plus the remaining time until death in CD4 < 200 ($h = 6$, AIDS). Since the duration in acute infection ($h = 2$) is randomly sampled, the remaining duration in CD4 > 500 ($h = 3$) is adjusted accordingly.

3.2.4.2 HIV Mortality

Mortality rates by CD4-count in the absence of ART were estimated in multiple African studies [76, 77, 6]; based on these data, I estimated yearly HIV-attributable mortality rates $\mu_{HIV,h}$ as: 0 during acute phase ($h = 2$); 0.4% during CD4 > 500 ($h = 3$); 2% during 350 < CD4 < 500 ($h = 4$); 4% during 200 < CD4 < 350 ($h = 5$); and 20% during CD4 < 200 ($h = 6$, AIDS).

3.2.5 Antiretroviral Therapy

Viral suppression via antiretroviral therapy (ART) influences the probability of HIV transmission, as well as rates of HIV progression and HIV-related mortality. The model considers individuals on ART before ($c = 3$) and after ($c = 4$) achieving full viral load suppression (VLS), as defined by undetectable HIV RNA in blood

¹⁰ Assuming exponential distributions for durations in each CD4 state (see § A.2.1 for more details).

samples. Among retained patients initiating ART (see § 3.2.6.2 for rates), time to VLS is usually described as “within 6 months” [78]. Mujugira et al. [79] estimated the median time to VLS as 3.1 [IQR: 2.8, 5.5] months from 1592 HIV serodiscordant couples; however this time may be underestimated due to the trial conditions and population. The distribution of time to VLS (Figure 1 in [79]) also featured a heavy tail, suggesting heterogeneity in time to VLS (see § 3.2.6.1 for implications). For example, time to VLS may be prolonged due to social and economic barriers to care [80, 81]. Considering these data, I sampled the time to VLS (duration in cascade state $c = 3$) from a gamma distribution with 95% CI (0.33, 1.0) years.

3.2.5.1 Probability of HIV Transmission on ART

All available evidence suggests that viral suppression by ART to undetectable levels prevents HIV transmission, i.e., undetectable = untransmittable (“U=U”) [82]. Thus, I assumed zero HIV transmission from individuals with VLS ($c = 4$). However, HIV transmission may still occur during the period between ART initiation to viral suppression ($c = 3$) [79]. Donnell et al. [41] estimate an adjusted incidence ratio of 0.08 (0.0, 0.57) for all individuals on ART. However, in [41] and [83], the 1 and 4 (respectively) genetically linked infections from individuals on ART all occurred within 90 days of ART initiation, suggesting that risk of transmission only persists before viral suppression. Adjusting the incidence denominator (person-time) to 90 days per individual who initiated ART in [41] results in approximately 3.13 times higher estimated incidence ratio: 0.25 for this specific period.¹¹ Thus, I sampled relative infectiousness on ART but before viral suppression ($c = 3$) from a BAB distribution with mean (95% CI) of 0.25 (0.01, 0.67). Finally, I assumed that the virally un-suppressed state ($c = 5$) had half the reduced infectiousness of $c = 3$, yielding 95% CI: (0.50, 0.83).

3.2.5.2 HIV Progression & Mortality on ART

Effective ART stops CD4 cell decline and results in some CD4 recovery [84, 85]. Most CD4 recovery occurs within the first year of treatment [84]. Due to the limited number of modelled treatment states, I model this initial recovery to be associated with the pre-VLS ART state ($c = 3$). Lawn et al. [85] and Gabillard et al. [86] estimate an increase of between 25–39 cells/mm³ per month during the first 3 months of treatment. After initial increases, CD4 recovery is modest and plateaus. Battegay et al. [84] report approximate increases of 22.4 cells/mm³ per year between years 1 and 5 on ART. Since HIV states $h = 4, 5, 6$ correspond to 150, 150, and 200-wide CD4 strata, I model rates of movement along $h = 6 \rightarrow 5 \rightarrow 4 \rightarrow 3$ as 0.167, 0.167, 0.125 per month, respectively, during pre-VLS ART ($c = 3$) and 0.1 per year after VLS ($c = 4$).

Since higher CD4 states are modelled to have lower mortality rates (see § 3.2.4.2), the modelled recovery of CD4 cells via ART described above implicitly affords a mortality benefit. However, HIV infection is associated with increased risk of death by non-AIDS causes — i.e., unrelated to CD4 count — including cardiovascular disease and renal disease [87]. Lundgren et al. [88] estimated 61% reduction in non-AIDS life-threatening events due to ART. For the same CD4 strata, Gabillard et al. [86] also report approximately 2-times higher mortality rates within the first year of ART vs. thereafter, suggesting that VLS is associated

¹¹ In [41], individuals who initiated ART contributed approximately 9.4 months per-person (273 persons / 349 person-years, Tables 2 and 3); thus the first 3 months of each individual represent $3/9.4 = 0.319$ fewer person-months of follow-up.

with 50% mortality reduction independent of CD4 increase. Thus, I modelled an additional 50% reduction in mortality among individuals with VLS ($c = 4$), and half this (25%) reduction before achieving VLS ($c = 3$).

3.2.6 Rates of HIV Diagnosis, ART Initiation, Viral Un-suppression & Re-suppression

Rates of HIV diagnosis δ , ART initiation τ , viral un-suppression ζ (including treatment failure, discontinuation, or loss to follow-up), and viral re-suppression σ' (Figure 3.1c) were defined to reflect historical trends and ART eligibility for Eswatini. These rates were further calibrated to reproduce observed cascade attainment over time in Eswatini (e.g., proportion on ART among those diagnosed with HIV). Similar to condom use, rates were interpolated between specified years using monotone piecewise cubic interpolation [71].

3.2.6.1 HIV Diagnosis

Multiple Eswatini studies report the proportions of women and men who tested for HIV in the p12m. However, this proportion may not directly reflect the yearly rate of diagnosis, because individuals may test more frequently based on their perceived risk [89]. Indeed, EmaSwati living with HIV were more likely to have reported previously testing for HIV in 2006 [2, Table 14.9], 2011 [90, Table 5], and 2016 [5, Table 7.3]. Additionally, the proportion tested in p12m likely underestimates the *rate* of testing due to repeat testers. Assuming an exponentially-distributed time spent untested in the period under consideration (consistent with inherent compartmental modelling assumptions), the testing rate λ can be calculated from the proportion tested ρ over period T via:

$$\begin{aligned}\rho &= 1 - \exp(-\lambda T) \\ \lambda &= -\log(1 - \rho)/T\end{aligned}\tag{3.2}$$

Moreover, [66] found approximately 70% underreporting of ever testing for HIV in face-to-face interviews vs. anonymous polling booth surveys, with consistent results across married and unmarried women and men.

Yet, preliminary model calibration using reported HIV testing rates (with 95% CI) described below as HIV diagnosis rates directly caused the model to overestimate HIV+ status awareness vs. the available data (see § 3.3.2.3, Table 3.9). This apparent discrepancy between reported population-level testing rates and HIV+ status awareness is in fact common, and could be explained by testing rate heterogeneity [91] — i.e., the existence of “fixed” sub-populations who test frequently and those who test rarely or never. Without further stratifying the modelled population along this testing frequency dimension, it is impossible to capture this heterogeneity directly. However, an alternative solution is to reduce modelled HIV diagnosis rates to reproduce the available data on HIV+ status awareness via model calibration. To this end, I parameterized HIV diagnosis rates over time based on reported testing rates (below), with a global reduction factor $f \sim \text{Unif}(0.5, 1)$. I further specified diagnosis rates using non-FSW women as a reference group, with separate time-varying *relative* rates defined for FSW and men. Confidence intervals for relative rates were assumed using a standard deviation of 0.2 for FSW and 0.1 for men (gamma priors).

HIV Testing Rates. Early HIV testing in Eswatini was mainly available to pregnant women via antenatal clinics, though a small number of youth and men also accessed HIV testing services [92, 93]. Based on

antenatal clinic data [94], I modelled a gradual increase in rates of HIV diagnosis among women from zero to 95% CI (5, 15)% (gamma prior) per year from 1990 to 2002, when the national HIV testing and counselling program was formally introduced [95]. I assumed no initial differences between FSW and other women, due to the lack of specific key populations prevention programs [96]. I further assumed that HIV diagnosis among men initially occurred at 10% the rate of women.

By 2006, $\rho = 21.9$ (20.6, 23.3)% of women and 8.9 (7.8, 10.0)% of men had tested for HIV and received the results in p12m [2]¹² — relative rate for men vs. women: 0.377 (0.207, 0.597). Further scale-up of HIV testing began in 2006 via provider-initiated testing and improved integration with the general health care system [95]. Between 2007 and 2010, such efforts doubled the number of testing locations (119 to 241) and tripled the number of total yearly tests (53,000 to 154,000) [97, 95]. By 2011, an estimated $\rho = 46.8\%$ of women, 28.4% of men, and 61.7 (55.6, 67.5)% of FSW had tested for HIV in p12m [90, 33],¹³ yielding testing rates of $\lambda = 0.631$, 0.333, and 0.962 per year, respectively — relative rates: 0.529 (0.352, 0.743) for men, and 1.521 (1.206, 1.980) for FSW.

Phase 1 of the MaxART program [98] ran from 2011 to 2014, with a primary objective to increase HIV testing. An estimated 284,680 people were reached with 389,658 tests by the end of Phase 1 (2014). By 2016, 57.1% of women and 47.8% of men had tested in p12m [5], yielding testing rates of $\lambda = 0.846$ and 0.650 per year, respectively. The relative rate for men increased to 0.770 (0.587, 0.978); however, this increase was *not* applied (2011 relative rate maintained) to improve model fit (see § 3.3). In 2014 [34] and 2020 [35] approximately $\rho = 75\%$ of FSW had tested in p12m ($\lambda = 1.386$) as such, I applied a relative rate of 1.62, (1.29, 2.07) for 2016. I held all rates of HIV diagnosis after 2016 fixed.

3.2.6.2 ART Initiation

Rates of ART initiation τ were modelled to reflect time-varying eligibility, availability, loss to follow-up, and differences between sex/activity groups.

Eligibility. Historical ART eligibility in Eswatini has generally followed the evolving World Health Organization (WHO) guidelines [99, 100, 101, 102]. Initial eligibility included one of [7]:

- CD4 < 200 cells/mm³ and any WHO clinical stage
- CD4 < 350 cells/mm³ and WHO clinical stage III
- any CD4 count and WHO clinical stage IV

Eligibility was revised in 2010 [8] to:

- CD4 < 350 cells/mm³ and any WHO clinical stage
- any CD4 count and WHO clinical stage III or IV

and again in 2015 [9] to:

- CD4 < 500 cells/mm³ and any WHO clinical stage
- in a discordant partnership or having a specified illness (any CD4 count or WHO clinical stage)

¹² Unless otherwise noted, “tested for HIV” will imply “and received the results” throughout this section.

¹³ The adjustment for missing ages 15–17 in [90] from § 3.3.2.1 was applied to the reported 50.1% of women and 31.7% of men aged 18–49 who tested in p12m, assuming 20% of women and 10% of men aged 15–17 tested in p12m.

before adoption of the current “ART for all” guidelines in late 2016 (modelled as effectively January 2017) [103, 10]. Phase 2 of MaxART also began in 2015, offering immediate ART via 14 health facilities in a stepped wedge design (6 facilities added per year) [103]. Relative to the 114 total facilities offering ART nationally at this time [104], I assumed this trial had minimal direct impact on population-level ART initiation — notwithstanding valuable insights gained regarding effective implementation [103].

I implemented the CD4-only eligibility criteria directly in the model, which is structured to match these 200, 350, and 500 CD4 cells/mm³ thresholds (Figure 3.1b). For eligibility by WHO clinical stages (not explicitly modelled), I estimated relative rates of ART initiation based on the following data from South Africa [105, Table 4] and Saudi Arabia [106, Table 2], respectively:

- 43/111 (39%) and 14/46 (30%) of PLHIV with $200 < \text{CD4} < 350$ were at stages III or IV; assumed: 35% PLHIV with $200 < \text{CD4} < 350$ were eligible for ART pre-2010
- 13/79 (16%) and 6/76 (8%) of PLHIV with $\text{CD4} > 350$ were at stage III; assumed: 15% PLHIV with $350 < \text{CD4} < 500$ were eligible for ART pre-2010 (5% with $\text{CD4} > 500$)
- 5/79 (6%) and 1/76 (1%) of PLHIV with $\text{CD4} > 350$ were at stage IV; assumed: 20% PLHIV with $350 < \text{CD4} < 500$ were eligible for ART 2010–2015 (5% with $\text{CD4} > 500$)

I assumed that roll-out of eligibility changes in 2010, 2015, and 2017 each occurred over a 1-year period.

Availability and Initiation. ART first became available in Eswatini in late 2003 via a one-hospital pilot project [95]. Early ART scale-up was modest, with 31 facilities offering ART by the end of 2009 [107]; however, this number increased rapidly to 110 facilities by the end of 2011 [95]. Phase 1 of MaxART (2011–2014) sought to further increase ART coverage among eligible PLHIV [98], including decentralization to lower level facilities, bringing the total number of facilities to 170 by 2015 [108]. Finally, national adoption of “Test and Start” in 2017 likely further reduced delays in ART initiation, while loss to follow-up was reduced throughout the years of ART scale-up [103].

Considering these data, I modelled the yearly ART initiation rate among eligible diagnosed PLHIV as: effectively $\tau = 0$ in 2003, gradually increasing to 1.5 (0.5, 3.0) by 2010; then to 9 (6, 12) by 2012; and stabilizing at 12 by 2018. This maximum rate of $\tau = 12$ corresponds to a mean effective delay of one month between diagnosis and ART initiation; this value was chosen in part to avoid numerical instability when solving the model with very high rates.

Group Differences. In 2011, conditional ART coverage (among diagnosed) was greater among men vs. women (Table 3.9), suggesting greater ART initiation among men vs. women. Yet, unconditional ART coverage (among PLHIV, regardless of diagnosis) were approximately equal (31.4 and 33.2%, respectively), and so conditional differences may be explained by the fact that women were more likely to be diagnosed at an earlier HIV stage via antenatal care, and thereafter not yet eligible for ART. Thus, I assumed no differences in ART initiation among men vs. women. A similar mechanism could partially explain differences in conditional coverage between FSW vs. women overall (36.9 vs. 48.0%), as FSW were more slightly likely to know their status (74.1 vs. 69.1%). However, FSW face unique barriers to accessing ART related to stigma and material insecurity [109]; as such, I sampled a relative rate for ART initiation among FSW from [0.5, 1] (uniform prior).

3.2.6.3 ART Failure

The modelled virally un-suppressed state ($c = 5$) reflects any combination of treatment failure (i.e., due to resistance mutations), discontinuation, or loss to follow-up (LTFU) after achieving viral suppression. The model does not explicitly simulate emergence and/or transmission of drug resistance, nor multiple unique ART regimens. As of 2016, resistance mutations to at least 1 of 3 drugs in combination regimens were identified in 10% ART-naïve PLHIV in Eswatini, and 16% PLHIV with prior ART exposure [110]. However, the extent to which these individual mutations can cause complete treatment failure remains unclear. Additionally, while transmissible resistance mutations could become more prevalent over time, emergence of new drugs (e.g., Dolutegravir) can combat the population-level impacts of this resistance [111].

All available data suggests that retention in ART care — i.e., not discontinued or LTFU — has improved over time in Eswatini [112, 113, 5]. Assuming an exponentially-distributed retention time (consistent with inherent compartmental modelling assumptions), I averaged the available data [113, Table 6] to calculated the effective yearly ART attrition rate as: 16.5% in 2008, 13.8% in 2010, 14.1% in 2012, and 8.3% in 2014. One-year LTFU was reported as 1% in 2016 [5], but it's not clear whether this definition was consistent with the earlier estimates. Many measures of LTFU may also overestimate true LTFU by failing to account for transfers between clinics and deaths [114, 115]; it's not clear whether the reported measures for Eswatini account for transfers or deaths.

LTFU was estimated to be 1.3 times higher among men vs. women in South Africa [114], which would be consistent with observed lower viral suppression among men vs. women on ART in Eswatini (Table 3.9) [114]. The same study estimated that LTFU did not significantly differ by the modelled CD4-strata [114]. No estimates of LTFU were available for FSW specifically in Eswatini, but among 354 FSW on ART in [35] (2021), 103 knew the results of viral load monitoring in p12m, of whom only 8 self-reported undetectable viral load. Such data may again reflect the unique barriers to accessing ART faced by FSW [109].

Considering all of the above data, I assumed: a yearly rate of viral un-suppression ζ among non-FSW women of 15% until 2010, decreasing to 5% by 2018; plus relative rates for men and FSW: [1, 1.5] (uniform priors).

3.2.6.4 Viral Re-suppression

The rate of viral re-suppression σ' aims to reflect the average delay associated with the steps of switching regimens (in case of treatment failure), or the steps of re-engaging in HIV care (in case of LTFU).

For treatment failure, viral un-suppression must first be identified. Availability of viral load monitoring in Eswatini was limited until at least 2010 [8], but incorporated into standard of care by 2015 (yearly testing) [9]. Without viral load testing, treatment failure can still be indicated clinically [8]. After suspecting treatment failure, at least three months of additional monitoring is typically required to rule-out issues of adherence [8, 9, 10], before another regimen is started. Moreover, second/third-line regimen options were limited in Eswatini until at least 2014 [116, 104]. Upon switching to an improved regimen, I assume that viral suppression occurs at the same rate as among ART-naïve PLHIV (see § 3.2.5).

For LTFU, no data directly indicate the average duration out of care in Eswatini. A recent model-based analysis of Kenyan data [117] suggests an average between 8 months and 2 years. Considering large-scale,

multisectorial efforts to improve ART care in Eswatini, it is likely that duration out of care has declined since 2010. Thus, I sampled the initial rate of viral re-suppression σ' from a gamma prior with 95% [0.5, 1.0], which increased by a factor of 1.5 over 2010–2018. I assumed no differences between groups.

3.2.7 Sex Work: Population Sizes & Partner Numbers

3.2.7.1 Population Sizes

Population sizes of all activity groups are modelled as proportions of the total population, which are assumed to remain roughly constant, although individuals can move between groups (see § 3.2.9.2), and disproportionate mortality due to HIV between groups may cause higher risk groups to shrink over time.

Female Sex Workers. The proportion of women who report sex work in national demographic and health surveys is generally considered unreliable due to social desirability bias, particularly if the survey is face-to-face and household-based [118, 119, 120, 121, 66]. Therefore, FSW population size estimates require targeted surveys and unique methodologies [122, 123]. In both [34] and [35], the Swati FSW population size was estimated using a combination of unique object method, service multiplier method, prior survey participation, and network scale-up method (NSUM) [122]. In 2011 [34], regional FSW population size estimates ranged from 0.7% to 6.5% of all women, with overall population-weighted mean across regions of 2.9%; in 2021 [35], the mean (95% CI) estimates were 2.43 (1.17, 5.02)%. To reflect this uncertainty in the model, a BAB distribution was fitted such that 95% of the probability fell between 0.7% and 6.5%, and used as the prior distribution for the proportion of women who are FSW: $P_{s_1 i_{34}}/P_{s_1}$. Then, following the analysis in § 3.2.1, the proportion of all FSW in the higher risk FSW group was fixed at 20%, and likewise the lower risk group at 80%.

Clients of FSW. Similar to FSW, household-based surveys are not considered reliable data sources for estimating the population size of clients of FSW [66]. However, few surveys are designed to reach clients of FSW, and no direct estimates of FSW size exist for Eswatini. So, I use a common approach for inferring the FSW client size [69], similar to the “multiplier method” [124]. Given the FSW population proportion $P_{s_1 i_{34}}$, the number of average yearly new and regular sex work clients per FSW $Q_{p_{34} s_1 i_{34}}$, the frequency of sex per partnership-year $F_{p_{34}}$, and the total number of yearly commercial sex acts per client year $Q_{p_{34} s_2 i_{34}} F_{p_{34}}$, the total client population $P_{s_2 i_{34}}$ is defined as:

$$\sum_i P_{s_2 i_{34}} = \frac{\sum_{pi} P_{s_1 i} Q_{p_{34} s_1 i_{34}} F_{p_{34}}}{\sum_{pi} Q_{p_{34} s_2 i_{34}} F_{p_{34}}} \quad (3.3)$$

Then, as with FSW, the proportion of total clients in the higher risk client group is defined as 20% of all clients, and likewise for the lower risk group at 80%. Using $Q_{p_{34} s_1 i_{34}}$, $Q_{p_{34} s_2 i_{34}}$, and $F_{p_{34}}$ as defined below in § 3.2.7.2, the client population size $P_{s_2 i_{34}}$ estimated by this method was 13.1 (2.1, 38.5)% of men.

3.2.7.2 Sex Work Partnerships

Female Sex Workers. Table 3.3 summarizes the numbers of numbers of new and regular clients *per month* reported by Swati FSW, stratified by higher vs. lower risk per the analysis in § 3.2.1.3. In general, the numbers of partners “C” reported for a given recall period γ (e.g., 1 month) do not directly inform a

partnership formation rate Q nor a number of concurrent partners K (see § A.2.3); rather, under certain assumptions, Q and K can be defined as:

$$Q = \frac{C}{\gamma + \delta} \quad (3.4)$$

$$K = \frac{C\delta}{\gamma + \delta} = Q\delta \quad (3.5)$$

The choice of force of infection model (see Chapter ??) will determine whether Q or K is used. Moreover, based on the survey questions,¹⁴ it's not clear whether these reported partner numbers C represent the numbers of unique men or unique client visits.

I assumed that all *new* clients were one-off visits; thus the reported partner numbers effectively represented $1/12$ th of the total numbers of yearly partnerships Q_{p_3} . As such, I sampled the yearly rate of new sex work partnerships among lower risk FSW from a gamma distribution with mean (95% CI) as $4.1 (2.5, 6.0) \times 12$, and the *relative* rate among higher risk FSW from $2.0 (1.6, 2.5)$. Since each partnership is assumed to include only one sex act, the partnership duration δ_{p_3} , frequency of sex F_{p_3} , and number of concurrent partnerships K_{p_3} are ill-defined, but can be defined for convenience as $\delta_{p_3} = 1/12$ (years), $F_{p_3} = 12$ (per year), and $K_{p_3} = Q_{p_3}/12$ (per year).

For *regular* sex work partnerships, uncertainties remain regarding partnership duration δ_{p_4} (see § 3.2.10.3), frequency of sex per month $F_{p_4}/12$, and survey responses C reflecting unique clients or total client visits per month. If C reflects the numbers of unique clients, then $Q_{p_4s_1i_3}$ can be defined via Eq. (3.4) using C directly; whereas if C reflects the numbers of unique visits, then $Q_{p_4s_1i_3}$ should be defined using $C/(F_{p_4}/12)$. I assumed that $\rho = 2/3$ of respondents interpreted the question as in the former case, and $1 - \rho = 1/3$ as in the latter, such that:

$$C' = \rho C + (1 - \rho) C / (F_{p_4}/12) \quad (3.6)$$

Taking $F_{p_4}/12 = 2$ as the prior mean from § 3.2.10.1, Eq. (3.6) simplifies to $C' = \frac{5}{6} C$. Then, sampling $C_{p_4s_1i_3}$ from a gamma distribution with mean (95% CI) $8.4 (6.0, 11.0)$ from Table 3.3, and δ_{p_4} as specified in § 3.2.10.3, I defined $Q_{p_4s_1i_3}$ and $K_{p_4s_1i_3}$ via Eq. (3.4) using $C'_{p_4s_1i_3}$ and $\gamma = 1/12$ year. For higher risk FSW, I sampled the *relative* number/rate of regular clients from $1.5 (1.3, 1.7)$ (Table 3.3) as before.

Clients. For Sub-Saharan African clients of FSW, data on the number of unique FSW visited and the frequency of sex is sparse. Among 64 clients in Kenya, the median number of sex work visits per week was 1.3 (68 per year); most clients (68%) had 1–3 regular FSW partners simultaneously, and visited 0–3 new FSW per year [125]. Among 261 truck drivers at sex work hotspots in Uganda, the mean number of sexual partners was 7.4 in the past 30 days and 44.7 in the past year [126]. Johnson and Dorrington [127] modelled yearly sex work visits among South African clients of FSW as gamma-distributed with age over 10, peaking at 64 visits per year for clients aged 37. To reflect these data, I specified clients overall to have mean (95% CI) 60 (35, 90) sex acts with FSW per year ($K_{p_3s_2i_3} F_{p_3}/12$, gamma prior). Then, the yearly sex acts among lower and higher risk clients are defined such that higher risk have $2.0 (1.6, 2.5)$ times the number risk. Finally, since the distribution of sex acts between new vs. regular sex work partnerships

¹⁴ The survey questions were: “In the last 30 days, how many (new/regular) clients have you had sex with?”, or similar.

must match that among FSW, the specific values of $K_{p_{34}s_2i_{34}}$ were computed automatically. See § 3.2.8.4 for numbers of main/spousal and casual partnerships among FSW and clients.

3.2.8 Non-Sex Work: Group Sizes & Partner Numbers

3.2.8.1 Reported Partner Numbers

The 2006-07 DHS [2], 2011 SHIMS [62], and 2016-17 SHIMS2 [5] surveys provide the numbers of respondents who reported 2+ partners in the past 12 months (p12m): 13.5, 18.2, 14.5% among men, and 1.6, 3.8, 4.1% among women, respectively.¹⁵ However, these data do not provide information on the types of partners reported — i.e., those reporting 1 partner in p12m are not necessarily in a main/spousal (vs casual) partnership, and neither are those reporting 2+ partners in p12m. Moreover, such reports are likely substantially biased by social desirability bias due to the face-to-face interview format [118, 128, 120, 66].

Regarding the types of partnerships reported. Both the 2006 DHS [2, Tables 14.6.1 and 14.6.2] and 2016-17 SHIMS [5, Tables 15.4.A and 15.4.B] summarize the numbers of women and men by partners in p12m and by marital/union status, although summaries are stratified by each factor separately, not jointly. However, making the following assumptions, I estimated the jointly-stratified proportions of individuals. Let W_{2+} , W_1 , and W_0 denote women reporting 2+, 1, and 0 partners, respectively, and likewise with M_{2+} , M_1 , M_0 for men (all partners reflect p12m).¹⁶ The assumptions were:

- W_{2+} included all women in non-polygynous unions (married or cohabiting) reporting sex with a “casual” (non-marital, non-cohabiting) partner
- M_{2+} included all men in polygynous unions, plus all men in non-polygynous unions reporting sex with a casual partner
- the remaining W_{2+} and M_{2+} formed only casual partnerships
- all women and men in non-polygynous unions reporting no sex with a casual partner reported 1 partner (W_1 and M_1)
- the remaining W_1 and M_1 formed only casual partnerships

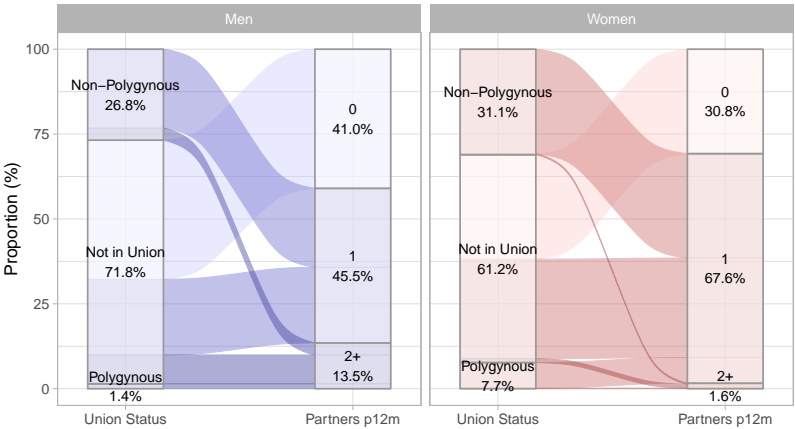
Figure 3.4 illustrates the resulting proportions of women and men in each union/partners in p12m stratum in 2006-07 (a) and 2016-17 (b).

Reporting Bias. Next, I consider the issue of reporting bias. M_{2+} is consistently much greater than W_{2+} . This difference is common in surveys [129, 130], and could be explained by either: (a) a small number of women with many partners, such as FSW, who may also not be reached by the survey, or who may not fully report partner numbers; (b) over-reporting of partnerships by men; or (c) under-reporting of partnerships by women. Further stratification of women reporting 2+ partners in [2, Table 14.7.1] revealed that 94% reported exactly 2 whereas 6% reported 3+, suggesting that explanation (a) is less likely unless women with 3+ partners are under-reported or indeed missing from the survey.

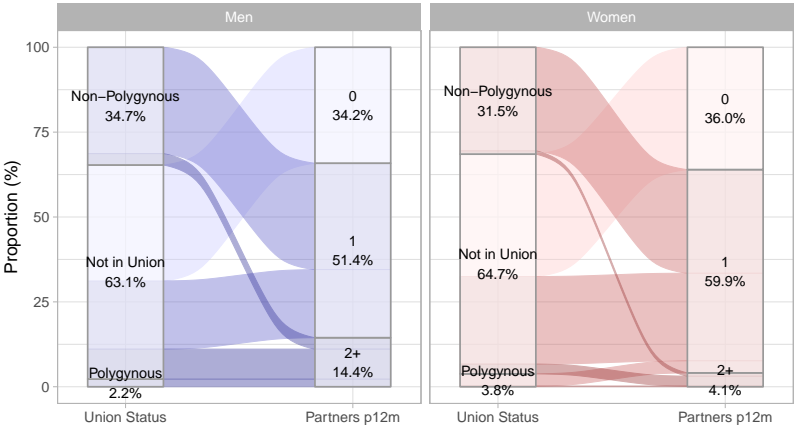
Gregson et al. [119] (Zimbabwe), Nnko et al. [131] (Tanzania) and Clark, Kabiru, and Zulu [132] (Kenya) explored explanations (b) and (c) through measures of consistency; their results suggested that under-

¹⁵ From Tables 14.7.1 and 14.7.2 (ages 15-49) in [2], Table 3 (ages 18-49) in [62], Table 15.3.A (ages 15+) in [5], with manual adjustment for survey skip patterns in [2, 5].

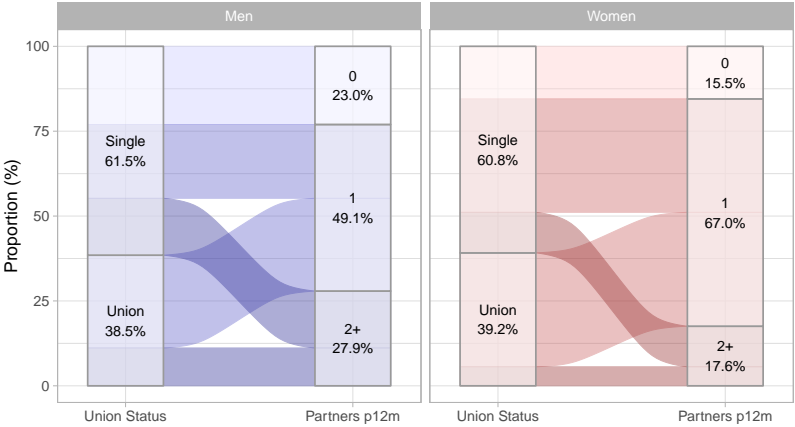
¹⁶ Regarding notation in this section, $W_{2+} = P_{s_1i_{234}}/P_{s_1}$, $W_1 + W_0 = P_{s_1i_1}/P_{s_1}$, and likewise for men (M , $s = 2$).



(a) 2006-07 [2]



(b) 2016 [5]



(c) Adjusted (mean)

Figure 3.4: Reported proportions of women and men aged 15–49, stratified by union status and numbers of partners in the past 12 months

reporting of non-spousal partnerships by women (c) was more likely, perhaps due to social norms and pressures; such norms in Eswatini are explored in [133, 134]. In fact, a review comparing computer-based tools vs. face-to-face interviews for surveying sexual behaviour [135] found that *both* women and men may under-report sexual partners, but women more so. A notable study in Benin [66] found that 7 times as many married women (21 vs. 3%) and 3 times as many married men (53 vs. 18%) reported any extramarital sex in p12m in a surveys via anonymous polling booth vs. face-to-face interview. Similarly, 5 times as many unmarried women (13.5 vs. 2.8%) reported exchanging sex for money, gifts or favours in p12m, while 4 times as many unmarried men (62 vs. 14%) reported non-transactional sex with a women in p12m. Such findings were similar to those from Zimbabwe (1990s) [119].

3.2.8.2 Bias Adjustment: Approach

Reflecting these potential reporting biases, I modelled the “true” proportions of Swati women and men in each union/partners in p12m stratum as follows. Let W_{s1} and W_{u1} denote sub-proportions of W_1 who are single and in a union, respectively, and likewise for W_{s2+} , W_{u2+} , M_{s1} , M_{u1} , M_{s2+} , and M_{u2+} . Further, let W_{s1} denote the reported proportion of women (average of 2006-07 and 2016-17), vs. W'_{s1} denoting the “true” (adjusted) proportion. I assumed that a fraction of W_0 belongs in W'_{s1} — i.e., a fraction of women reporting 0 partners in p12m truly had 1 casual (non-main/spousal) partner. I modelled this relationship through an odds ratio $\varphi_{W_{s1}:0}$, which is roughly equivalent in interpretation to the proportion ratios estimated by Béhanzin et al. [66]:¹⁷

$$\varphi_{W_{s1}:0} = \frac{W'_{s1}}{W'_0} \bigg/ \frac{W_{s1}}{W_0} \quad (3.7)$$

I defined similar odds ratios $\varphi_{W_{s2+:s1}}$, $\varphi_{W_{u2+:u1}}$, $\varphi_{W_{u1}:0}$, $\varphi_{W_{u1}:s1}$, and $\varphi_{W_{u2+:s2+}}$, and likewise for men. The corresponding transitions of women from reported to “true” strata are illustrated in Figure 3.5. To resolve the adjusted values W' then requires solving the (nonlinear) system of 6 equations corresponding to the 6 odds ratios φ , subject to $\sum_i W'_i = 1$ and $0 \leq W'_i < 1$. An exact solution is not guaranteed, but the sum squared error from all equations can be minimized. The odds ratios φ were then defined as follows, including sampling distributions.

Union Status. I assumed that under-reporting of main/spousal partnerships was minimal, but that some “main” partnerships may not be captured in the definition “married/cohabiting” from [2, 5]; thus $\varphi_{u1:0}$, $\varphi_{u1:s1}$, and $\varphi_{u2+:s2+}$ would be small but greater than 1 (horizontal transitions in Figure 3.5). Moreover, based on the median age of marriage, 23–29 [2], approximately half of respondents aged 15–49 would have been married, whereas only 28–39% of women and men reported being in a union (Figure 3.4a and 3.4b), although some marriages end in divorce/widowing [2]. Thus, I sampled each of $\varphi_{u1:0}$, $\varphi_{u1:s1}$, and $\varphi_{u2+:s2+}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = .5$ for women and $\alpha = .3$ for men, yielding mean (95% CI): 1.50 (1.00, 3.51) and 1.30 (1.00, 2.90), respectively.

Partner Numbers. Next, I defined $\varphi_{s1:0}$, $\varphi_{s2+:s1}$, and $\varphi_{u2+:u1}$ as follows (vertical transitions in Figure 3.5). The median age of first sex in Eswatini was approximately 18 for women and 19.5 for men [2]. Thus, the 31–36% of women and 34–41% of men aged 15–49 reporting no partners in p12m (Figure 3.4a and 3.4b) is likely overestimated, although some individuals may be abstinent in p12m following sexual debut. I

¹⁷ Odds ratios ensure no proportions become greater than one or negative.

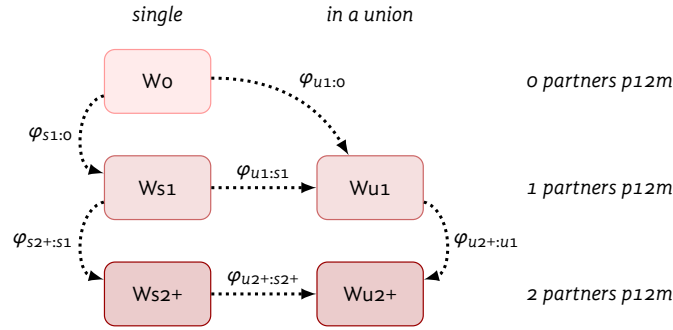


Figure 3.5: Illustration of how women (and equivalently men) are reallocated between union/partners in p12m strata based on odds ratios φ

p12m: within the past 12 months Wo: 0 partners in p12m; Ws1: single (not married/cohabiting) and 1 partner in p12m; Wu1: in a union (married/cohabiting) and 2+ partners in p12m; Ws2+: single and 2+ partners in p12m; Wu2+: in a union and 2+ partners in p12m. φ : odds of truly being in the second (arrowhead) vs first (tail) group.

assumed that women had 3 and men had 2 times the odds of actually having 1 casual partner in p12m while reporting no partners. Thus, I sampled $\varphi_{s1:0}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = 2$ for women and $\alpha = 1$ for men, yielding mean (95% CI): 3.00 (1.24, 6.57) and 2.00 (1.03, 4.69), respectively. Drawing on [66], I assumed that “single” women and men (not married/cohabiting) were less likely to report multiple partners in p12m, but women more so. Thus, I sampled $\varphi_{s2+:s1}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = 4$ for women and $\alpha = 1$ for men, yielding 5.00 (2.09, 9.77) and 2.00 (1.03, 4.69). I made a similar assumption about married/cohabiting women and men, with the same odds for men, but even greater odds of non-reporting among women. I sampled $\varphi_{u2+:u1}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = 6$ for women and $\alpha = 1$ for men, yielding 7.00 (3.20, 12.67) and 2.00 (1.03, 4.69).

3.2.8.3 Bias Adjustment: Resulting Group Sizes & Partner Numbers

The mean resulting adjusted proportions W' and M' from solving the system with the assumed odds ratios φ are illustrated in Figure 3.4c, which can be compared to the reported proportions in a and b. Figure C.5 also illustrates the empiric density distributions for each element W'_i and M'_i . Numerically, the mean (95% CI) estimates were:

- $W'_0 = 17$ (9, 27)% of women and $M'_0 = 25$ (13, 35)% of men had 0 partners in p12m
- $W'_1 = 66$ (57, 75)% of women and $M'_1 = 49$ (37, 61)% of men had 1 partners in p12m
- $W'_{2+} = 17$ (10, 27)% of women and $M'_{2+} = 26$ (15, 44)% of men had 2+ partners in p12m
- $W'_{u1}/W'_{o1} = 38$ (21, 57)% women and $M'_{u1}/M'_{o1} = 35$ (23, 50)% men with 0–1 partners in p12m were in a main/spousal partnership
- $W'_{s1}/W'_{o1} = 41$ (19, 65)% women and $M'_{s1}/M'_{o1} = 31$ (15, 55)% men with 0–1 partners in p12m were in a single casual partnership
- $W'_{u2+}/W'_{2+} = 32$ (9, 55)% women and $M'_{u2+}/M'_{2+} = 38$ (13, 62)% men with 2+ partners in p12m were in a main/spousal partnership, and the rest had only casual partnerships.

Group Sizes. From these results, I defined the sizes of the modelled lower and medium activity groups, and the average numbers of main/spousal partnerships per person. I assumed that W'_{2+} and M'_{2+} included

FSW and client population sizes, respectively (see § 3.2.7.1). Thus, the populations size of medium activity women was defined as $P_{s_1 i_2} = W'_{2+} - P_{s_1 i_{34}}$. Sampling W'_{2+} from a BAB distribution with 95% CI (10, 27)%, the resulting 95% CI for medium activity women $P_{s_1 i_2}$ was (6, 25)% of women. The lowest activity women population size was then defined as $1 - P_{s_1 i_{234}}$, representing (73, 90)% of women. Since there is greater uncertainty in the client population size, the same approach for the medium activity men population size $P_{s_2 i_2}$ could yield negative values. Instead, I sampled $P_{s_2 i_2}$ directly from a BAB distribution with 95% CI (10, 17)%, yielding 95% CI for $P_{s_2 i_{234}}$ of (15, 50)% of men, which is close to (15, 44)% from M_{2+} . The lowest activity men were then defined as $1 - P_{s_2 i_{234}}$, representing (50, 85)% of men.

Main/Spousal Partnerships. To simplify model fitting, I sampled a common proportion of individuals reporting a main/spousal partnership from a BAB distribution with 95% CI (25, 50)%, applied to all women and men in the lowest activity groups ($C_{p_1 s_{12} i_1}$), as well as all women in the median activity group ($C_{p_1 s_1 i_2}$). Then, Eqs. (3.4) and (3.5) were used to define Q and K , respectively. Since FSW and clients had fewer main/spousal partnerships (see § 3.2.8.4), I calculated the proportion of men in the medium activity group having main/spousal partnerships $K_{p_1 s_2 i_2}$ to balance the total number of main/spousal partnerships among women and men.

Casual Partnerships. I similarly defined a common proportion of women and men in the lowest activity groups reporting casual partnership $C_{p_2 s_{12} i_1}$ with 95% CI (20, 55)%. However, the number of casual partnerships among W_{2+} and M_{2+} remains uncertain. The analysis above provides no information on these values, but the number of partners in p12m for the medium activity groups must be at least about 1.5 to ensure these women and men actually have 2+ partners in p12m. Thus, I sampled the number of casual partners reported by women in the medium activity group $C_{p_2 s_1 i_2}$ from a gamma distribution with 95% CI (1.2, 2), and computed Q and K via Eqs. (3.4) and (3.5). As before, I calculated the numbers of casual partnerships among men in the medium activity group $K_{p_2 s_2 i_2}$ to balance total casual partnerships.

3.2.8.4 Main/Spousal & Casual Partnerships among FSW & Clients

Among Swati FSW, the mean number of total non-paying partners in the past month was approximately 1–1.5 (Table 3.3), which may include both main/spousal partners and casual partners. Among FSW in South Africa [136] and Kenya [137], while 54 and 72% (respectively) reported being in a relationship, only 6 and 3% were married, although many non-marital partners may still constitute effectively “main” partnerships with respect to condom use and duration. Thus, I assumed that: 50% of all FSW reported a main/spousal partner (i.e., $C_{p_1 s_1 i_{34}} = 0.5$); lower risk FSW reported $C_{p_2 s_1 i_3} = 0.5$ casual partners; and higher risk FSW reported $C_{p_2 s_1 i_4} = 1.0$ casual partners, on average.

Available data suggest that about half of clients also report non-sex work partners, which are not always distinguished as main/spousal vs. casual partnerships [138, 74]. Non-paying partners of FSW are also often clients of other FSW [137, 139]. Yet, clients of FSW also tend to be younger and more likely to be never/formerly married vs. non-client men [138, 140]. So, I assumed that clients reported half the numbers of main/spousal partnerships compared to lowest activity men: $C_{p_1 s_2 i_{34}} = 0.5 C_{p_1 s_1 i_1}$, and 25–100% the numbers of casual partnerships compared to medium activity women (uniform prior). As before, I computed Q and K via Eqs. (3.4) and (3.5).

3.2.9 Turnover

3.2.9.1 Births & Deaths

The modelled population considers ages 15–49, reflecting commonly reported data and the majority of sexual activity. In the absence of mortality, individuals would therefore remain within the modelled “open cohort” population for 35 years. The estimated average yearly mortality rate for these ages was 1.44% around 2006 [2, Table 15.2]. However, this estimate includes HIV/AIDS-attributable mortality, which I model separately (see § 3.2.4.2), accounting for approximately 64% of deaths around that time [141]. Thus, the overall exit rate from the modelled cohort due to reaching age 50 (“aging out”) and non-HIV-attributable mortality was: $\mu = 1/35 + (1 - .64)1.44\% = 3.78\%$.

I estimated the rate of entry into the modelled population ν to fit population size of ages 15–49 in Eswatini [14], and approximate population growth rates [142], given that I model HIV/AIDS-attributable mortality separately. Specifically, I assumed a population growth rate $g = \nu - \mu$ in the absence of HIV/AIDS of 4% in 1980, 3% in 2000, 1.5% in 2010, and 1.5% in 2020 (monotonic cubic interpolation). I sampled g in 2050 from a uniform prior with 95% CI (0.7%, 1.5%), reflecting uncertainty in estimated projections [142]. Finally, I calculated the population entry rate as $\nu = g + \mu$. These parameter values were informally validated by comparison of model outputs with Swati population sizes for ages 15–49 from [14]. The distribution of activity groups among individuals *entering* the model, denoted E_{si} , is different from the distribution among individuals *currently* in the model P_{si} , but E_{si} is computed automatically as described below in § 3.2.9.2.

3.2.9.2 Activity Group Turnover

In addition to overall population turnover (entry/exit from the open population), I model movement of individuals between activity groups within the model. Activity group turnover reflects the fact that risk is not constant over sexual life course, and reported duration in higher activity contexts can be short [16]. Previous modelling has shown that activity group turnover (sometimes called “episodic risk”) can strongly influence parameter fitting and intervention impact [143, 144]. I model turnover from activity group si to si' as a constant rate $\theta_{si'i'}$, which implies an assumption that (in the absence of HIV) duration in group si is exponentially distributed with mean D_{si} [145]:

$$D_{si} = \frac{1}{\mu + \sum_{i'} \theta_{si'i'}} \quad (3.8)$$

where μ is the overall exit rate from § 3.2.9.1. As shown previously [144], the relative sizes of each sex-activity group P_{si} can be maintained at fixed values by satisfying the following “mass-balance” equation:

$$\nu P_{si} = \nu E_{si} + \sum_{i'} \theta_{si'i'} P_{si'} - \sum_i \theta_{si'i'} P_{si} \quad (3.9)$$

Specific turnover rates $\theta_{si'i'}$ and entrant activity group sizes E_{si} can then be uniquely resolved by specifying $N_i(N_i - 1) = 12$ non-redundant and compatible constraints, where specifying each D_{si} is one such constraint.

Duration Selling Sex. The FSW survey data for 2011 [33], 2014 [34], and 2021 [35] include questions on the respondent’s current age, and age of first selling sex; the difference between these ages can then define a “duration selling sex”. Using this approach, the unadjusted years selling sex among Swati FSW were median [IQR]: 4 [2, 7] in 2011 and 5 [3, 9] in 2014, with histograms shown in Figure C.3. However, such estimates have three sources of bias: sampling error, censoring, and measurement error.

Sampling error was addressed through RDS-adjustment in 2011 and 2021, yielding estimates of the proportions of FSW who have been selling sex for 0–2, 3–5, 6–10, and 10+ years. The adjusted proportions are not significantly different between 2011 and 2021, and indicate fewer years selling sex vs. the unadjusted proportions, which would be consistent with challenges in reaching women in the first year(s) of sex work [146]. I fit an exponential distribution to the cumulative adjusted proportions (Figure C.4), yielding an estimated distribution mean λ^{-1} of 4.2 (3.5, 5.3) years. However, the reported years selling sex in a cross sectional survey will underestimate the eventual duration in sex work among respondents by a factor $f \leq 2$, because respondents continue selling sex after the survey — i.e., the observed duration is right censored (see § A.2.2 for derivation and further discussion). Thus, the overall mean duration in sex work would be given by $\bar{D} = f \lambda^{-1}$. Yet, additionally, the current definition of duration selling sex includes a hidden assumption that FSW sell sex continuously after starting. In fact, 348/777 (45%) FSW reported having ever stopped selling sex in the 2014 survey [34] (other surveys did not ask). Among these FSW, the expected duration selling sex in the current period (i.e., since re-starting most recently) must be less than half ($\rho < 1/2$) of the durations calculated above. Thus, an adjusted overall mean duration can be calculated as $\bar{D} = (0.45\rho + 0.55)f\lambda^{-1}$. Taking $\rho \sim \text{Unif}(0.2, 0.4)$ and $f \sim \text{Unif}(1.5, 2)$, we obtain \bar{D} with mean (95% CI): 5.13 (3.87, 6.72), similar to the pooled estimate for African FSW up to 2010: 5.5 years [147].

Finally, I assumed that higher risk FSW stay in sex work longer by a factor of R_D with 95% CI (1.54, 3.25) (gamma prior, Table 3.3). Thus, durations in sex work among higher risk (D_{HR}) and lower risk (D_{LR}) FSW can be resolved using:

$$\begin{aligned}\bar{D} &= 0.2 D_{HR} + 0.8 D_{LR} \\ R_D &= D_{HR}/D_{LR}\end{aligned}\tag{3.10}$$

yielding mean (95% CI) D_{LR} : 4.07 (2.96, 5.48) and D_{HR} : 9.33 (6.30, 13.13) (gamma priors).

Duration Buying Sex. Data to inform the average duration spent buying sex among clients is limited. Fazito et al. [147] estimated mean durations of 4.6–5.5 years based on studies in Benin [138] and Kenya [125]. Hodgins et al. [148, Table G] also gives pooled estimates for the proportions of men in Sub-Saharan Africa who paid for sex ever vs. in p12m during 2000–2020. Estimates ranged from 8.8 (6.5, 11.7)% of men aged 25–34 who ever bought sex, to 2.2 (1.5, 3.2)% of men aged 35–54 who bought sex in p12m. Based on these data, I defined a gamma prior distribution for the duration buying sex with 95% CI (4, 15) years, applied to both higher and lower risk clients.

Lowest & Medium Activity Groups. Data on individual-level changes to numbers of non-sex work partners in p12m is even more sparse than data related to sex work; so, it’s unclear to what extent individuals move between the lowest and medium activity groups throughout their sexual life course. Data from Uganda, Zimbabwe, and South Africa [129] suggested that sexual activity (proportion sexually active and mean numbers of partners) was approximately stable with age (after sexual debut and before age 49), with modest trends toward lower activity at older age. However, these population-level data do

not necessarily suggest that the *same* individuals have multiple partnerships each year. Reflecting this uncertainty, I sampled the rate of turnover from medium to lowest activity for both women and men from a gamma prior with 95% CI (5, 50)% per year.

Additional Turnover Assumptions. The above assumptions specify 3 key constraints for each sex: two durations D_{si} and one turnover rate θ_{siv} . Since higher and lower risk FSW (and clients) are conceptualized as mutually exclusive groups, I modelled no turnover between these groups: $\theta_{s_{i3}i_4} = \theta_{s_{i4}i_3} = 0$ (+2 constraints). Next, since FSW often enter sex work shortly after sexual debut [146, 149], and sexual activity is roughly constant or slightly declining with age [129], I assumed that $E_{si} = f P_{si}$,¹⁸ with $f = 2$ for FSW, $f = 1.5$ for clients, and $f = 1$ for medium activity women and men (+3 constraints); then $f < 1$ for the lowest activity women and men is computed automatically. Finally, since exiting sex work is unlikely to be an abrupt transition to monogamous or zero sexual activity [16, 150], I further assumed that (50, 90)% of women exiting sex work transition to the medium activity group (BAB prior) (+2 constraints). In the absence of relevant data, I made a similar assumption regarding clients, with (25, 90)% former clients transitioning to the medium activity group. These 10 < 12 total constraints then allow two degrees of freedom to resolve the values of θ_{siv} and E_{si} . A non-negative solution to the system of constraints is solved as described in [144],¹⁹ repeated at each timestep as v varies with time.

3.2.10 Sex Frequency & Partnership Duration

3.2.10.1 Sex Frequency

The Eswatini general population data sources [2, 62, 5] did not report on frequency of sex. In South Africa, average numbers of sex acts per week per partnership (non-sex work) was reported as mean 2.5 (IQR: 1–3) [151], with consistent reports across main/spousal partnerships and casual partnerships. Sex frequency among South Africans per month overall (not per-partnership) is also summarized in [152, Figure 3.15], which is roughly consistent with [151], but motivates a smaller lower bound. Median sex frequency per partnership-year in 1998 Rakai, Uganda was approximately 90 acts with the “more frequent” of concurrent partners, and approximately 20 acts with the “less frequent” [153]. Considering these data, I sampled the number of sex acts per year in main/spousal partnerships F_{p_1} from a gamma prior distribution with 95% CI (13, 156), and a relative rate for casual partnerships $F_{p_2}/F_{p_1} \sim \text{Unif}(0.25, 1)$. As described in § 3.2.7.2, I defined $F_{p_3} = 12$ for occasional sex work partnerships, and $F_{p_4} \sim \text{Unif}(12, 36)$ for regular sex work partnerships. I also constrained samples of F_{p_4} such that higher risk FSW never have commercial sex more than twice daily, on average.

3.2.10.2 Anal Sex

Among Eswatini data sources, only [34] (FSW, 2014) counted sex acts separately for anal and vaginal sex. Among all FSW, the proportion of “average sex acts per week” that were anal (vs vaginal) was 2.9%. However, a previous coital diary study in neighbouring KwaZulu-Natal suggested much higher proportions were anal [154], and face-to-face interview survey design may result in under-reporting [70]. Owen

¹⁸ Subject to $f \leq (v - \mu + D_{si}^{-1})v^{-1}$, which can be derived from Eq. (10) in [144].

¹⁹ Using docs.scipy.org/doc/scipy/reference/generated/scipy.optimize.nnls.html

et al. review studies of anal sex in South Africa, and estimate that 0.6–16.5% of sex acts among the general population are anal [155], vs 2.4–15.9% among FSW [70]. To reflect this greater uncertainty, the proportions of sex acts which are anal in main/spousal and casual partnerships are sampled from a gamma prior distribution with 95% CI (0.6, 16.5)%, and likewise for occasional and regular sex work partnerships with 95% CI (2.4, 15.9)%. Finally, I ensure a greater proportion of anal sex in sex work vs. main/spousal and casual partnerships per § A.1.3.

3.2.10.3 Partnership Duration

As explored in Chapter ??, the durations of sexual partnerships can be key determinants of epidemic dynamics and intervention impact.²⁰ Eswatini-specific data on partnership duration are lacking. Moreover, accurate estimation of partnership duration remains challenging even when data exist, due to censoring, truncation, and sampling biases [156]. Similar to challenges in estimating sex work duration (§ A.2), we must distinguish the definition of an “average partnership” as (a) among all partnerships in a population over a given *time period*, vs. (b) among all partnerships in a population *cross-section*. Case (b) will be biased by partnership duration, so the estimated mean duration will longer, while case (a) reflects an unbiased estimate.²¹ The difference between the exponential distribution mean and median should also be kept in mind (see § A.2.1).

Main/Spousal Partnerships. Detailed data on marriage in Eswatini was only captured in 2006 [2, Table 6.1]. The median age of first marriage was 24.3 among women and 27.7 among men (26.0 overall). Approximately 64% of women and 88% of men (76% overall) who were ever married or living together were in a union at age 50–54. However, no data indicated whether any respondents had remarried or entered into a secondary union. Among women aged 40–49, the most recent data on median age of first marriage and proportions ever remarried were 33 years old and 6.6% in South Africa, 20.9 and 3.7% in Lesotho, and 18.7 and 28.4% in Mozambique [157]; such data may not capture non-marital secondary unions. Thus, I assumed 5–20% of unions among EmaSwati aged 50–54 were secondary. Further assuming an exponential distribution for the proportion of enduring partnerships ρ vs. time T per Eq. (3.2), I defined $\rho \in (0.56, 0.71)$, $t = 52 - 26 = 26$ years, yielding an effective partnership termination rate of $\lambda \in (1.32, 2.23)\%$ per year, and an effective partnership duration of $\delta_{p_1} = \lambda^{-1} \in (45, 76)$ years.

Classically, partnership duration is used to define the total numbers of sex acts per modelled partnership (see § ??); with this approach, we should therefore use $\delta_{p_1} = \rho(49 - 26) \in (14.5, 18.5)$ years, since the modelled population only includes ages 15–49. However, the proposed approach to modelling partnerships introduced in § ?? can make use of the effective termination rate. In fact, the proposed approach uses a partnership *change* rate, which would be even slower than the partnership termination rate, as the change rate would also consider whether and when divorced/separated individuals form *new* main/spousal partnerships. The change rate could even be tied to the modelled baseline and HIV-attributable mortality, given that the majority of unions ended via spousal death (83% of unions among women and 56% among men by age 50–54) [2]. For simplicity, I assumed an effective main/spousal partnership change rate of

²⁰ Chapter ?? also discusses the related phenomenon of partnership concurrency, and how concurrency is represented in compartmental models.

²¹ If case (a) durations are exponentially distributed, the durations in case (b) will be gamma-distributed with $\alpha = 2$, $\beta = \lambda$; thus the mean duration in case (b) will be $\alpha/\beta = 2\lambda$ (twice as long).

1–2% per year with the proposed approach (regardless of mortality), and effective duration of 14.5–18.5 years with the classic approach (both uniform priors).

Casual Partnerships. No data is available regarding durations of non-marital sexual partnerships in Eswatini, and regional data on are also limited. I synthesized the available partnership duration data from South Africa [158, 159, 160], Rural Tanzania [131], and four cities in Kenya, Zambia, Benin, and Cameroon [161]. Based on these data, I defined a gamma prior distribution for the mean duration of casual partnerships δ_{p_2} with 95% CI (0.25, 1.5) years, roughly consistent with prior models [162].

Sex Work Partnerships. As noted in § 3.2.7.2, duration of occasional sex work partnerships is ill defined, but can be defined to comprise a single sex act with $F_{p_3} \delta_{p_3} = 1$. Data on regular sex work partnerships is severely limited, and sometimes regular paying clients later become non-paying emotional partners [137, 163]. Based on [125], I defined a gamma prior distribution for the mean duration of regular sex work partnerships δ_{p_4} with 95% CI (0.5, 2.0) years.

3.2.11 Mixing

In addition to more concentrated transmission among FSW and their clients via regular and occasional sex work partnerships — which are *only* formed among FSW and clients — other types of partnerships may be formed preferentially between particular activity groups. For example, FSW and clients may be more likely to form main or casual partnerships with each other than with other activity groups. Such preferences are captured in a “mixing matrix” M , where $M_{pii'}$ denotes the total number of type- p partnerships formed between groups i and i' in the population (ignoring sex indices s, s' temporarily) — i.e., who has sex with whom. The mixing matrix $M_{pii'}$ must be symmetric, and have row/column sums equal to the total numbers of partnerships “offered” by any group: $M_{pi} = P_i C_{pi}$ (group size \times partnerships per-person).

3.2.11.1 Classic ϵ Mixing

In many risk/activity-stratified compartmental transmission models, mixing is parameterized via a single parameter $\epsilon \in [0, 1]$, which controls the degree of like-with-like mixing [164]. This approach is often attributed to [165], wherein a key adjustment for imbalanced partner numbers among women vs. men was introduced. The approach defines the *probability* of someone from group i forming a *given* type- p partnership with someone from group i' as:

$$\rho_{pii'} = (\epsilon) l_{ii'} + (1 - \epsilon) \pi_{ii'}, \quad l_{ii'} = \begin{cases} 1 & i = i' \\ 0 & i \neq i' \end{cases}, \quad \pi_{ii'} = \frac{M_{pi'}}{\sum_j M_{pj}} \quad (3.11)$$

where: l represents complete like-with-like mixing (an identity matrix), π represents random mixing (random but proportional to the number of partnerships “offered”), and ϵ effectively interpolates between these two extremes. Thus, $\epsilon = 0$ reflects fully random mixing, and $\epsilon = 1$ reflects fully like-with-like mixing. Then, the total numbers of type- p partnerships between groups i and i' can be defined as $M_{pii'} = M_{pi} \rho_{pii'}$. Three advantages of Eq. (3.11) are: (1) simplicity; (2) ϵ can be directly interpreted as the proportion of partnerships which are formed among like-with-like vs. randomly; and (3) it guarantees that M will be symmetric, even if P and/or C change. Yet, the simplicity of this approach precludes implementation of

more complex mixing patterns, although some modest extensions can be made, such as asymmetric age mixing among women and men (e.g., [166]).

3.2.11.2 Log-Linear Mixing

A more general approach to mixing is developed in [167]. This “log-linear” approach defines the mixing matrix elements $M_{pi i'}$ as follows. The expected total numbers of partnerships between risk groups under random mixing are defined as:

$$\Pi_{pi i'} = \frac{M_{pi} M_{pi'}}{\sum_j M_{pj}} \quad (3.12)$$

Next, a matrix $\Phi_{pi i'}$ is defined, representing the odds of a type- p partnership forming between groups i and i' , compared to random mixing. The matrix Φ must be symmetric, and can be estimated directly from the right kind of data (which is rarely available) [167]. Then, an initial estimate of $M_{pi i'}$ is:

$$\begin{aligned} M_{pi i'}^{(0)} &= \exp \left[\log \left(\Pi_{pi i'} \right) + \Phi_{pi i'} \right] \\ &= \Pi_{pi i'} \exp \left(\Phi_{pi i'} \right) \end{aligned} \quad (3.13)$$

However, this estimate changes the total numbers of partnerships formed by each group: $M_{pi}^{(0)} \neq \Pi_{pi}$, where $M_{pi} = \sum_{i'} M_{pi i'}$ and $\Pi_{pi} = \sum_{i'} \Pi_{pi i'}$. There is no *a priori* definition of $M_{pi i'}$ or adjustment to $\Phi_{pi i'}$ that can guarantee the numbers of partnerships will not change.²² However, an iterative proportional fitting procedure [168] can resolve an estimate $M_{pi i'}^{(n)}$ that maintains the total numbers of partnerships:

$$M_{pi i'}^{(n+1)} = M_{pi i'}^{(n)} \frac{\Pi_{pf}}{M_{pf}^{(n)}} \quad f = \begin{cases} i & \text{if } n \text{ is even} \\ i' & \text{if } n \text{ is odd} \end{cases} \quad (3.14)$$

Each step of this procedure can be understood as a re-scaling of the current estimate $M_{pi i'}^{(n)}$ row-wise (i) or column-wise (i') to match the numbers of partnerships offered by individuals (Π_{pi}) or their partners ($\Pi_{pi'}$). Each row-step re-introduces discrepancies in the columns, and vice versa, but overall convergence is guaranteed [169].

In practice, Eq. (3.14) adds approximately one decimal of precision per $2n$ for the 4×4 case, thus 15–20 iterations is often sufficient to come within computational precision limits. Since the partnerships matrix $M_{pi i'}$ should adapt to reflect changes in group sizes (e.g., due to HIV mortality) or numbers of partnerships offered (e.g., see § ??), the matrix must be re-computed at every time point. Thus, the procedure Eq. (3.14) could be considered computationally expensive. However, this approach provides great flexibility and interpretability to specify complex mixing patterns via the odds matrix $\Phi_{pi i'}$.

Adding back the sex dimension indices $i \rightarrow si$, $i' \rightarrow s'i'$, two final adjustments are needed for the bipartite (i.e., heterosexual) system. First, I ensure that $M_{s=s'} = \Pi_{s=s'} = 0$. Second, for the case when the total numbers of partnerships offered by women and men do not balance ($\sum_j M_{ps_1j} \neq \sum_j M_{ps_2j}$), I revise the denominator of Eq. (3.12) to $\sum_j \omega_s M_{psj}$, where ω_s are weights such that $\sum_s \omega_s = 1$. Similar to the “compromise” parameter θ in [165], if $\omega = \{1, 0\}$, then women’s partnership numbers are matched exactly

²² I hypothesize that this lack of *a priori* solution is the reason this approach has not been widely used.

while men adapt their partner numbers to balance; and conversely for $\omega = \{0, 1\}$. I fixed $\omega = \{0.5, 0.5\}$ for equal adaptation among women and men.

3.2.11.3 Odds of Mixing

Despite the flexibility in the odds of mixing matrix $\Phi_{pi'i'}$, limited data are available to inform specific elements, especially for Eswatini in particular. In Kenya [137], Benin, Guinea, and Senegal [139], and Uganda [163], a disproportionate fraction of non-paying partners of FSW were former and/or current clients. Given this fraction ψ and the proportion of all men who are clients ρ , the odds of these partnerships forming can be computed as:

$$\Phi = \frac{\psi(1-\rho)}{(1-\psi)\rho} \quad (3.15)$$

Taking $\psi \in (0.33, 0.70)$ [137, 139] and $\rho \in (5, 20)\%$ [148], we obtain $\Phi \in (2, 19)$. As noted in § 3.2.8.4, it's not clear whether such partnerships reflect main/spousal or casual partnerships. As such, I sampled a common value for both partnership types, as well as for higher/lower risk FSW and clients: $\Phi_{p_{12}i_{34}i'_{34}}$ from a gamma prior with 95% CI of (2, 19). I further assumed that lowest activity women and men had greater odds of forming main/spousal partnerships with each other, based loosely on age cohorting effects [170], observed like-with-like sexual mixing preferences in numerous other contexts [167, 171, 172], and prior modelling work [173]. I sampled $\Phi_{p_{11}i_{11}i'_{11}}$ from a gamma prior with 95% CI of (1.5, 3). I made no further assumptions about preferential mixing (i.e., all other elements $\Phi = 1$). Thus, I assumed that occasional and regular sex work partnerships form randomly with respect to higher vs. lower FSW and their clients.

3.3 Calibration

The parameters described in § 3.2 represent model inputs, many of which are uncertain. For each uncertain parameter, I have specified a prior distribution based on the available data and/or assumptions. Model calibration then aims to reduce this uncertainty — i.e., estimate the parameter posterior distributions — by comparing model *outputs* to additional data called “calibration targets”, under different combinations of input parameters. Section 3.3.1 describes the approach to calibration, while § 3.3.2 details the calibration targets used, including estimates of HIV incidence, prevalence, and the cascade of care for the population overall, and stratified by risk group where available.

3.3.1 Approach

I used a Bayesian approach for model calibration [174]. Let θ denote the complete set of 74 calibrated model parameters (Table C.1), and T the complete set of calibration targets. The goal of calibration is to obtain samples from the posterior distribution of parameters given the targets $p(\theta | T)$. This posterior distribution can be defined via Bayes' rule as:

$$p(\theta | T) = \frac{p(T | \theta) p(\theta)}{p(T)} \quad (3.16)$$

The posterior distribution was characterized empirically via Monte Carlo simulation — i.e., by randomly sampling parameter sets $\theta_s \sim p(\theta)$, and for each set computing the likelihood $p(T | \theta_s)$. This likelihood was defined via independent uncertainty distributions for each calibration target T_i . For example, overall HIV prevalence in Eswatini was estimated as 27.2%, 95% CI: (25.8, 28.7) in 2016 [5]; using this information, I defined a BAB distribution as the likelihood function for this calibration target $p(T_i | \theta)$. Thus, a parameter set θ_{s_1} which yields model-estimated overall HIV prevalence $T_i(\theta_{s_1}) = 25\%$ in 2016 would have a higher likelihood for this target than a parameter set θ_{s_2} which yields $T_i(\theta_{s_2}) = 20\%$ in 2016. The independent likelihoods for each target were aggregated on logarithmic scale to give the overall likelihood:

$$\log p(T | \theta_s) = \sum_i \log p(T_i | \theta_s) \quad (3.17)$$

Any individual log-likelihood which was beyond computational precision was replaced with an arbitrarily large negative number (-10^6). In order to obtain good coverage of the sampling space, most (57) calibrated parameters were sampled using Latin hypercube sampling [175]. The remaining 17 calibrated parameters were sampled randomly and iteratively until they satisfied a set of relational constraints (see § C.3.1).

Although several iterative methods exist to update the sampling distributions based on the likelihoods, and thereby characterize the posterior distribution more efficiently [174], I did not update the sampling distributions. Rather, I simply took the top 1% of parameter sets θ_s by likelihood, and assume these are approximately representative of the posterior distribution. Within the top 1%, I also did not weight parameter sets by likelihood.

3.3.2 Calibration Targets

The data sources for Eswatini calibration targets are mainly the same as for Eswatini-specific parameters. I assumed that population-level surveys in 2006 [2], 2011 [3, 4], and 2016 [5] reached FSW and their clients, although respondents may not report selling or buying sex in the context of these surveys.

3.3.2.1 HIV Prevalence

Table 3.5 summarizes the available HIV prevalence data for Eswatini. Uncertainty around each estimate was modelled using a BAB distribution. I made several adjustments to the estimates as follows.

Sampling Error. Population-level HIV prevalence estimates in 2006 and 2016 included expanded 95% CI (vs. standard binomial 95% CI) due to sampling error for women, men, and the population overall (Table B.2 in [2] and Table C.2 in [5]). This expanded 95% CI corresponds to a reduction in effective N vs. the sample N for the binomial distribution, by a factor of 41–75%. I applied this factor to equivalently expand the estimated 95% CI for the corresponding lower risk and non-lower risk women, men, and population overall in 2006 and 2016, and also for all 2011 HIV prevalence estimates [3].

Biased Partner Number Reporting. As discussed in § 3.2.8.2, I assumed that the proportion of the population reporting 0–1 sexual partners p6m (“lower risk”) is overestimated, and the proportion reporting 2+ (“non-lower risk”) is underestimated. While overall HIV prevalence estimates would not be affected by this reporting bias, HIV prevalence among the lower risk group would be overestimated. To correct

Table 3.5: Estimates of HIV prevalence in Eswatini

Population ^a	Year	N	Raw	Adjusted		Used	Ref	Notes
			%	%	(95% CI)			
Overall	2006	8,187	25.9	—	(24.4, 27.3)	✓	[2]	b
	2011	18,172	32.1	28.0	(27.0, 29.0)	✓	[3]	cd
	2016	8,533	27.2	—	(25.8, 28.7)	✓	[5]	b
Women Overall	2006	4,424	31.1	—	(29.4, 32.9)	✓	[2]	b
	2011	9,843	38.8	34.2	(33.0, 35.4)	✓	[3]	cd
	2016	4,878	34.3	—	(32.6, 36.0)	✓	[5]	b
Men Overall	2006	3,763	19.7	—	(17.9, 21.4)	✓	[2]	b
	2011	8,329	24.1	20.7	(19.6, 21.8)	✓	[3]	cd
	2016	3,655	18.8	—	(17.3, 20.4)	✓	[5]	b
LR Overall	2006	7,589	24.9	—	—	✗	[2]	
	2011	16,145	31.9	—	—	✗	[3]	
	2016	7,887	32.2	—	—	✗	[5]	
Non-LR Overall	2006	579	38.3	—	—	✗	[2]	
	2011	1,887	33.3	29.0	(25.9, 32.2)	✗	[3]	cd
	2016	914	28.7	—	(25.8, 31.7)	*	[5]	f
LR Women	2006	4,346	30.7	26.8	(22.7, 28.7)	*	[2]	e
	2011	9,843	38.2	30.8	(28.9, 32.8)	*	[3]	ce
	2016	5,203	36.5	31.5	(30.0, 33.1)	*	[5]	e
Non-LR Women	2006	72	53.0	—	(41.5, 64.3)	*	[2]	f
	2011	373	54.5	48.1	(41.5, 54.8)	*	[3]	cd
	2016	263	45.3	—	(39.3, 51.3)	*	[5]	f
LR Men	2006	3,243	17.1	14.1	(6.5, 16.7)	*	[2]	e
	2011	6,733	23.2	19.0	(18.0, 20.1)	*	[3]	ce
	2016	2,684	25.1	16.9	(15.7, 18.1)	*	[5]	e
Non-LR Men	2006	506	36.1	—	(32.0, 40.3)	*	[2]	f
	2011	1,515	28.1	24.1	(21.4, 26.9)	*	[3]	cd
	2016	651	22.8	—	(19.7, 26.1)	*	[5]	f
FSW Overall	2011	328	70.3	60.5	(52.1, 69.0)	✓	[33]	g
	2014	781	37.8	—	—	✗	[34]	h
	2021	676	60.8	58.8	(53.9, 63.6)	✓	[33]	g

^a LR: lower risk, reporting 0-1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; ^b 95% CI as reported from sampling adjustment; ^c adjusted from ages 18-49 to 15-49 (see § 3.3.2.1); ^d 95% CI expanded via inferred sampling adjustment; ^e adjusted for biased reporting of risk behaviours (see § 3.2.8.2 and § 3.3.2.1); ^f 95% CI inferred from N; ^g RDS-adjusted; ^h self-reported; * used within prevalence ratio only; all estimates used the BAB distribution.

Table 3.6: Estimated HIV prevalence ratios in Eswatini

Numerator ^a	Denominator ^a	Year	Ratio	(95% CI)	Used	Ref	Notes
Non-LR Women	LR Women	2006	2.02	(1.84, 2.34)	✓	[2]	b
		2011	1.54	(1.47, 1.66)	✓	[3]	b
		2016	1.42	(1.37, 1.51)	✓	[5]	b
Non-LR Men	LR Men	2006	2.57	(2.16, 5.28)	✓	[2]	b
		2011	1.24	(1.20, 1.34)	✓	[3]	b
		2016	1.32	(1.26, 1.45)	✓	[5]	b
FSW Overall	Women Overall	2011	2.16	(1.87, 2.50)	✓	[33, 3]	b
HR FSW	LR FSW	2011	1.46	(1.30, 1.63)	✓	[33]	c
		2014	2.30	(1.92, 2.75)	✗	[34]	cd

^a LR: lower risk, reporting 0–1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; HR/LR FSW: higher/lower risk FSW, as defined in § 3.2.1; ^b mean and 95% CI estimated via Monte Carlo sampling; ^c per analysis in § 3.2.1.3; ^d self-reported; see Table 3.5 for more notes on data sources and adjustments.

this overestimate, I further assumed that HIV prevalence among “observed” non-lower risk (had 2+ partners p6m, reported 2+) was representative of HIV prevalence among “unobserved” non-lower risk (had 2+, reported 0–1). Thus, HIV prevalence among the “true” lower risk (had 0–1, reported 0–1) can be estimated as:

$$H_{01} = \frac{H - H_{2+}W'_{2+}}{W'_{01}} \quad (3.18)$$

where H denotes HIV prevalence, and W' denotes the adjusted proportions calculated in § 3.2.8.3.

Respondent Ages. The 2006 and 2016 surveys provide data for ages 15–49 (the age range intended to be captured by the model) while the 2011 survey was limited to ages 18–49. Since HIV prevalence is much lower among ages 15–17, the 2011 estimates would be biased high; so, I adjusted all 2011 HIV prevalence estimates in as follows. Drawing on age-stratified data in 2006 [2] and 2011 [3], I assumed that HIV prevalence among ages 15–17 was 5% among girls/women, 2% among boys/men, and 3.5% overall. Next, I estimated the fraction of women aged 15–17 among all women aged 15–49 (13.5%), and likewise for men (15.4%) and overall (14.4%) [176]. I then estimated HIV prevalence among women, men, and overall for ages 15–49 using a weighted average of the 15–17 and 18–49 estimates. Finally, I computed the resulting relative reduction in HIV prevalence for women overall, and applied this reduction equally to the HIV prevalence estimates for lower risk and non-lower risk women, and likewise for men and the population overall.

Since risk heterogeneity is a key determinant of epidemic dynamics, it is important to capture HIV prevalence ratios across risk groups. For this objective, directly specifying prevalence ratio targets is more efficient than using independent prevalence targets for lower risk and non-lower risk. Based on the available data, I defined the prevalence ratio targets in Table 3.6.

The raw (unadjusted) estimates suggest that HIV prevalence strongly peaked between 2006 and 2016. After adjustment for respondent ages, 2011 estimates remained highest, but the magnitude of differences with 2006 and 2016 was reduced substantially. The largest reduction in HIV prevalence via adjustment was among lower risk women in 2011: from 38.2% to 30.8%, due to the modelled “addition” of women/girls aged 15–17 (lower HIV prevalence), and “subtraction” of women with 2+ partners p6m (higher HIV

Table 3.7: Estimates of HIV incidence in Eswatini

Population ^a	Year	N	Raw	Adjusted		Used	Ref	Notes
			%	%	(95% CI)			
Overall	2016	9,476	1.48	—	(0.96, 1.99)	✓	[5]	bc
Women Overall	2011	5,486	3.1	2.94	(2.52, 3.47)	✓	[4]	de
	2016	5,227	1.99	—	(1.16, 2.80)	✓	[5]	bc
Men Overall	2011	5,746	1.7	1.50	(1.16, 1.84)	✓	[4]	de
	2016	4,249	0.99	—	(0.39, 1.59)	✓	[5]	bc
LR Women	2011	4,924	3.21	1.58	(0.40, 2.24)	*	[4]	def
Non-LR Women	2011	93	10.10	9.62	(4.76, 18.29)	*	[4]	de
LR Men	2011	3,855	1.64	0.76	(0.01, 1.17)	*	[4]	def
Non-LR Men	2011	874	3.87	3.42	(2.21, 4.94)	*	[4]	de
FSW Overall	2021	676	11.71	—	(8.31, 16.92)	✓	[35]	b

^a LR: lower risk, reporting 0–1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; ^b via HIV-1 Limiting Antigen recency testing; ^c 95% CI as reported from sampling adjustment; ^d via 6 month cohort (94.4% follow-up); ^e adjusted from ages 18–49 to 15–49 (see § 3.3.2.1); ^f adjusted for biased reporting of risk behaviours (see § 3.2.8.2 and § 3.3.2.1); * used within incidence ratio only; all estimates used the skew normal distribution.

prevalence).

3.3.2.2 HIV Incidence

Population-level incidence was first measured in the 2011 Swaziland HIV Incidence Measurement Survey (SHIMS) via 6-month cohort (gold standard) [62, 4], in which 145 seroconversions were observed among 11,232 re-tested (LTFU was 5.6%). The follow-up SHIMS2 study in 2016–17 used the HIV-1 Limiting Antigen Enzyme Immunoassay (LAG EIA) “recency test”, which detects infections acquired within the past 141 days, 95%CI: (119, 160) [177]; this LAG EIA incidence measure was validated during SHIMS1 [62]. Recency testing was also recently integrated into Eswatini standard of care [63].

Table 3.7 summarizes the available HIV incidence data for Eswatini. Uncertainty around each estimate was modelled using a skewnormal or inverse gaussian distribution. As with prevalence, the 2011 estimates were adjusted for the missing 15–17 age range, this time assuming 2% and 0.4% annual incidence among girls/women and boys/men aged 15–17, respectively (extrapolating from age-stratified incidence estimates from [4]). The 2011 estimates for lower risk women and men were also adjusted for biased partner number reporting using the same approach as for HIV prevalence. Two incidence ratios were also defined (Table 3.8).

No study of FSW in Eswatini estimated incidence directly, but [35] reported that 30 of 676 prevalent HIV infections among FSW were identified as recent via LAG EIA per national guidelines [5, 63]. Using Eq. (3.2) with $\rho = 30/676 = 4.44\%$ and $T = 130$ days, I computed an incidence rate of $\lambda = 11.7\%$ per year. I further estimated uncertainty for this rate by combining the 95% CI from $\rho \sim \text{Binom}(\rho = 4.44\%, N = 676)$ and $T \in (118, 140)$, yielding 95% CI for λ of (8.3, 16.9).

Table 3.8: Estimated HIV incidence ratios in Eswatini

Numerator ^a	Denominator ^a	Year	Ratio	(95% CI)	Used	Ref	Notes
Non-LR Women	LR Women	2011	5.74	(2.47, 22.26)	✓	[3]	^b
Non-LR Men	LR Men	2011	4.16	(1.69, 23.09)	✓	[3]	^b

^a LR: lower risk, reporting 0-1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; ^b mean and 95% CI estimated via Monte Carlo sampling; see Table 3.7 for more notes on data sources and adjustments.

3.3.2.3 HIV Cascade of Care

Table 3.9 summarizes the available data for the HIV cascade of care in Eswatini, including estimates stratified by risk group where possible. Both conditional (e.g., on ART among diagnosed, “90-90-90”) and unconditional (e.g., on ART among PLHIV, “90-81-73”) cascade data were included, which is redundant but may improve calibration quality. Unlike HIV prevalence and incidence calibration targets, no adjustments were applied to these data. A recent meta-analysis [178] suggested substantial under-reporting of known HIV+ status, including 9 (4, 15)% among the population overall (10 studies), and 32 (22, 44)% among FSW specifically (2 studies). However, data from SHIMS2 [5] suggested much lower under-reporting (2.2%) in Eswatini.

3.4 Results

This section presents the results of model calibration, including: the posterior distributions of calibrated parameters, and the modelled patterns of transmission among risk groups in Eswatini over time.

3.4.1 Posterior Parameter Distributions

Figure 3.6 illustrates the distributions of calibrated model parameters, stratified by top 1% (posterior) vs bottom 99% according to calibration likelihood. Many of the distributions do not significantly differ (Kolmogorov-Smirnov Test [180]), indicating that calibration did not reduce uncertainty in these parameters. While more advanced model calibration techniques might improve parameter inference [174], the overall model fit was judged to be sufficient for the downstream research questions (§ ??). A total of 19 parameters had highly significant differences ($p < 10^{-5}$) between prior and posterior distributions:

- **Mean increased:** aRbeta_gud_inf, aRbeta_gud_sus, beta_0, C12m_cas_wm, C1m_swr_fsw_l, dur_acute, dur_cas, F_msp, F_swr, PF_ai_mcx, PX_w_fsw, Rbeta_acute, RC_cas_cli.wm, RF_cas.msp
- **Mean decreased:** dur_cli, dur_fsw_l, dx_wq_2011, Rdx_global, Rdx_m.wq_2011

Such differences overwhelmingly tended towards increasing overall HIV transmission, suggesting that the set of prior distributions tended to underestimate transmission risk, despite several adjustments towards increasing transmission risk (§ 3.2). Indeed, the high HIV prevalence in Eswatini, and other generalized epidemics, has long been challenging to explain based on the available data [181, 182].

Figure 3.7 further illustrates bivariate rank correlations among posterior parameter values (subset of parameters with at least one correlation ± 0.1). Of these 19 parameters, 12 were subject to relational con-

Table 3.9: Estimated HIV cascade of care in Eswatini

Step ^a	Population ^a	Year	N	%	(95% CI)	Used	Ref	Notes
Diagnosed among PLHIV	Overall	2011	5,807	62.6	(61.4, 63.8)	✓	[90]	bc
		2016	2,417	86.1	(84.7, 87.6)	✓	[5]	e
	Women overall	2011	3,810	69.1	(67.6, 70.6)	✓	[90]	b
		2016	1,690	90.2	(88.6, 91.8)	✓	[5]	e
	Men overall	2011	1,997	50.1	(47.9, 52.3)	✓	[90]	b
		2016	727	77.3	(74.0, 80.6)	✓	[5]	e
	FSW	2011	313	74.1	(61.7, 89.8)	✓	[179]	d
		2021	411	88.3	(85.1, 91.2)	✓	[35]	bf
On ART among Diagnosed	Overall	2011	3,635	52.1	(50.5, 53.7)	✓	[90]	bcd
		2016	2,113	87.8	(86.0, 89.6)	✓	[5]	e
	Women overall	2011	2,633	48.0	(46.1, 49.9)	✓	[90]	bd
		2016	1,532	87.5	(85.4, 89.6)	✓	[5]	e
	Men overall	2011	1,002	62.7	(59.7, 65.7)	✓	[90]	bd
		2016	581	88.4	(85.2, 91.6)	✓	[5]	e
	FSW	2011	174	36.9	(30.1, 44.2)	✓	[179]	
		2021	363	97.5	(95.7, 98.9)	✓	[35]	bf
On ART among PLHIV	Overall	2011	5,807	31.9	(30.7, 33.1)	✓	[90]	bc
		2016	2,417	75.6	(73.6, 77.5)	✓	[5]	e
	Women overall	2011	3,810	33.2	(31.7, 34.7)	✓	[90]	b
		2016	1,690	78.9	(76.8, 81.1)	✓	[5]	e
	Men overall	2011	1,997	31.4	(29.4, 33.4)	✓	[90]	b
		2016	727	68.3	(64.7, 72.0)	✓	[5]	e
	FSW	2011	313	27.4	(20.9, 35.7)	✓	[179]	d
		2021	411	86.1	(82.6, 89.3)	✓	[35]	bf
VLS among On ART	Overall	2016	1,858	90.3	(89.0, 91.6)	✓	[5]	e
	Women overall	2016	1,342	91.4	(89.9, 92.8)	✓	[5]	e
	Men overall	2016	516	87.6	(84.4, 90.9)	✓	[5]	e
VLS among PLHIV	Overall	2016	2,417	68.2	(66.1, 70.4)	✓	[5]	e
	Women overall	2016	1,690	72.1	(69.7, 74.5)	✓	[5]	e
	Men overall	2016	727	59.9	(56.1, 63.7)	✓	[5]	e

^a PLHIV: people living with HIV; ART: antiretroviral therapy; VLS: HIV viral load suppressed, defined as ≤ 1000 RNA copies/mL in [5]; FSW: female sex worker; ^b 95% CI inferred from N; ^c estimated from combining women & men; ^d estimated from conditional steps, with 95% CI via simulation; ^e 95% CI as reported from sampling adjustment; ^f not RDS-adjusted.

3.4 RESULTS

39

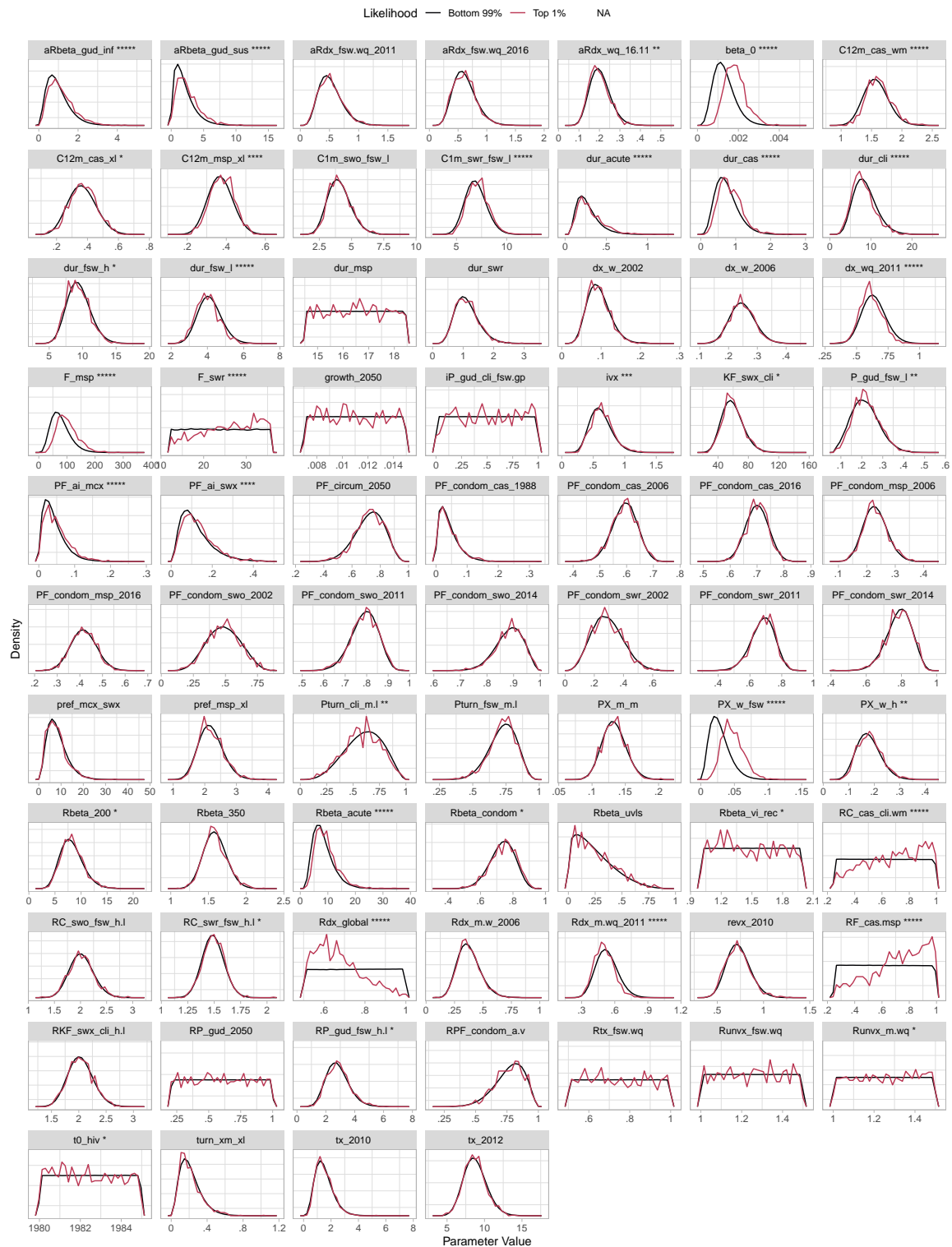


Figure 3.6: Distributions of calibrated model parameters, stratified by top 1% (posterior) vs bottom 99% according to calibration likelihood

Asterisks denote significance of Kolmogorov-Smirnov (KS) Test [183] for comparing distributions, where $p < 0.1$: *, $p < 0.01$: **, etc; see Table C.1 for parameter definitions

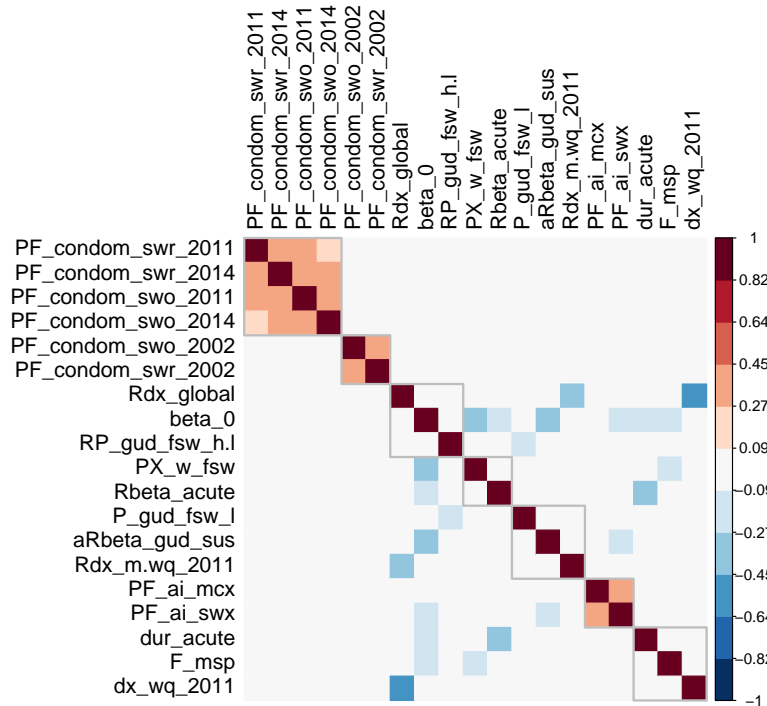


Figure 3.7: Rank correlations among selected posterior model parameters

Subset of parameters with at least one correlation ± 0.1 ; layout computed via hierarchical clustering using the Ward-2 criterion [180]; gray squares denote computed clusters; see Table C.1 for parameter definitions

straints (§ C.3.1) and 11 had highly significant differences between prior and posterior distributions. For example, condom use levels were *positively* correlated across regular and occasional sex work partnerships, including over time (PF_condom_swr*), as were the proportions of anal sex acts in sex work vs. non-sex work partnerships (PF_ai_*). Multiple combinations of parameters with similar influence on transmission dynamics were *negatively* correlated, such as the baseline per-act probability of transmission (beta_0) vs. relative susceptibility due to GUD (aRbeta_gud_sus), and diagnosis rates overall (Rdx_global) vs. among specific risk groups (dx_wq_2011, Rdx_m.wq_2011).

These correlated parameters reflect challenges of non-identifiability [184], although no parameters in the model are perfectly non-identifiable. Thus, the variance of posterior distributions may be inflated for these parameters [184], but so long as the joint posterior maintains the observed correlations — i.e., individual parameter values are not permuted among posterior parameter sets — the resulting epidemic simulations should remain plausible.

3.4.2 Calibration

Figure 3.8 illustrates the modelled HIV prevalence and incidence among selected risk groups and the associated calibration targets.

Figure 3.9 illustrates the modelled HIV cascade of care among selected risk groups and the associated calibration targets.

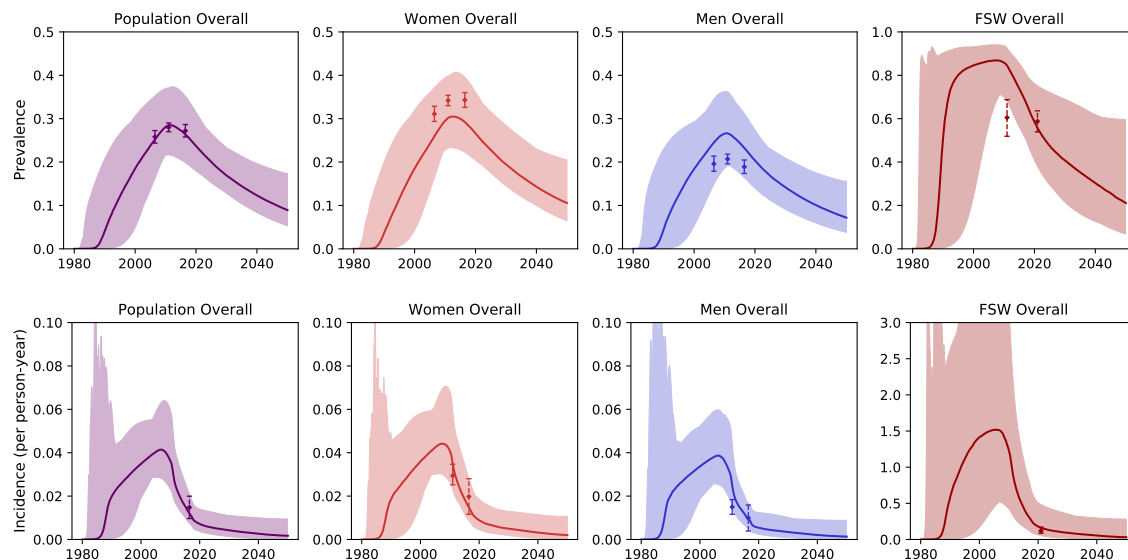


Figure 3.8: Modelled HIV prevalence and incidence among selected risk groups and associated calibration targets

1000 model fits (top 1% by likelihood among 100,000 sampled parameter sets); ribbon and curve: range and median of model fits; points and error bars: mean and 95% CI for each calibration target.

Additional Figures are given in § C.3.2, including: HIV prevalence ratios (C.6), HIV incidence ratios (C.7), total Eswatini population size aged 15–49 (C.8), and condom use within each partnership type (C.9).

3.4.3 Eswatini HIV Epidemic

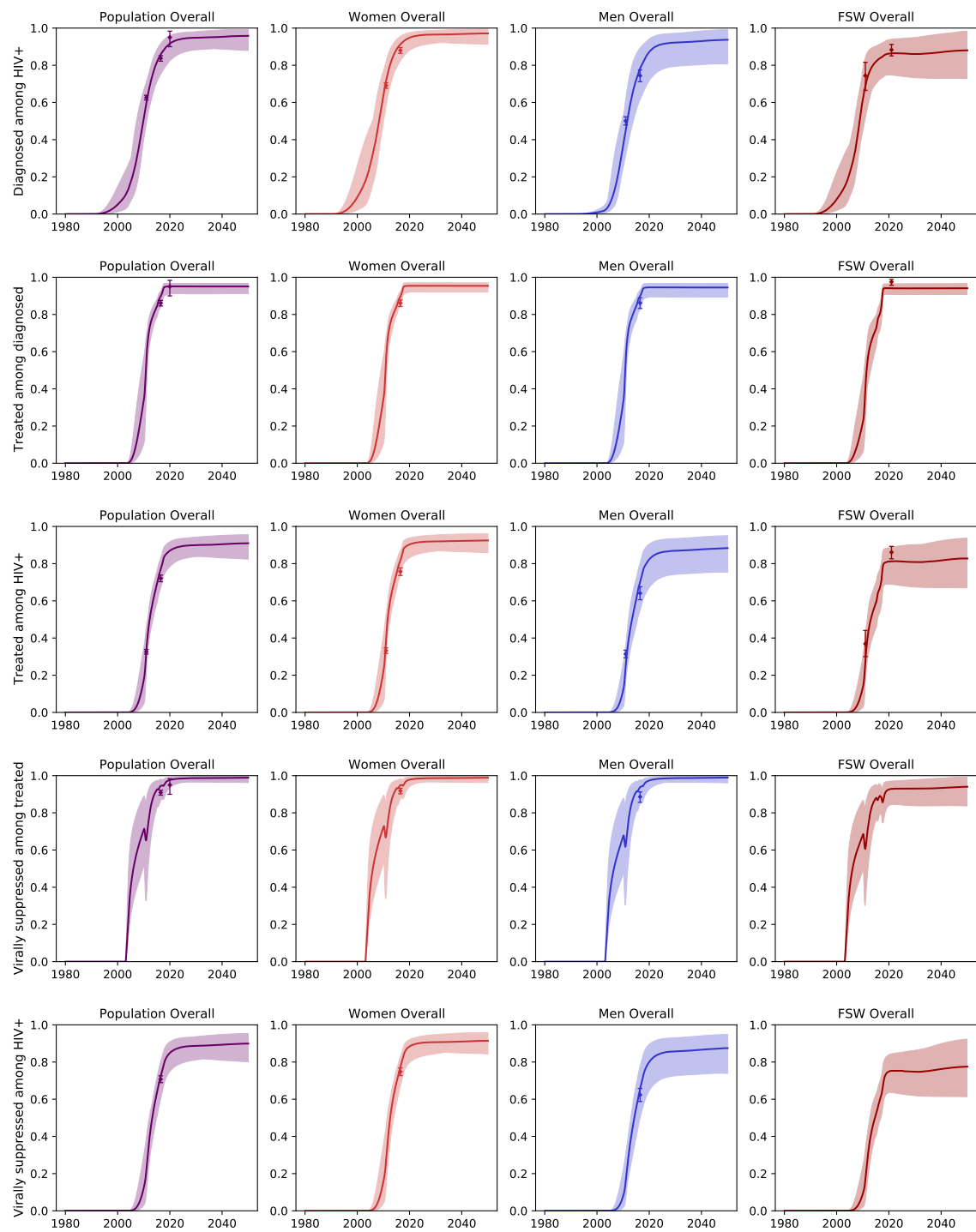


Figure 3.9: Modelled HIV cascade of care among selected risk groups and associated calibration targets
1000 model fits (top 1% by likelihood among 100,000 sampled parameter sets); ribbon and curve: range and median of model fits; points and error bars: mean and 95% CI for each calibration target.

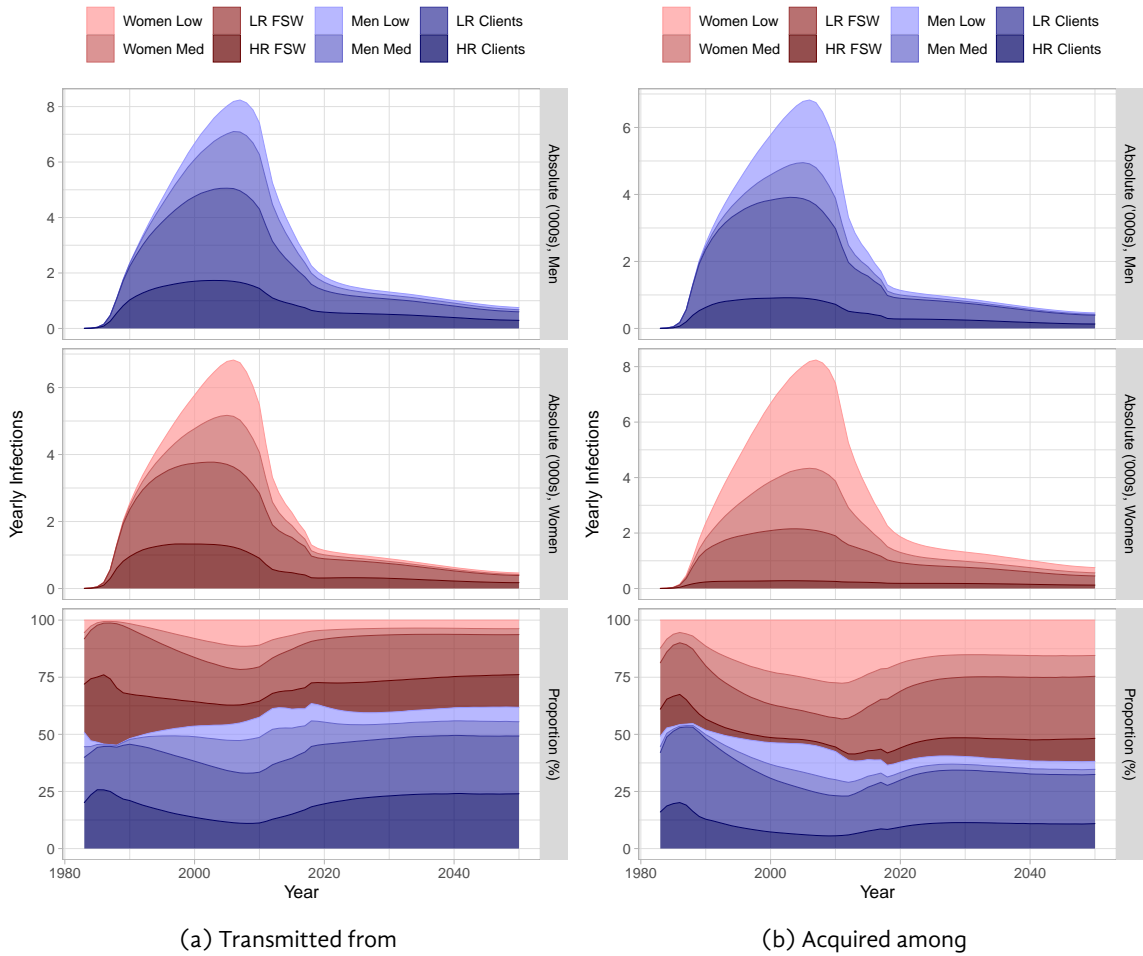


Figure 3.10: Absolute numbers and proportions of modelled yearly HIV infections (a) transmitted from and (b) acquired among risk groups in Eswatini

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 shown.

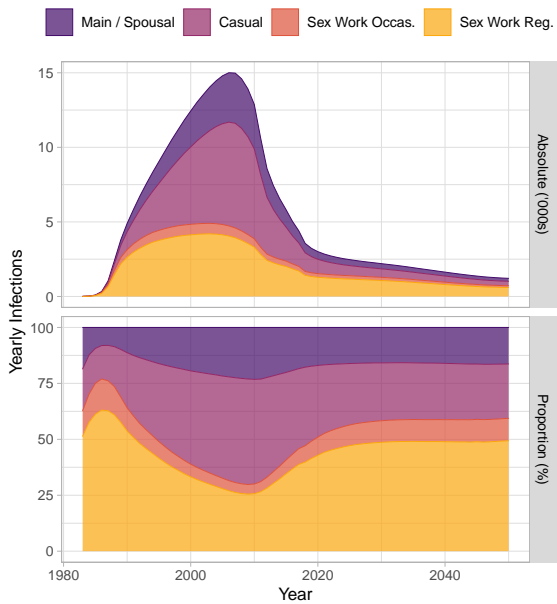


Figure 3.11: Absolute numbers and proportions of modelled yearly HIV infections transmitted via different partnership types in Eswatini

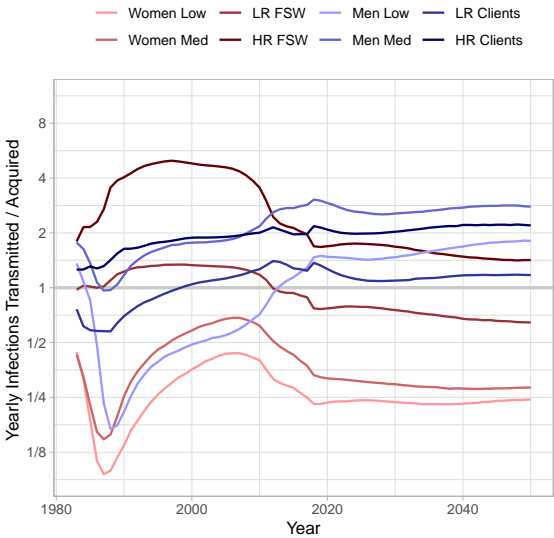


Figure 3.12: Ratio of modelled yearly infections transmitted from vs acquired among risk groups in Eswatini

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 shown.

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Appendix A

Supporting Mathematics

A.1 Distributions

A.1.1 Fitting Distributions

Uncertainty distributions for all parameters and calibration targets were estimated by fitting a parametric distribution to specified quantiles. Let $f(x | \theta)$ be the probability density function of random variable x (parameter or target) given distribution parameters θ . Then $F(x | \theta) = \int_0^x f(\tau) d\tau$ is the cumulative distribution function, and $Q(p | \theta) = F^{-1}(p | \theta)$ is the quantile function. Our objective is to estimate θ , given a set of quantiles (e.g., $q = \{q_{2.5}, q_{97.5}\}$ for the 95% CI). For each estimation, I minimized¹ the the following error function:

$$J(\theta) = \sum_i |q_i - Q(p_i | \theta)|^\omega \quad (\text{A.1})$$

where ω can specify absolute differences ($\omega = 1$) or squared differences ($\omega = 2$) to improve convergence. Distribution fit was validated visually using a plot of the distribution quantiles $Q(p_i | \theta)$ vs. the target quantiles q_i , overlaid on the density distribution $f(x | \theta)$; e.g., Figure A.1.

A.1.2 Beta Approximation of the Binomial (BAB) Distribution

Numerous model parameters and calibration targets represent population proportions. Such proportions can be estimated as $\rho = n/N$, where N is the sample size and n is the number of individuals with the characteristic of interest. The uncertainty around n is then given by the binomial distribution:

$$p(n) = \binom{N}{n} \rho^n (1 - \rho)^{N-n} \quad (\text{A.2})$$

However, Eq. (A.2) is only defined for discrete values of n . It is more convenient to have a continuous distribution for ρ , for sampling parameters and evaluating the likelihood of calibration targets, since compartmental models can have non-whole-number population sizes. For this purpose, I use a beta

¹ Using docs.scipy.org/doc/scipy/reference/optimize.minimize-lbfgsb.html

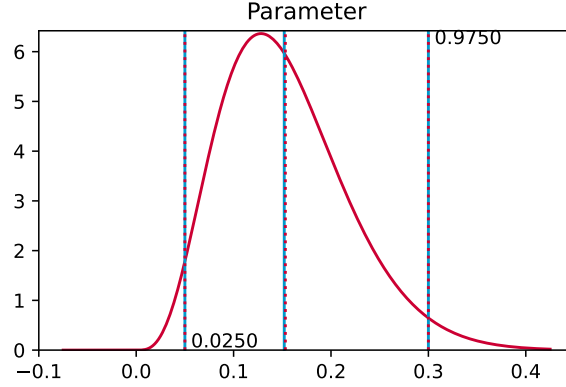


Figure A.1: Example distribution fitting validation plot

BAB distribution fit to $\{q_{2.5} = .05, q_{97.5} = .30\}$; blue solid lines: target quantiles q_i ; red dotted lines: distribution quantiles $Q(p_i | \theta)$; red solid line: density distribution $f(x | \theta)$.

approximation of the binomial distribution (BAB):

$$p(\rho) = \frac{\Gamma(\alpha + \beta)}{\Gamma(\alpha)\Gamma(\beta)} \rho^{\alpha-1} (1 - \rho)^{\beta-1} \quad (\text{A.3})$$

with $\alpha = N\rho$ and $\beta = N(1 - \rho)$. Unlike the approximation by a normal distribution, the beta distribution ensures that $\rho \in [0, 1]$. Figure A.2 illustrates the approximation for $N = \{10, 20, 40\}$ and $\rho = \{0.01, 0.1, 0.5\}$.

A.1.3 Joint Sampling with Relational Constraints

Figure A.3 illustrates the posterior (sampled) distributions for variables X_1, X_2, X_3 , having uniform priors but subject to $X_1 < X_2 < X_3$. Three approaches to enforcing $X_1 < X_2 < X_3$ were explored:

- **joint:** sample X_1, X_2, X_3 simultaneously; then discard any samples failing $X_1 < X_2 < X_3$.
- **forward:** sample X_1 ; then sample X_2 until $X_1 < X_2$; then sample X_3 until $X_2 < X_3$.
- **backward:** sample X_3 ; then sample X_2 until $X_2 < X_3$; then sample X_1 until $X_1 < X_2$.

All three methods result in a different posterior vs. the prior, but the forward and backward methods severely distort the distributions for X_3 and X_1 , respectively, while leaving the distributions for X_1 and X_3 unchanged. By contrast, the joint method influences the posterior distributions of each variable in a more “equitable” way, which is preferred.

A.2 Durations

A.2.1 Exponential Duration Assumption in Compartmental Models

Let λ be the fixed exit rate from compartment A, which is assumed to be homogeneous. Then $\delta \sim \lambda e^{-\lambda\delta}$ is the exponentially distributed duration time in the group.

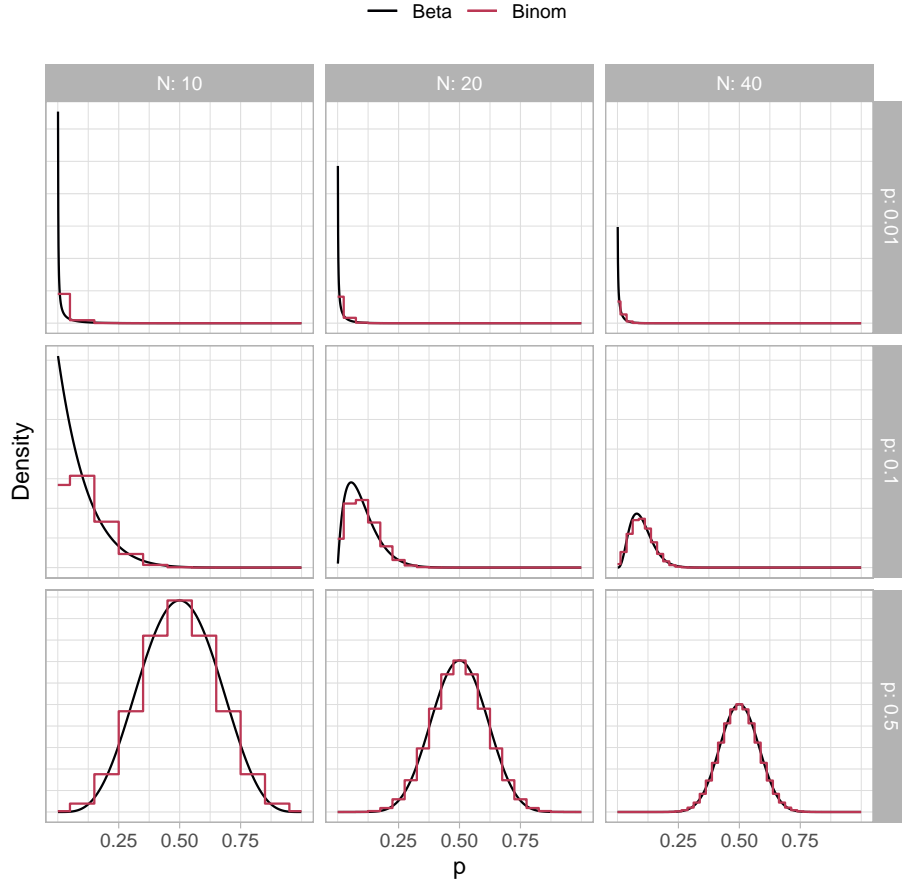


Figure A.2: Beta approximation of the binomial distribution (BAB)

Mean & Median Duration. The mean duration is $\mu = 1/\lambda$ and the median is $m = \log(2)/\lambda \approx 0.69 \mu$. Thus, if 50% of individuals progress from compartment A to B by time τ (median duration), the exit rate λ is given by $\log(2)/\tau$.

Collapsing Compartments in Series. Let compartments A and B be in series, with exit rates λ_A and λ_B respectively. Collapsing A and B into AB will sum the mean durations: $\delta_{AB} = 1/\lambda_A + 1/\lambda_B$; thus, the exit rate from AB will be $\lambda_{AB} = 1/(1/\lambda_A + 1/\lambda_B)$.

Collapsing Compartments in Parallel. Let compartments A and B be in parallel, with exit rates λ_A and λ_B respectively. Collapsing A and B into AB will sum the exit rates: $\lambda_{AB} = \lambda_A + \lambda_B$; thus, the mean duration in AB will be $\delta_{AB} = 1/(\lambda_A + \lambda_B)$.

A.2.2 Estimating Duration in Sex Work from Cross Sectional Data

Cross sectional sex work surveys will often ask respondents about their duration in sex work. These durations might then be taken to be the average durations in sex work; however, this will be an underestimate,

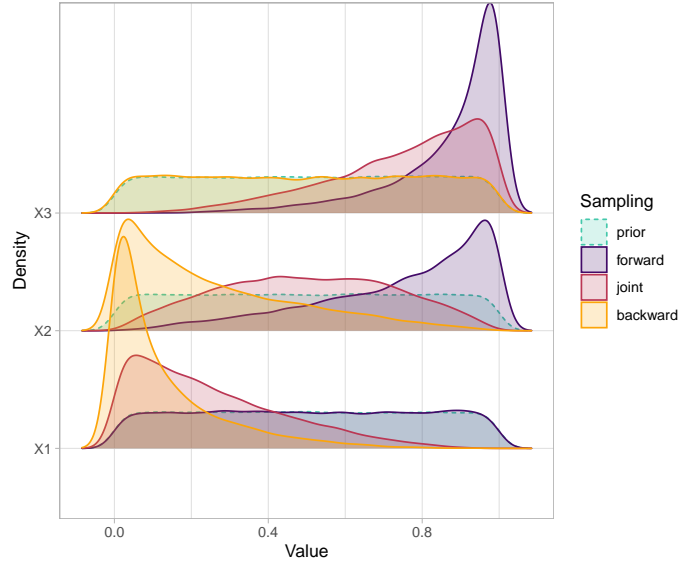


Figure A.3: Illustration of different sampling biases when enforcing $X_1 < X_2 < X_3$

because respondents will continue selling sex after the survey [1].²

Figure A.4 illustrates a steady-state population with 7 women selling sex at any given time. The steady-state assumption implies that a women leaving sex work after δ years will be immediately replaced by a women entering sex work whose eventual duration will also be δ years. Let δ be this true duration, and δ_s be the duration reported in the survey. If we assume that the survey reaches women at a random time point during the duration δ , then $\delta_s \sim \text{Unif}(0, \delta)$, and the mean reported duration is $E(\delta_s) = \frac{1}{2}E(\delta)$. Thus, $E(\delta) = 2E(\delta_s)$ would be an estimate of the true mean duration from the sample. In reality, sex work surveys may be more likely to reach women who have already been selling sex for several months or years, due to delayed self-identification as sex worker [2]. Thus, we would expect that $f = E(\delta)/E(\delta_s) \in (1, 2)$, which we can use to compute the mean exit rate as described in § A.2.1.

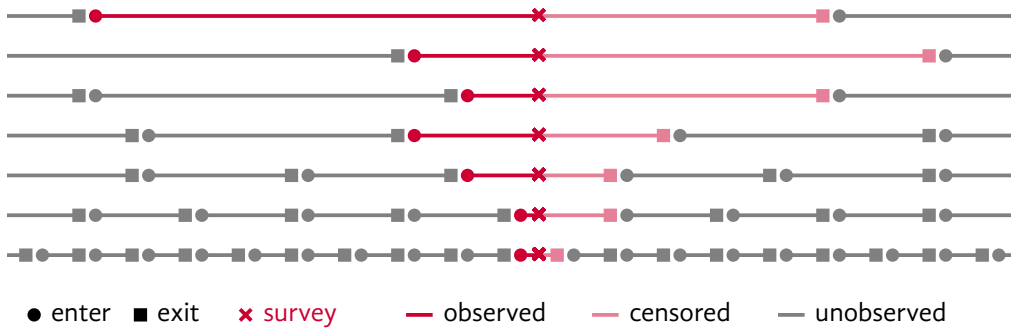


Figure A.4: Illustrative steady-state population of 7 FSW, with varying true durations in sex work δ , vs. the observed durations in sex work δ_s via cross-sectional survey.

² An alternate example would be to take the mean age of a population as the life expectancy! Thanks to Saulius Simcikas and Dr. Jarle Tufto for help identifying and discussing this bias: stats.stackexchange.com/questions/298828.

Another observation we can make from Figure A.4 is that women who sell sex longer are more likely to be captured in the survey. That is, while the sampled durations are representative of women who *currently* sell sex, these durations are biased high vs. the population of women who *ever* sell sex. It's not clear whether this observation is widely understood and kept in mind when interpreting sex work survey data.

A.2.3 Quantifying Partnerships

Similar to § A.2.2, sexual partnerships are often quantified using cross-sectional surveys. In this case, respondents are typically asked to report the numbers of unique partners during a standardized recall period γ — e.g., “How many different people have you had sex with during the past year?” Such data can then be used to inform modelled rates of partnership change Q and/or numbers of concurrent partnerships K .

If partnership duration is long and the recall period is short — including $\gamma \approx 0$ for “Are you currently in a long-term sexual partnership?” — the reported partnerships mostly reflect *ongoing* partnerships, and thus $C \approx K$. If partnership duration is short and the recall period is long, — including $\delta \approx 0$ for “How many one-off sexual partners have you had during the past year?” — the reported partnerships mostly reflect *complete* partnerships, and thus $C/\gamma \approx Q$. However, if partnership duration and recall period are similar in length, the reported partnerships reflect a mixture of tail-ends, complete, and ongoing partnerships, and thus C overestimates K , but C/γ also overestimates Q . In summary:

- $\gamma \ll \delta$: mostly ongoing partnerships; $C \approx K$ (concurrent)
- $\gamma \gg \delta$: mostly complete partnerships; $C/\gamma \approx Q$ (change rate)
- $\gamma \approx \delta$: some tail-ends, some complete, some ongoing; $C > K$, $C/\gamma > Q$ (neither)

I developed an approach to estimate Q and K from C and γ . The approach draws on a similar assumption as in § A.2.2: that survey timing is effectively random with respect to partnership duration. Then, if either end of the recall period would capture an ongoing partnership, the intersection point would be, on average, at the partnership mid-point. Thus, the recall period is effectively extended by half the partnership duration $\delta/2$ on each end, and δ overall, as illustrated in Figure A.5. As such, we can define Q and K as:

$$Q = \frac{C}{\gamma + \delta} \tag{A.4}$$

$$K = \frac{C\delta}{\gamma + \delta} = Q\delta \tag{A.5}$$

As an example, Figure A.5 illustrates a recall period of $\gamma = 6$ years, for which $C = 9$ partnerships are reported, having durations of $\delta = 3$ years. Thus, we can compute $Q = 9/(6 + 3) = 1$ and $K = 1(3) = 3$, which can be verified by careful examination of Figure A.5.

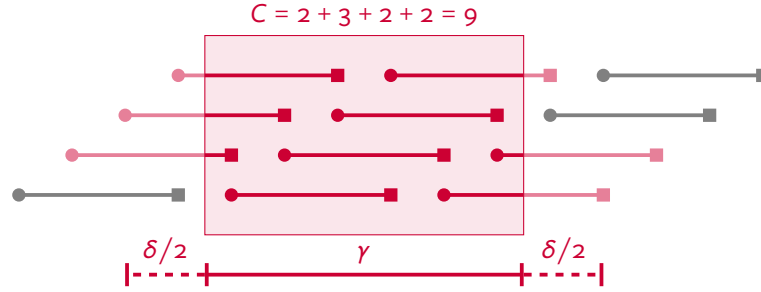


Figure A.5: Illustration of conceptual framework for quantifying partnerships from the number reported during a given recall period

Circle: partnership start; line: ongoing partnership; square: partnership end; red: reported partnership; grey: partnership not reported; γ /red: recall period; δ : partnership duration; C : number of reported partnerships for γ .

A.3 Miscellaneous

A.3.1 Proof that $B_{WPH} \geq B_{BPH}$

In § ??, I claimed that the per-partnership probability of transmission B is larger for within- vs. between-partnership heterogeneity — $B_{WPH} \geq B_{BPH}$, from Eqs. (??) and (??), respectively — given the same set of transmission modifiers R_f, α_f . Here is a proof of that claim:

$$B_{WPH} \geq B_{BPH} \\ 1 - \prod_f (1 - \beta_f)^{A\alpha_f} \geq 1 - \sum_f \alpha_f (1 - \beta_f)^A \quad (A.6)$$

Let $x_f = (1 - \beta_f)^A$; then

$$\prod_f x_f^{\alpha_f} \leq \sum_f \alpha_f x_f \quad (A.7)$$

Since $\sum_f \alpha_f = 1$ and $\alpha_f \in [0, 1]$ are effectively weights, Eq. (A.7) is the weighted arithmetic mean–geometric mean (AM–GM) inequality [3]. In fact, Aldaz [3] further shows that the the gap between B_{WPH} and B_{BPH} increases with the α_f -weighted variance in $\beta_f^{\frac{1}{2}}$ (although the increase is not exact), which supports the results of § ?? mathematically.

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Appendix C

Supplement to Chapter 3

C.1 Female Sex Worker Data

C.1.1 FSW Risk Factor Variable Distributions

Figures C.1 and C.2.

C.1.2 Years Since First Sold Sex

Figure C.3. Figure C.4.

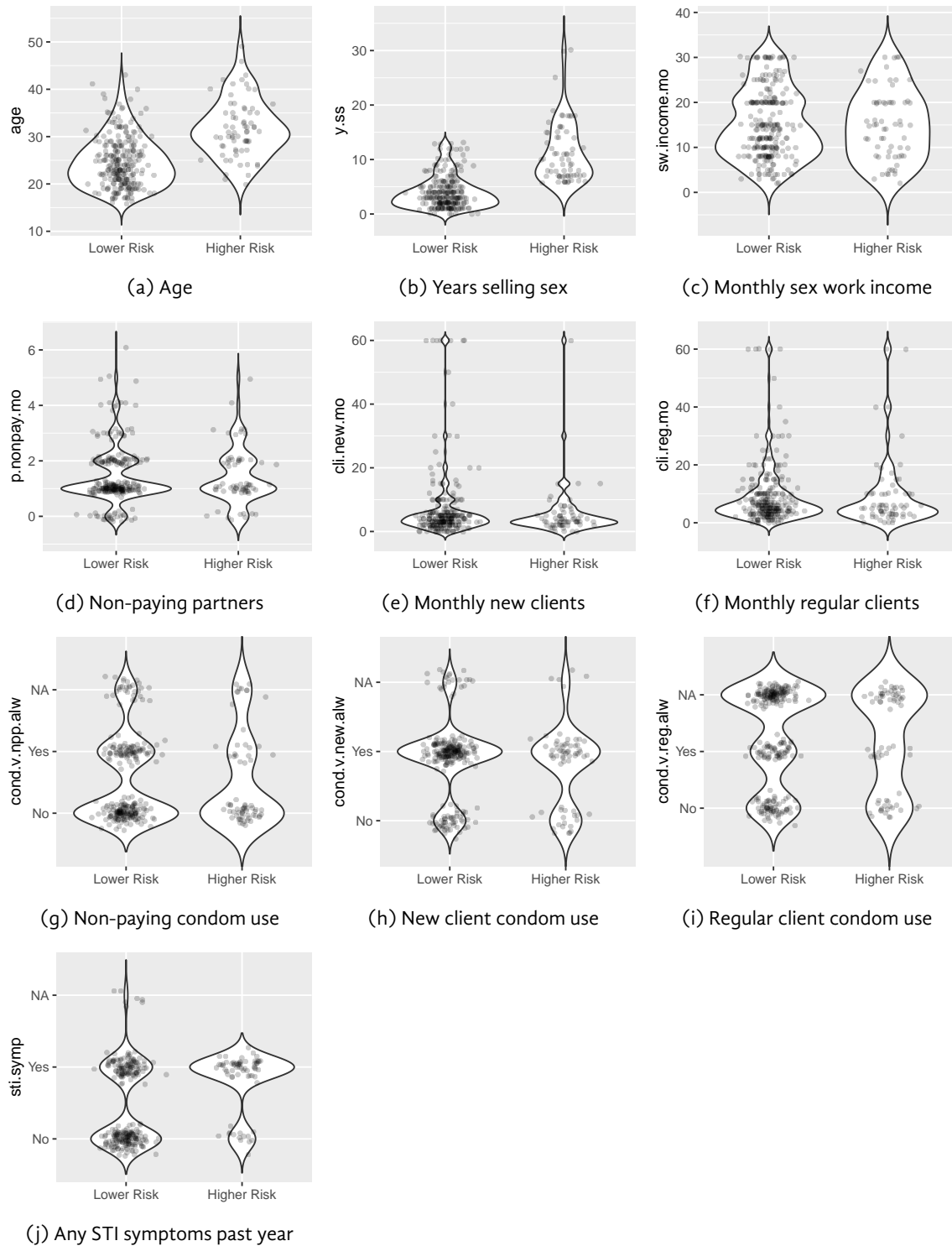


Figure C.1: HIV risk factor variables among higher vs. lower risk FSW in Eswatini, as estimated by multi-variate logistic regression model for serologic HIV status (2011)

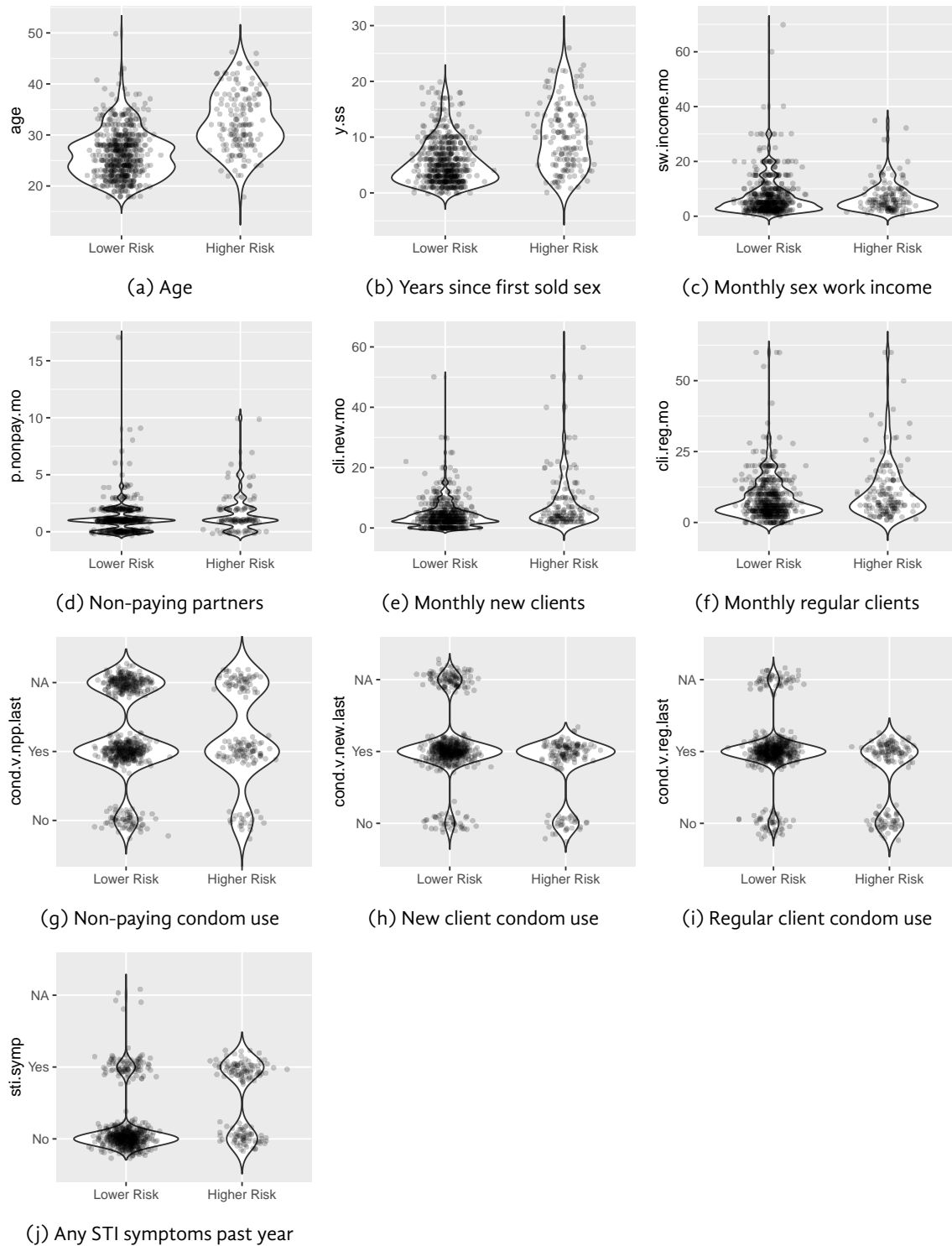


Figure C.2: HIV risk factor variables among higher vs. lower risk FSW in Eswatini, as estimated by multi-variate logistic regression model for self-reported HIV status (2014)

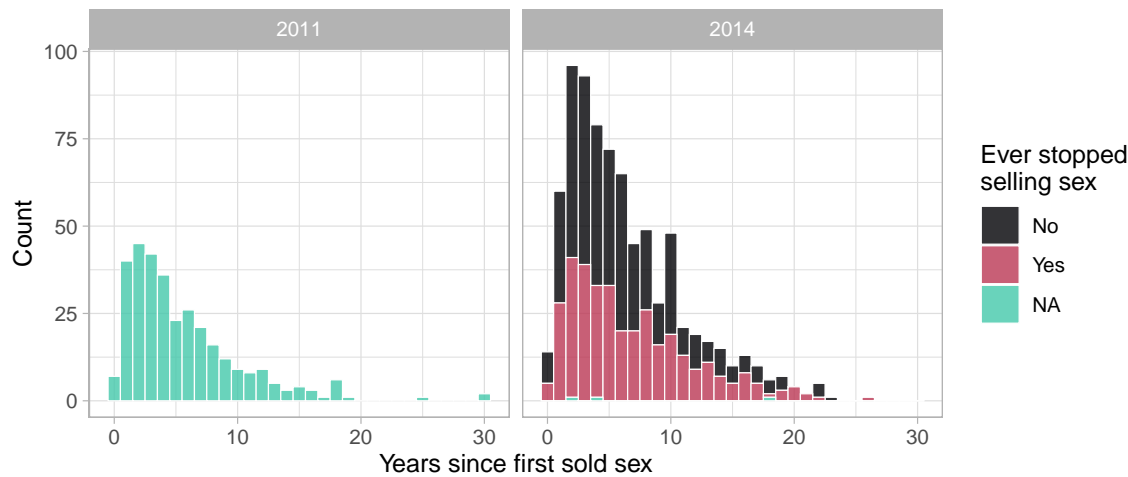


Figure C.3: Years since first sold sex among FSW in Eswatini (unadjusted)

Data sources: 2011 [1], 2014 [2]

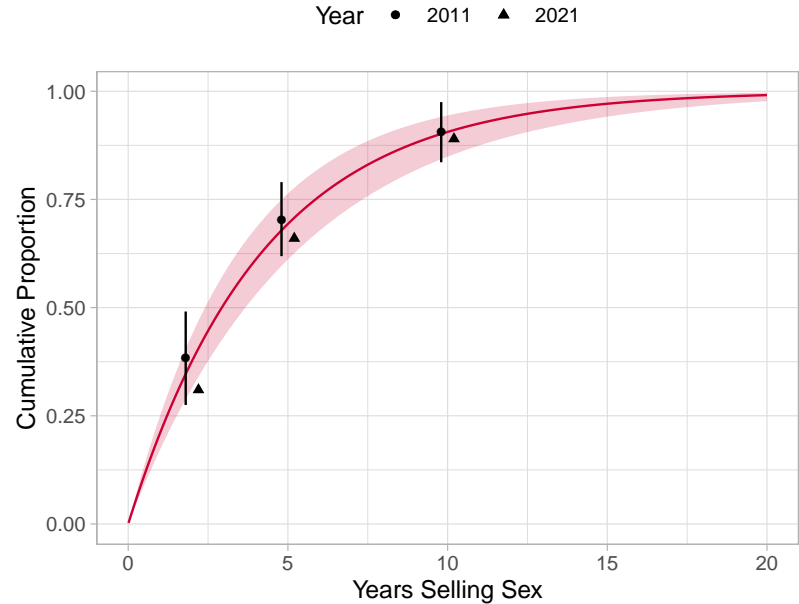


Figure C.4: Cumulative distribution of years selling sex among FSW in Eswatini (RDS-adjusted)

The line and shaded region illustrate the median and 95% CI of sampled exponential distributions, respectively; calibration data from [1] (2011) and [3] (2011).

C.2 Non-Sex Work: Adjusted Partner Numbers

Figure C.5. § 3.2.8

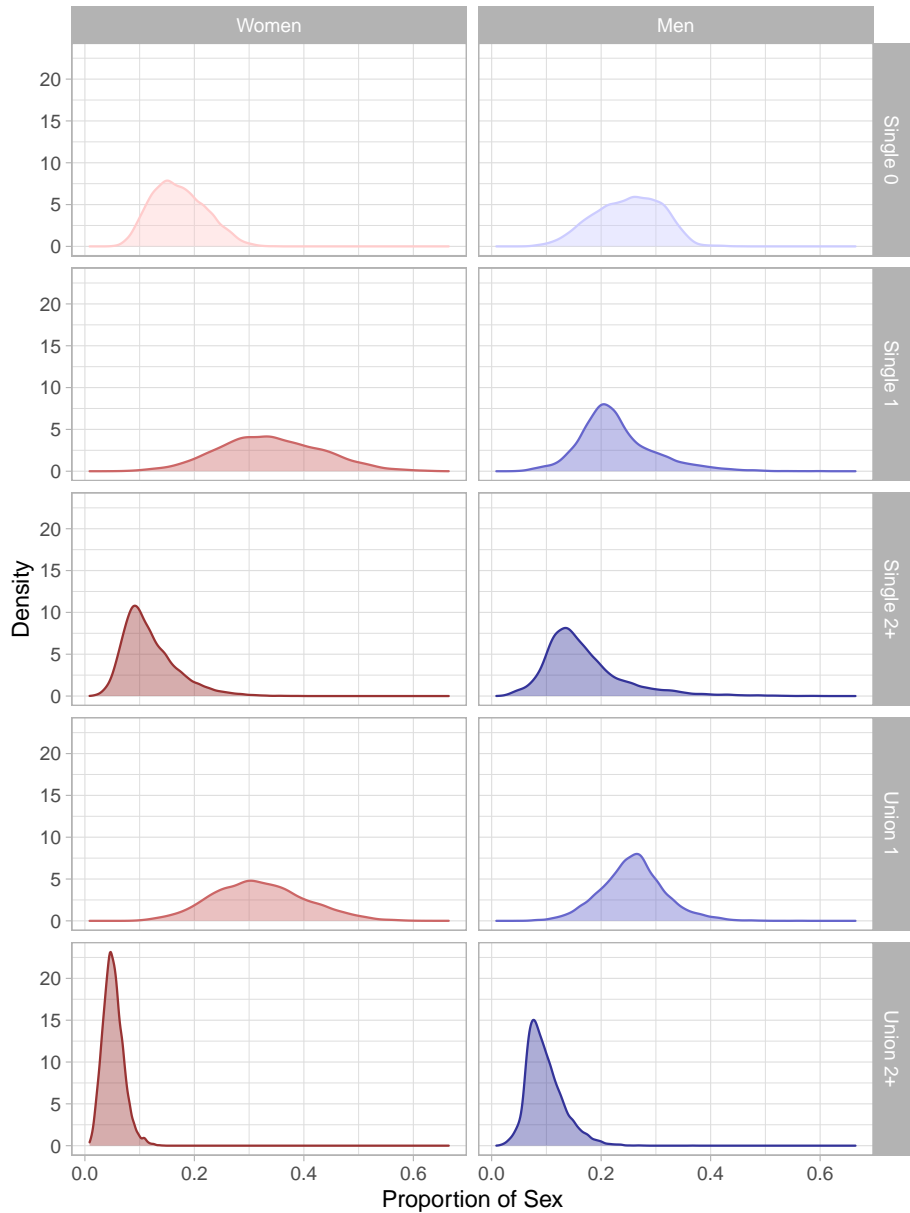


Figure C.5: Density distribution for adjusted proportions of women and men aged 15–49, stratified by union status and numbers of partners in the past 12 months

C.3 Model Calibration

Table C.1

Table C.1: Definitions of calibrated parameters

Parameter	Definition
to_hiv	year of HIV introduction to Eswatini
PX_w_fsw	proportion of women who are FSW
PX_w_h	proportion of women who have 2+ partners in p12m
PX_m_m	proportion of men who have 2+ partners in p12m
dur_fsw_l	duration in sex work among lower risk FSW
dur_fsw_h	duration in sex work among higher risk FSW
dur_cli	duration buying sex among clients
turn_xm_xl	turnover rate from medium to lowest activity (women and men)
Pturn_fsw_m:l	proportion of FSW who transition to medium activity
Pturn_cli_m:l	proportion of clients who transition to medium activity
growth_2050	rate of Eswatini population growth in 2050
C12m_msp_xl	number of main/spousal partners in p12m among lowest activity
C12m_cas_xl	number of casual partners in p12m among lowest activity
C12m_cas_wm	number of casual partners in p12m among medium activity women
RC_cas_cli:wm	relative number of casual partners among clients vs medium activity women
C1m_swo_fsw_l	number of occasional sex work partners in p1m among lower risk FSW
C1m_swr_fsw_l	number of regular sex work partners in p1m among lower risk FSW
RC_swo_fsw_h:l	relative number of occasional sex work partners among higher vs lower risk FSW
RC_swr_fsw_h:l	relative number of regular sex work partners among higher vs lower risk FSW
KF_swx_cli	rate of visiting FSW (sex acts) among clients overall
RKF_swx_cli_h:l	relative rate of visiting (sex acts) among higher vs lower risk clients
F_msp	rate of sex acts in main/spousal partnerships
RF_cas:msp	relative rate of sex acts in casual vs main/spousal partnerships
dur_msp	duration of main/spousal partnerships
dur_cas	duration of casual partnerships
dur_swr	duration of regular sex work partnerships
F_swr ^a	rate of sex acts in regular sex work partnerships
PF_ai ^b	proportion of sex acts which are anal in all partnerships
pref_msp_xl	log-odds of main/spousal partnership formation among lowest activity
pref_mcx_swx	log-odds of non-sex work partnership formation among FSW and clients
Rbeta_condom	relative per-act probability of HIV transmission with a condom
RPF_condom_a:v	relative condom use in anal vs vaginal sex
RPF_condom_1996	relative condom use in all partnerships in 1996 vs 2002 or 2006
PF_condom_msp_2006 ^c	condom use in main/spousal partnerships in 2006
PF_condom_msp_2016 ^c	condom use in main/spousal partnerships in 2006
PF_condom_cas_2006 ^c	condom use in casual partnerships in 2006
PF_condom_cas_2016 ^c	condom use in casual partnerships in 2016
PF_condom_swo_2002 ^c	condom use in occasional sex work partnerships in 2002
PF_condom_swo_2011 ^c	condom use in occasional sex work partnerships in 2011
PF_condom_swo_2014 ^c	condom use in occasional sex work partnerships in 2014
PF_condom_swr_2002 ^c	condom use in regular sex work partnerships in 2002
PF_condom_swr_2011 ^c	condom use in regular sex work partnerships in 2011
PF_condom_swr_2014 ^c	condom use in regular sex work partnerships in 2014
PF_circum_2050	prevalence of circumcision by 2050
beta_0	per-act probability of HIV transmission β for CD4 > 350 (reference)
Rbeta_acute ^d	relative β during acute infection
Rbeta_350	relative β for 200 < CD4 < 350
Rbeta_200	relative β for CD4 < 350
Rbeta_vi_rec	relative β for receptive vaginal sex

continued ...

... continued

Parameter	Definition
aRbeta_gud_sus	additional relative β for GUD among susceptible partner
aRbeta_gud_inf	additional relative β for GUD among infectious partner
dur_acute ^d	duration of acute infection
P_gud_fsw_l ^e	prevalence of GUD among lower risk FSW
RP_gud_fsw_h:l ^e	relative prevalence of GUD among higher vs lower risk FSW
RP_gud_2050	relative prevalence of GUD overall in 2050 vs 2020
iP_gud_h:l	prevalence interpolator for GUD among medium activity vs DHS and FSW
Rbeta_uvls	relative β on ART but before VLS
Rdx_global	relative rate of diagnosis overall
dx_w_2002	rate of diagnosis among women in 2002
dx_w_2006	rate of diagnosis among women in 2006
Rdx_m:w_2006	relative rate of diagnosis among men vs women in 2006
dx_wq_2011	rate of diagnosis among non-FSW women in 2011
Rdx_m:wq_2011	relative rate of diagnosis among men vs non-FSW women in 2011
aRdx_fsw:wq_2011	additional relative rate of diagnosis among FSW vs non-FSW women in 2011
aRdx_wq_16:11	additional relative rate of diagnosis among non-FSW women in 2016 vs 2011
aRdx_fsw:wq_2016	additional relative rate of diagnosis among FSW vs non-FSW women in 2016
tx_2010	rate of ART initiation among diagnosed and eligible in 2010
tx_2012	rate of ART initiation among diagnosed and eligible in 2012
Rtx_fsw:wq	relative rate of ART initiation among FSW vs non-FSW women
ivx	duration on ART before achieving VLS initially
Runvx_m:wq	relative rate of viral unsuppression among men vs non-FSW women
Runvx_fsw:wq	relative rate of viral unsuppression among FSW vs non-FSW women
revx_2010	rate of viral re-suppression in 2010

FSW: female sex worker; p12m: past 12 months; β : per-act probability of HIV transmission; GUD: any genital ulcer disease in p12m; ART: antiretroviral therapy; VLS: viral load suppression; additional relative (aR): relative value beyond one, e.g., $R = 1.5 \rightarrow aR = 0.5$; prevalence interpolator (iP): e.g., $P_0 = 0.2, P_1 = 0.4, iP_x = 0.5 \rightarrow P_x = 0.3$; all rates in per-year; all durations in years; all parameters reflect stratum averages; ^{a,b,c,d,e} parameters with relational sampling constraints (see § C.3.1).

C.3.1 Relational Sampling Constraints

Several relational constraints were imposed on calibrated parameter values during sampling. For each set of constraints below, the selected parameters were repeatedly sampled (randomly, not via Latin hypercube) until all constraints were satisfied:

- $K_{\text{sw}_0\text{fsw}_l} * RC_{\text{sw}_0\text{fsw}_h:l} * F_{\text{sw}_0} + K_{\text{swr}_\text{fsw}_l} * RC_{\text{swr}_\text{fsw}_h:l} * F_{\text{swr}} < 2*365$
where: $K_{\text{sw}_\text{fsw}_l} = C_{1\text{m}_\text{sw}_\text{fsw}_l} * \text{dur}_{\text{sw}_\text{fsw}} / (\text{dur}_{\text{sw}_\text{fsw}} + 1/12)$
- $PF_{\text{ai}} \leq 0.5$
- Let c denote PF_{condom} :
 - $c_{\text{msp}_2006} < c_{\text{msp}_2016}$
 - $c_{\text{cas}_2006} < c_{\text{cas}_2016}$
 - $c_{\text{sw}_02002} < c_{\text{sw}_02011} < c_{\text{sw}_02014}$
 - $c_{\text{swr}_2002} < c_{\text{swr}_2011} < c_{\text{swr}_2014}$
 - $c_{\text{msp}_2006} < c_{\text{cas}_2006}$
 - $c_{\text{msp}_2016} < c_{\text{cas}_2016}$
 - $c_{\text{swr}_2002} < c_{\text{sw}_02002}$
 - $c_{\text{swr}_2011} < c_{\text{sw}_02011}$
 - $c_{\text{swr}_2014} < c_{\text{sw}_02014}$
- $1 \leq (R\text{beta}_{\text{acute}} * \text{dur}_{\text{acute}}) \leq 63$

C.3 MODEL CALIBRATION

67

$$\begin{aligned} \text{e. } & P_{\text{gud_fsw_l}} > .07 \\ & (P_{\text{gud_fsw_l}} * RP_{\text{gud_fsw_h:l}}) < 1 \end{aligned}$$

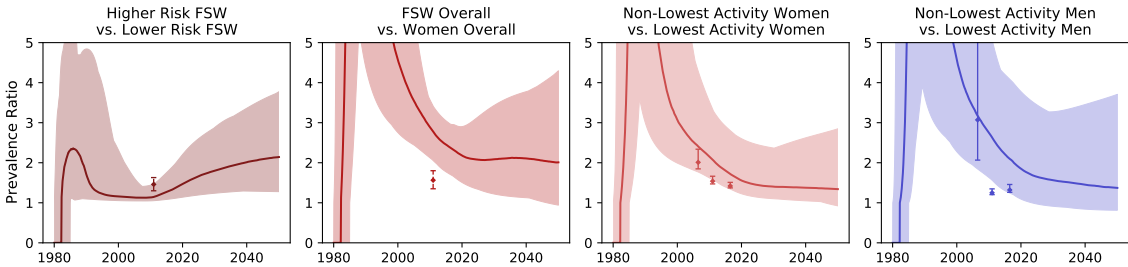


Figure C.6: Modelled HIV prevalence ratios between selected risk groups and associated calibration targets
1000 model fits (top 1% by likelihood among 100,000 sampled parameter sets); ribbon and curve: range and median of model fits; points and error bars: mean and 95% CI for each calibration target.

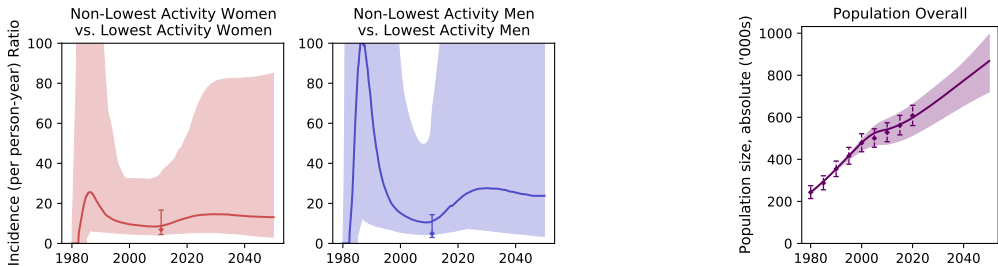


Figure C.7: Modelled HIV incidence ratios between selected risk groups and associated calibration targets
1000 model fits (top 1% by likelihood among 100,000 sampled parameter sets); ribbon and curve: range and median of model fits; points and error bars: mean and 95% CI for each calibration target.

Figure C.8: Modelled Eswatini population aged 15–49 and associated calibration targets

C.3.2 Results

Figure C.6 Figure C.7 Figure C.8 Figure C.9

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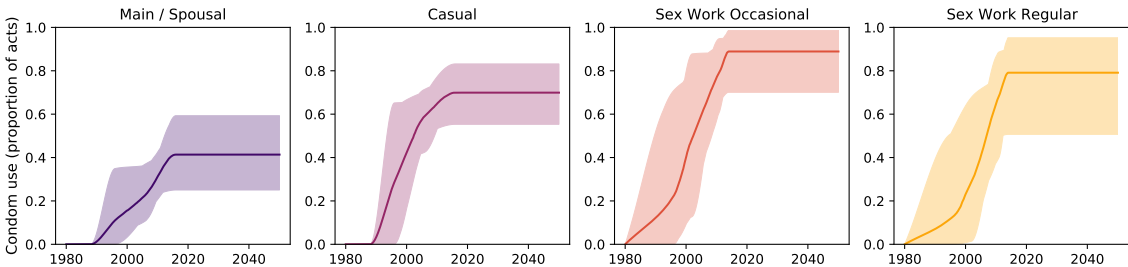
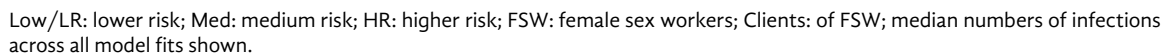


Figure C.9: Modelled condom use within different partnership types

1000 model fits (top 1% by likelihood among 100,000 sampled parameter sets); ribbon and curve: range and median of model fits.



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