

REEXAMINING ASSUMPTIONS IN
COMPARTMENTAL MODELS OF HETEROSEXUAL HIV TRANSMISSION
APPLIED TO eSWATINI



by

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Abstract

Acknowledgements

slow is smooth

smooth is fast

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Table 1: Acronyms

Acronym	Definition
HIV	human immunodeficiency virus
AIDS	acquired immunodeficiency syndrome
CD4	cluster of differentiation 4 (lymphocyte type)
ART	antiretroviral therapy
PrEP	pre-exposure prophylaxis
VMMC	voluntary medical male circumcision
FSW	female sex worker
MSM	men who have sex with men
AGYW	adolescent girls and young women
STI	sexually transmitted infection
GUD	genital ulcer disease
p12m	past 12 months
CI	credible interval

Chapter 1

Introduction

Chapter 2

Systematic Review of Compartmental HIV Transmission Model Structures

Chapter 3

Model Structure, Parameterization, & Calibration

Drawing on the insights from Chapter 2, 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 Unlinked from Care
Partnership types	(p)	1 Main / Spousal
		2 Casual
		3 Occasional Sex Work
		4 Regular Sex Work
Sex act types	(a)	1 Vaginal
		2 Anal

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, 12–25 years [??]); short-term partnerships ($p = 2$, medium condom use, 1–6 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 [assumed]). 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], and, with CD4 as a proxy for viral load, infectiousness [9]. The modelled ART cascade (Figure 3.1c) includes the major steps associated with the “90-90-90” targets, plus a generic “unlinked” state reflecting any combination of treatment failure, discontinuation, or loss to follow-up.

3.1.1 Initialization & Solving

The first cases of HIV and AIDS in eSwatini were diagnosed in 1986 and 1987, respectively [10], although HIV may have been present several years earlier [11]. As such, I initialize the model in 1980 with no HIV, and simulate introduction of HIV at a random year between 1980 and 1985 (uniform prior). HIV

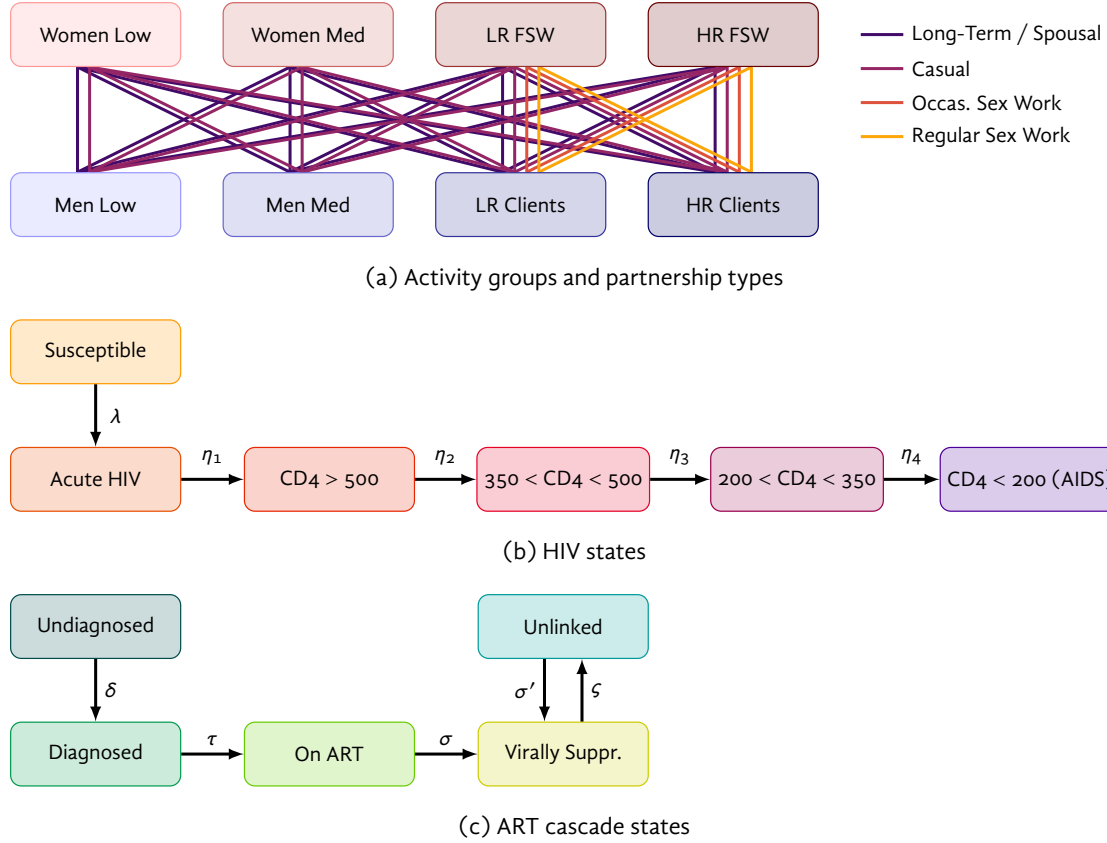


Figure 3.1: Model structure and transitions

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).

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 $350 < \text{CD4} < 500$ ($h = 4$), all undiagnosed ($c = 1$).³ The population size of EmaSwati aged 15–49 in 1980 was defined as 243,000 from [12].

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 (see § B.2.2), while rates and ratios were generally modelled using a gamma or skewnormal 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 [11]. 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

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 [13, 14]; yet such heterogeneities likely influence transmission dynamics. Among the studies identified in Chapter 2, only three sub-stratified FSW by risk-related factors: Cremin et al. [15] defined three levels of risk via regression analysis, Low et al. [16] distinguished between occasional and full-time FSW, while Shannon et al. [17] sub-stratified FSW by work environment, violence exposure, and context-specific structural factors. Seven other studies, reflecting two unique models [18, 19], 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 [20, 21, 14, 22]. However, serostatus reflects cumulative risk exposure, whereas sexual risk behaviour is dynamic [23, 24], as is use of prevention resources [25]. For example, while HIV prevalence often increases with age, HIV incidence among women can peak shortly after sexual debut [26]. 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 [27]. Cohort studies that measure incidence can help identify risk factors for HIV acquisition [28, 29], but large sample sizes are often required to accurately estimate overall incidence rate, let alone risk factors [30].

3.2.1.1 FSW Survey Data

Three surveys, in 2011 [31] ($N = 325$), 2014 [32] ($N = 781$), and 2021 [33] ($N = 676$) provide HIV and biobehavioural data on FSW in eSwatini. The 2011 survey employed respondent driven sampling (RDS, details in [34]), 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 [35]. I analyzed the individual-level data from 2011 and 2014 (data from 2021 not yet 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.

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.

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.

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%) [31]. 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 [35], 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 [36], 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.

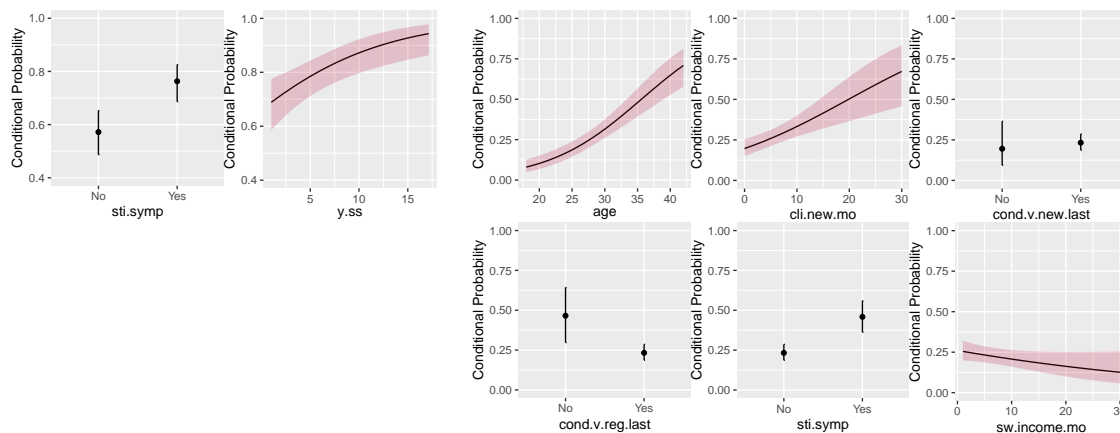
⁵ Logistic regression models were implemented using `lrm` from: cran.r-project.org/package=rms.

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

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.



(a) 2011 (serologic HIV status)

(b) 2014 (self-reported HIV status)

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

sti.sym: 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, $p < 0.05$.

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 [37] to support model parameterization; these ratios are summarized in Table 3.3, and the distributions of variable values are illustrated in Figures B.1 and B.2.

3.2.1.4 Discussion

TODO

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 k) 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:

$$\beta_{asis'i'h'c'} = \beta_0 R_{\beta,k_1} \dots R_{\beta,k_N} \quad (3.1)$$

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. [9] 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 [9]. Such differences in transmission are most likely due to differences in viral load, which is associated with HIV stage [38, 39]. The probability of transmission during the middle asymptomatic period, was reported as mean (95% CI) 0.072 (0.053, 0.097)% per act, which was used to define a skewnormal 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. [9] 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 [40, 41, 42]. In a recent reanalysis of the Rakai cohort data, Bellan et al. [43] 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 [9], 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 [44, 9, 39] 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 [44, 45], and others reporting up to 2-times higher male-to-female ($s' = 2, s = 1$) transmission vs female-to-male ($s' = 1, s = 2$) [46, 9]. To reflect this uncertainty, I defined a gamma prior distribution for the relative rate of male-to-female vs female-to-male transmission with 95% CI: (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. [47] synthesized the per-act transmission probability for anal intercourse, with most data from MSM studies. Analyses in [47] 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 [48] (without ART): 0.14 (0.04, 0.29)% vs vaginal intercourse [9] (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 [47] (without ART): 1.67 (0.44, 3.67)% vs vaginal intercourse [9] (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 § 3.2.9 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) [9, 45, 49]. Since circumcision status is unrelated to the research question, I fixed this effect at 50% relative risk. For anal intercourse, Wiysonge et al. [50] 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 [51, 50], 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. [52] 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 [53]. Thus, condom effectiveness was fixed at 74%. See § 3.2.3.2 for levels of condom use in eSwatini over time.

3.2.2.5 Genital Ulcer Disease

Genital ulcer disease (GUD) is another established risk factor for HIV transmission [54, 55]. Some, but not all GUD is associated with sexually transmitted infections (STIs), and some, but not all STIs can cause GUD [55]. GUD is thought to increase both HIV susceptibility and infectiousness through a variety of mechanisms [55, 56, 57], but HIV may also facilitate transmission of various STIs through immunosuppression [58]. The meta-analysis by Boily et al. [9] 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 [59] 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. As such, I applied factors for increased susceptibility and infectiousness due to GUD

⁶ See § 3.2.1 for more discussion.

in accordance with group-specific p12m GUD prevalence (see § 3.2.3.3), with 95% CI (1.43, 15) (skew normal distribution) and (1.03, 5.69) (gamma), 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 [60], 30.0% in 2017 [5], and 37% in 2021 [61]. Since VMMC continues to be a key element of eSwatini's HIV response [61], 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 [60], 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 § ?? In Zambia, circumcision status was not associated with paying for sex [62].

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 [63] suggesting over-reporting of condom use, and [64] 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 § ??) 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 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 [67] suggested that FSW were more likely than their clients to report having used a condom. As

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.

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)	[65]	b
		Men	currently	7.3	(5.9, 12.1)	[65]	b
	2002	FSW	last sex	60	—	[66]	cd
			always	45.8	—	[66]	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)	[31]	de
			always	20.8	(14.7, 26.9)	[31]	de
	2014	FSW	last sex	80.6	(64.7, 89.6)	[32]	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	—	[66]	d
			always	74.4	—	[66]	d
	2020	FSW	always	50	—	[33]	
New Sex Work	2011	FSW	last sex	84.8	(57.9, 92.4)	[31]	ef
			always	56.7	(47.8, 65.6)	[31]	d
	2014	FSW	last sex	88.5	(54.9, 95.9)	[32]	g
Regular Sex Work	2011	FSW	last sex	82.9	(56.8, 90.0)	[31]	ef
			always	38.6	(29.5, 47.7)	[31]	e
	2014	FSW	last sex	85.6	(47.9, 95.0)	[32]	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.

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 [66] 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. [68] 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 [31, 32], 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 beta 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 beta 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 assume that condom use was effectively zero in 1980 [65]. 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 § B.2.3, this sampling strategy minimizes differences between the prior and posterior (sampled) distributions. For each partnership type, I then smoothly interpolate between sampled levels of condom use over the available years using monotone piecewise cubic interpolation [69].

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 40% of the lowest activity group reported being not sexually active during p12m [2, 5] (see § ??); thus I reduced GUD prevalence by 40% among this group.

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 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 beta 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 [70]. Thus, to reflect uncertainty in STI/GUD prevalence trends, I

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”.

sampled a relative reduction in GUD prevalence for all populations by 2050 from a uniform distribution spanning [0.2, 1].

Finally, no eSwatini-specific data are available for clients of FSW, but studies in Zimbabwe [71], Senegal [72] and Zambia [62] 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 versus 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 $\mu_{\text{HIV},h}$, and treatment via antiretroviral therapy (ART). Lodi et al. [73] estimate median times from seroconversion to $\text{CD4} < 500$, < 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 $\text{CD4} > 500$ ($h = 3$); 3.74 years in $350 < \text{CD4} < 500$ ($h = 4$); and 5.26 years in $200 < \text{CD4} < 350$ ($h = 5$); plus the remaining time until death in $\text{CD4} < 200$ ($h = 6$, AIDS). Since the duration in acute infection ($h = 2$) is randomly sampled, the remaining duration in $\text{CD4} > 500$ ($h = 3$) 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 [74, 75, 6]; based on these data, I estimated yearly HIV-attributable mortality rates $\mu_{\text{HIV},h}$ as: 0 during acute phase ($h = 2$); 0.4% during $\text{CD4} > 500$ ($h = 3$); 2% during $350 < \text{CD4} < 500$ ($h = 4$); 4% during $200 < \text{CD4} < 350$ ($h = 5$); and 20% during $\text{CD4} < 200$ ($h = 6$, 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 ($c = 4$) and after ($c = 5$) achieving full viral load suppression (VLS), as defined by undetectable HIV RNA in blood samples. Among retained patients initiating ART, time to VLS is usually described as “within 6 months” [76]. More specifically, Mujugira et al. [77] estimate the median time to VLS as 3 months, yielding an estimated *mean* duration for $c = 4$ of 4.3 months (see § B.2.4).

¹⁰ Assuming exponential distributions for durations in each CD4 state (see § B.2.4 for more details).

3.2.5.1 Probability of HIV Transmission

All available evidence suggests that viral suppression by ART to undetectable levels prevents HIV transmission, *i.e.*, undetectable = untransmittable (“U=U”) [78]. Thus, I assumed zero HIV transmission from individuals with VLS ($c = 5$). However, HIV transmission may still occur during the period between ART initiation to viral suppression ($c = 4$) [77]. Donnell et al. [39] estimate an adjusted incidence ratio of 0.08 (0.0, 0.57) for all individuals on ART. However, in [39] and [79], 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 [39] 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 ($c = 4$) from a beta distribution with mean (95% CI) of 0.25 (0.01, 0.67).

3.2.5.2 HIV Progression & Mortality

Effective ART stops CD4 cell decline and results in some CD4 recovery [80, 81]. Most CD4 recovery occurs within the first year of treatment [80]. Due to the limited number of modelled treatment states, I model this initial recovery to be associated with the 4.3-month pre-VLS ART state ($c = 4$). Lawn et al. [81] and Gabillard et al. [82] estimate an increase of between 25–39 cells/mm³ per month during the first 3 months of treatment. Since HIV states $h = 4, 5, 6$ correspond to 150, 150, and 200-wide CD4 strata, I model rates of movement along $h = 6 \rightarrow 5 \rightarrow 4 \rightarrow 3$ during pre-VLS ART ($c = 4$) as 0.20, 0.20, 0.17 per month, respectively. After initial increases, CD4 recovery is modest and plateaus. Battegay et al. [80] report approximate increases of 22.4 cells/mm³ per year between years 1 and 5 on ART. Thus, I model rates of movement along $h = 6 \rightarrow 5 \rightarrow 4 \rightarrow 3$ after VLS ($c = 5$) as 0.15 per year.

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 [83]. Lundgren et al. [84] estimated 61% reduction in non-AIDS life-threatening events due to ART. For the same CD4 strata, Gabillard et al. [82] also report approximately 2-times higher mortality rates within the first year of ART versus thereafter, suggesting that VLS is associated with 50% mortality reduction independent of CD4 increase. Thus, I modelled an additional 50% reduction in mortality among individuals with VLS ($c = 5$), and half this (25%) reduction before achieving VLS ($c = 4$).

3.2.6 Sex Work: Population Sizes & Partner Numbers

3.2.6.1 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 § 3.2.8.2), and disproportionate mortality due to HIV between groups may cause higher risk groups to shrink over time.

¹¹ In [39], 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.

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 [85, 86, 87, 88, 64]. Therefore, FSW population size estimates require targeted surveys and unique methodologies [89, 90]. In both [32] and [33], 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) [89]. In 2011 [32], 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 [33], the mean (95% CI) estimates were 2.43 (1.17, 5.02)%. To reflect this uncertainty in the model, a beta 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 [64]. 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 [67], similar to the “multiplier method” [91]. Given the FSW population proportion $P_{s_1 i_{34}}$, the number of yearly new and regular sex work clients per FSW $C_{p_{34} s_1 i_{34}}$, the frequency of sex per partnership-year $F_{p_{34}}$, and the total number of yearly commercial sex acts per client year $C_{p_{34} s_2 i_{34}} F_{p_{34}}$, the total client population $P_{s_2 i_{34}}$ is defined as:

$$\sum_i P_{s_2 i_{34}} = \frac{\sum_{i,p} P_{s_1 i_{34}} C_{p_{34} s_1 i_{34}} F_{p_{34}}}{\sum_{i,p} C_{p_{34} s_2 i_{34}} F_{p_{34}}} \quad (3.2)$$

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 $C_{p_{34} s_1 i_{34}}$, $C_{p_{34} s_2 i_{34}}$, and $F_{p_{34}}$ as defined in § 3.2.6.2, the client population size $P_{s_2 i_{34}}$ estimated by this method was 13.1 (2.1, 38.5)% of men.

3.2.6.2 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. Based on the survey questions,¹² it's not clear whether these numbers 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 1/12th of the total number of yearly partnerships $C_{p_{34} s_1 i_{34}}$. As such, I sampled the yearly numbers 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* number among higher risk FSW from 2.0 (1.6, 2.5). Since each partnership includes only one sex act, the frequency of sex F_{p_3} and partnership duration δ_{p_3} are ill-defined, but can be defined for convenience as $F_{p_3} = 12$ (per year) and $\delta_{p_3} = 1/12$ (years). The correction for partnership duration explored in § ?? was not applied to new sex work partnerships.

For *regular* sex work partnerships, uncertainties remain regarding partnership duration δ_{p_4} , frequency of sex per month $F_{p_4}/12$, and interpretation of survey responses “N” as unique clients or total client visits per

¹² The survey questions were: “In the last 30 days, how many (new/regular) clients have you had sex with?”, or similar.

month. If N reflects the numbers of unique clients, then $C_{p_4s_1i_3}$ should be defined as N directly; whereas if N reflects the numbers of unique visits, then $C_{p_4s_1i_3}$ should be defined as $N/(F_{p_4}/12)$. I therefore derived a sampling distribution for $C_{p_4s_1i_3}$ empirically as follows. I assumed that $F_{p_4}/12$ was 1–4 visits per client per month (uniform), and that a random proportion of respondents ($\rho \in [0, 1]$, uniform) reported unique clients or unique visits. Then, I sampled N from a gamma distribution with mean (95% CI) 8.4 (6.0, 11.0) (Table 3.3), and defined:

$$C_{p_4s_1i_3} \sim (\rho)N + (1 - \rho)N / (F_{p_4}/12) \quad (3.3)$$

I obtained mean (95%CI): 6.1 (2.7, 9.7) for $C_{p_4s_1i_3}$, yielding 14.7 (7.3, 29.6) total sex acts per month with regular clients among lower risk FSW. For higher risk FSW, I sampled the *relative* number 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 [92]. 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 [93]. Johnson and Dorrington [94] 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 ($C_{p_{34}s_2i_{34}} F_{p_{34}}$, 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 must match that among FSW, the specific values of $C_{p_{34}s_2i_{34}}$ were computed automatically. See § 3.2.7.4 for numbers of main/spousal and casual partnerships among FSW and clients.

3.2.7 Non-Sex Work: Group Sizes & Partner Numbers

3.2.7.1 Reported Partner Numbers

The 2006-07 DHS [2], 2011 SHIMS [60], 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.¹³ 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 [85, 95, 87, 64].

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).¹⁴ The assumptions were:

¹³ From Tables 14.7.1 and 14.7.2 (ages 15-49) in [2], Table 3 (ages 18-49) in [60], Table 15.3.A (ages 15+) in [5], with manual adjustment for survey skip patterns in [2, 5].

¹⁴ 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 , $s = 2$).

- 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

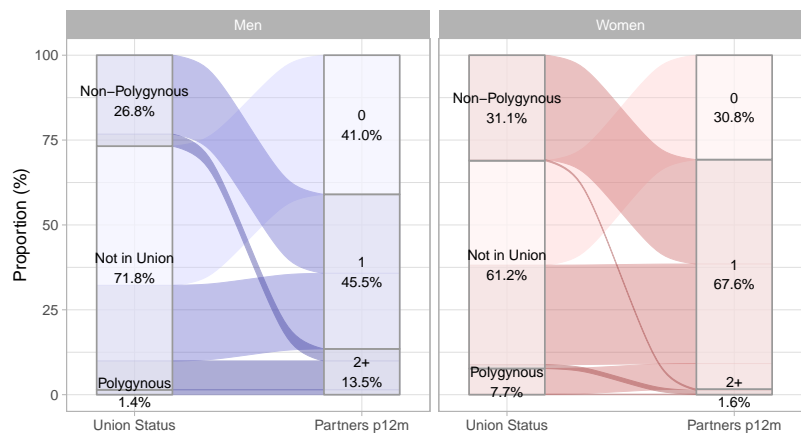
Figure 3.4 illustrates the resulting proportions of women and men in each union/partners in p12m stratum in 2006-07 (a) and 2016-17 (b).

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 [96, 97], 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.

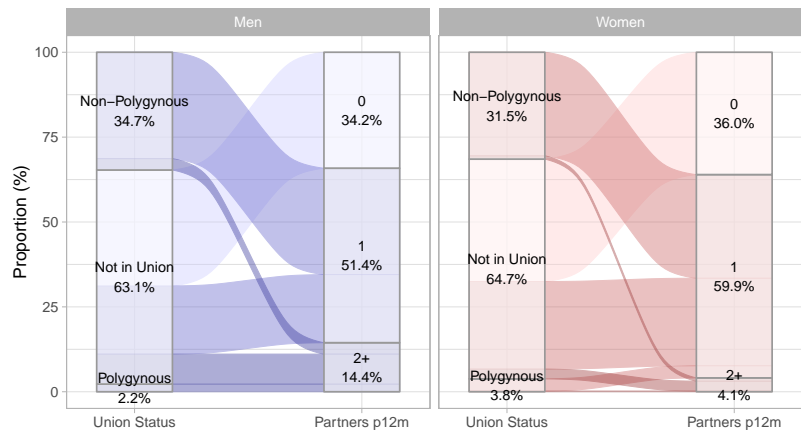
Gregson et al. [86] (Zimbabwe), Nnko et al. [98] (Tanzania) and Clark, Kabiru, and Zulu [99] (Kenya) explored explanations (b) and (c) through measures of consistency; their results suggested that under-reporting of non-spousal partnerships by women (c) was more likely, perhaps due to social norms and pressures; such norms in eSwatini are explored in [100, 101]. In fact, a review comparing computer-based tools versus face-to-face interviews for surveying sexual behaviour [102] found that *both* women and men may under-report sexual partners, but women more so. A notable study in Benin [64] 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) [86].

3.2.7.2 Bias Adjustment: Approach

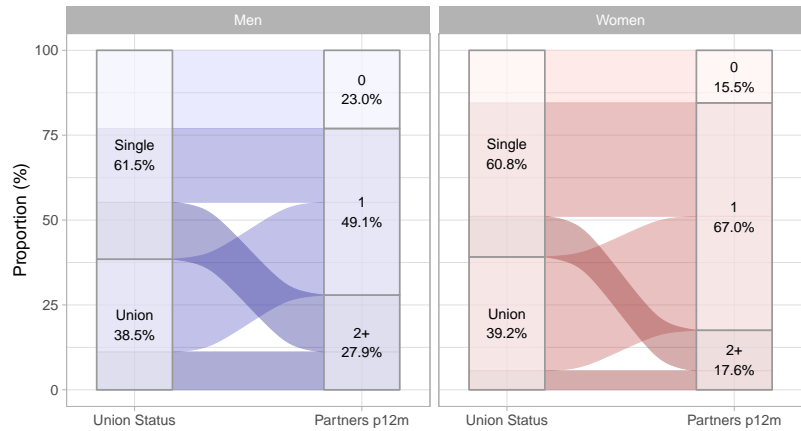
Reflecting these potential reporting biases, I modelled the “true” proportions of Swati women and men in each union/partners in p12m stratum as follows. Let W_{s1} and W_{u1} denote sub-proportions of W_1 who are single and in a union, respectively, and likewise for W_{s2+} , W_{u2+} , M_{s1} , M_{u1} , M_{s2+} , and M_{u2+} . Further, let W_{s1} denote the reported proportion of women (average of 2006-07 and 2016-17), versus 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 $\phi_{W,s1;0}$, which is roughly equivalent in interpretation to the proportion



(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

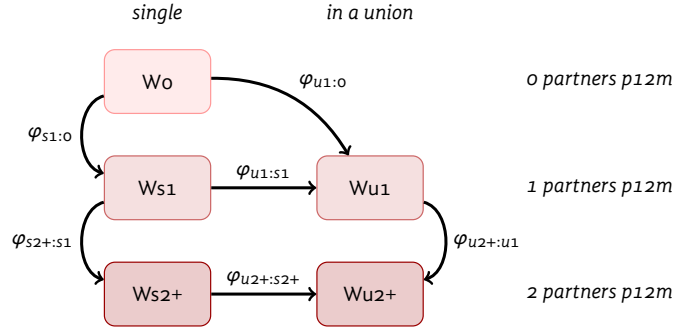


Figure 3.5: Illustration of how women (and equivalently men) are reallocated between union/partners in p12m strata based on odds ratios φ

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.

ratios estimated by Béhanzin et al. [64]:¹⁵

$$\varphi_{Ws1:0} = \frac{W'_{s1}}{W'_0} \bigg/ \frac{W_{s1}}{W_0} \quad (3.4)$$

I defined similar odds ratios $\varphi_{Ws2+:s1}$, $\varphi_{Wu2+:u1}$, $\varphi_{Wu1:0}$, $\varphi_{Wu1:s1}$, and $\varphi_{Wu2+:s2+}$, 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 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 [64], I assumed that “single” women and men (not married/cohabiting) were less likely to report

¹⁵ Odds ratios ensure no proportions become greater than one or negative.

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).

3.2.7.3 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 B.9 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 § 3.2.6.1). Thus, the populations size of medium activity women was defined as $P_{s1i2} = W'_{2+} - P_{s1i34}$. Sampling W'_{2+} from a beta distribution with 95% CI (10, 27)%, the resulting 95% CI for medium activity women P_{s1i2} was (6, 25)% of women. The lowest activity women population size was then defined as $1 - P_{s1i234}$, 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_{s2i2} could yield negative values. Instead, I sampled P_{s2i2} directly from a beta distribution with 95% CI (10, 17)%, yielding 95% CI for P_{s2i234} of (15, 50)% of men, which is close to (15, 44)% from M_{2+} . The lowest activity men were then then defined as $1 - P_{s2i234}$, representing (50, 85)% of men.

Main/Spousal Partnerships. To simplify model fitting, I sampled a common proportion of individuals having a main/spousal partnership from a beta distribution with 95% CI (25, 50)%, applied to all women and men in the lowest activity groups ($C_{p1s12i1}$), as well as all women in the median activity group (C_{p1s1i2}). Since FSW and clients had fewer main/spousal partnerships (see § 3.2.7.4), I calculated the proportion of men in the medium activity group having main/spousal partnerships C_{p1s2i2} 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 having casual partnership $C_{p2s12i1}$ 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 among women in the medium activity group $C_{p_2s_1i_2}$ from a gamma distribution with 95% CI (1.2, 3). As before, I calculated the numbers of casual partnerships among men in the medium activity group $C_{p_2s_2i_2}$ to balance total casual partnerships.

3.2.7.4 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 [103] and Kenya [104], 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 had a main/spousal partner (*i.e.*, $C_{p_1s_1i_34} = 0.5$); lower risk FSW had $C_{p_2s_1i_3} = 0.5$ casual partners; and higher risk FSW had $C_{p_2s_1i_4} = 1.0$ casual partners, on average.

Available data suggest that about half of clients also have non-sex work partners, which are not always distinguished as main/spousal versus casual partnerships [105, 72]. Non-paying partners of FSW are also often clients of other FSW [104, 106]. Yet, clients of FSW also tend to be younger and more likely to be never/formerly married versus non-client men [105, 107]. So, I assumed that clients had half the numbers of main/spousal partnerships compared to lowest activity men: $C_{p_1s_2i_34} = 0.5 C_{p_1s_2i_1}$, and 25–100% the numbers of casual partnerships compared to medium activity women (uniform prior).

3.2.8 Turnover

3.2.8.1 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 [108]. 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 [12], and approximate population growth rates [109], 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 [109]. 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 [12].

3.2.8.2 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 [14]. Previous modelling has shown that activity group turnover (sometimes called “episodic risk”) can strongly influence parameter fitting and intervention impact [110, 111]. I model turnover from activity group si to si' as a constant rate $\theta_{sii'}$, which implies an assumption that duration in group si is exponentially distributed with mean D_{si} [112]:

$$D_{si} = \frac{1}{\mu + \sum_{i'} \theta_{sii'}} \quad (3.5)$$

where μ is the overall exit rate from § 3.2.8.1. As shown previously [111], for fixed activity group sizes, the elements of $\theta_{sii'}$ may be uniquely resolved by specifying $N_i(N_i - 1)$ non-redundant constraints, where specifying D_{si} is one such constraint.

Duration Selling Sex. The unadjusted reported years selling sex among Swati FSW were median 4 (IQR: 2–7) in 2011 [31] and 5 [3, 9] in 2014 [32], with raw distributions shown in Figure B.3. RDS-adjusted proportions of FSW who report selling sex for 0–2, 3–5, 6–10, and 10+ years are also given for 2011 [31] and 2021 [33]. The adjusted proportions are not significantly different between 2011 and 2021, and indicate fewer years selling sex versus the unadjusted proportions, which would be consistent with challenges in reaching women in the first year(s) of sex work [113]. I fit an exponential distribution to these adjusted proportions (Figure B.4), yielding an estimated distribution mean λ^{-1} of mean (95% CI) 4.2 (3.5, 5.3) years selling sex.

Even after RDS-adjustment, the reported years selling sex in a cross sectional survey underestimate the eventual duration in sex work among respondents by a factor $f \leq 2$, because respondents will continue selling sex after the survey; see § B.2.5 for an example and further discussion. Thus, the overall mean duration in sex work is given by $\bar{D} = f \lambda^{-1}$. Taking $f \sim \text{Unif}(1.5, 2)$, \bar{D} is estimated to have mean (95% CI) of 7.4 (5.7, 9.6). This estimate is slightly longer than the pooled estimate for Africa up to 2010 [114]. 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:

$$\begin{aligned} \bar{D} &= 0.2 D_{HR} + 0.8 D_{LR} \\ R_D &= D_{HR}/D_{LR} \end{aligned} \quad (3.6)$$

yielding $D_{LR} \sim 5.8$ (4.4, 7.9) and $D_{HR} \sim 13.4$ (9.3, 19.0). I fit gamma distributions to these data as priors.

Duration Buying Sex. Data to inform the average duration spent buying sex among clients is limited. Fazito et al. [114] estimated mean durations of 4.6–5.5 years based on studies in Benin [105] and Kenya [92]. Hodgins et al. [115, Table G] also gives pooled estimates for the proportions of men in Sub-Saharan Africa who paid for sex *ever* versus 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.

Wider Population. 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 [96] 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. I modelled an equal number of individuals turning over from lowest to medium activity per year (the actual rate depends on the activity group sizes).

Next, I defined the distribution of activity groups from which women enter and exit sex work. Since higher and lower risk FSW (and clients) are conceptualized as mutually exclusive groups, I modelled no turnover between these groups. Emerging data suggest that entry into sex work can be a fuzzy process which may include transactional sex [113, 116]. Thus, I assumed that most — 95% CI (50, 90)% — of women entering sex work originate from the medium activity group (beta prior). I further assumed that exiting sex work is unlikely to be an abrupt transition to monogamous or zero sexual activity [14, 117], and thus modelled an equal proportion of women *exiting* sex work transitioning to the medium activity group. To maintain activity group sizes, I modelled an equal number of women entering and exiting sex work each year. Finally, in the absence of relevant data, I made equal assumptions regarding clients, except that the proportion of men entering from and exiting to the medium risk group was sampled from a beta distribution with 95% CI (25, 90)%.

3.2.9 Sex Frequency & Partnership Duration

3.2.9.1 Sex Frequency

The eSwatini general population data sources [2, 60, 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) [118], 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 [119, Figure 3.15], which is roughly consistent with [118], 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” [120]. Considering these data, I sample the number of sex acts per year in both main/spousal and casual partnerships ($F_{p_1} = F_{p_2}$) from a gamma prior distribution with 95% CI (13, 156). As described in § 3.2.6.2, I defined $F_{p_3} = 12$ for occasional sex work partnerships, and $F_{p_4} \sim \text{Unif}(12, 48)$ for regular sex work partnerships.

3.2.9.2 Anal Sex

Among eSwatini data sources, only [32] (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 [121], and face-to-face interview survey design may result in under-reporting [122]. Owen et al. [123] review studies of anal sex in South Africa, and estimate that 0.6–16.5% of sex acts among

the general population are anal, vs 0.6–29.2% among higher-risk populations.¹⁶ To reflect this greater uncertainty, the proportions of sex acts which are anal in main/spousal and casual partnerships are sampled from a beta prior distribution with 95% CI (0.6, 16.5)%, and likewise for occasional and regular sex work partnerships with 95% CI (0.6, 29.2)%.

3.2.9.3 Partnership Duration

As explored in Chapter ??, the durations of sexual partnerships can be key determinants of epidemic dynamics and intervention impact.¹⁷ 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 [124]. Similar to challenges in estimating sex work duration (§ B.2.5), we must distinguish the definition of an “average partnership” as (a) among all partnerships in a population over a given *time period*, versus (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.¹⁸ The difference between the exponential distribution mean and median should also be kept in mind (see § B.2.4).

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 [125]; 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 versus time t :

$$\begin{aligned}\rho &= 1 - \exp(-\lambda t) \\ \lambda &= -\log(1 - \rho)/t\end{aligned}\tag{3.7}$$

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,

¹⁶ “Higher-risk” populations in [123] were defined as: “STI clinic patients, FSW, their clients, and HIV-infected individuals”.

¹⁷ Chapter ?? also discusses the related phenomenon of partnership concurrency, and how concurrency is represented in compartmental models.

¹⁸ 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).

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 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 [126, 127, 128], Rural Tanzania [98], and four cities in Kenya, Zambia, Benin, and Cameroon [129]. 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 [130]

Sex Work Partnerships. As noted in § 3.2.6.2, 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 [104, 131]. Based on [92], 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.

3.2.10 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 $M_{pi i'}$ 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 $M_{pi i'}$ 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).

3.2.10.1 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 [132]. This approach is often attributed to [133], 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:

$$\rho_{pi i'} = (\epsilon) I_{ii'} + (1 - \epsilon) \pi_{ii'}, \quad I_{ii'} = \begin{cases} 1 & i = i' \\ 0 & i \neq i' \end{cases}, \quad \pi_{ii'} = \frac{M_{pi i'}}{\sum_j M_{pj}} \quad (3.8)$$

where: I 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 $M_{pi i'} = M_{pi} \rho_{pi i'}$. Three advantages of Eq. (3.8) are: (1) simplicity; (2) ϵ can be directly interpreted as the proportion of

partnerships which are formed among like-with-like versus 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 [TODO].

3.2.10.2 Log-Linear Mixing

A more general approach to mixing is developed in [134]. 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:

$$\Pi_{pi i'} = \frac{M_{pi} M_{pi'}}{\sum_j M_{pj}} \quad (3.9)$$

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) [134]. Then, an initial estimate of $M_{pi i'}$ is:

$$\begin{aligned} M_{pi i'}^{(0)} &= \exp \left[\log \left(\Pi_{pi i'} \right) + \Phi_{pi i'} \right] \\ &= \Pi_{pi i'} \exp \left(\Phi_{pi i'} \right) \end{aligned} \quad (3.10)$$

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.¹⁹ However, an iterative proportional fitting procedure [135] can resolve an estimate $M_{pi i'}^{(n)}$ that maintains the total numbers of partnerships:

$$M_{pi i'}^{(n+1)} = M_{pi i'}^{(n)} \frac{\Pi_{pf}}{M_{pf}^{(n)}} \quad f = \begin{cases} i & \text{if } n \text{ is even} \\ i' & \text{if } n \text{ is odd} \end{cases} \quad (3.11)$$

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 [136].

In practice, Eq. (3.11) 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. (??) 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. (3.9) to $\sum_j \omega_s M_{psj}$, where ω_s are weights such that $\sum_s \omega_s = 1$. Similar to the

¹⁹ I hypothesize that this lack of a *a priori* solution is the reason this approach has not been widely used.

“compromise” parameter θ in [133], if $\omega = \{1, 0\}$, then women’s partnership numbers are matched exactly 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.

3.2.10.3 Odds of Mixing

Despite the flexibility in the odds of mixing matrix $\Phi_{p_i i'}$, limited data are available to inform specific elements, especially for eSwatini in particular. In Kenya [104], Benin, Guinea, and Senegal [106], and Uganda [131], 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:

$$\Phi = \frac{\psi(1-\rho)}{(1-\psi)\rho} \quad (3.12)$$

Taking $\psi \in (0.33, 0.70)$ [104, 106] and $\rho \in (5, 20)\%$ [115], we obtain $\Phi \in (2, 19)$. As noted in § 3.2.7.4, its 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 [137], observed like-with-like sexual mixing preferences in numerous other contexts [134, 138, 139], and prior modelling work [140]. 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 versus lower FSW and their clients.

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Appendix A

Supplement to Chapter 2

These materials are copied verbatim from the appendix of [95].

A.1 Search Strategy

We designed our search strategy with guidance from an information specialist at the University of Toronto Library.

A.1.1 Search Terms

Our search strategy and step-wise results are as follows (Table A.1), where `term/` denotes a MeSH term, and `.mp` searches the main text fields, including title, abstract, and heading words. We searched MEDLINE and EMBASE via Ovid on 2020 March 20. Duplicate studies were removed automatically by Ovid and by Covidence; four additional duplicates with subtly different titles were later identified and removed manually.

Table A.1: Systematic review search terms and hits

	Term	Hits
M1	238,076	model, theoretical/
M2	334,921	model, biological/
M3	302,802	computer simulation/
M4	196,814	patient-specific modeling/
M5	67,459	monte carlo method/
M6	32,801	exp stochastic processes/
M7	455,312	(model* ADJ3 (math* OR transmission OR dynamic* OR epidemi* OR compartmental OR deterministic OR individual OR agent OR network OR infectious disease* OR markov OR dynamic* OR simulat*)).mp
M8	1,369,153	OR/ M1-M7
H1	290,863	exp HIV/
H2	651,624	exp HIV infections/
H3	753,274	(HIV OR HIV1* OR HIV2* OR HIV-1* OR HIV-2*).mp
H4	369,182	hiv infect*.mp
H5	538,214	(human immunodeficiency virus OR human immun* deficiency virus).mp

continued ...

A.1 SEARCH STRATEGY

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... continued		
	Term	Hits
H6	216,228	exp Acquired Immunodeficiency Syndrome/
H7	235,971	(acquired immun*deficiency syndrome OR acquired immun* deficiency syndrome).mp
H8	954,470	OR/ H1-H7
G1	3,512	Angola/ OR Angola.mp
G2	9,273	Benin/ OR Benin.mp
G3	5,809	Botswana/ OR Botswana.mp
G4	9,983	Burkina Faso/ OR Burkina Faso.mp
G5	2,055	Burundi/ OR Burundi.mp
G6	16,822	Cameroon/ OR Cameroon.mp
G7	1,196	Cape Verde/ OR Cape Verde.mp
G8	15,416	Central African Republic/ OR Central African Republic.mp OR CAR.ti.
G9	3,075	Chad/ OR Chad.mp
G10	995	Comoros/ OR Comoros.mp
G11	13,737	Democratic Republic of the Congo/ OR Democratic Republic of the Congo.mp OR DRC.mp
G12	959	Djibouti/ OR Djibouti.mp
G13	1,131	Equatorial Guinea/ OR Equatorial Guinea.mp
G14	1,437	Eritrea/ OR Eritrea.mp
G15	35,959	Ethiopia/ OR Ethiopia.mp
G16	4,500	Gabon/ OR Gabon.mp
G17	6,626	Gambia/ OR Gambia.mp
G18	25,213	Ghana/ OR Ghana.mp
G19	360,920	Guinea/ OR Guinea.mp
G20	2,625	Guinea-Bissau/ OR Guinea-Bissau.mp
G21	9,730	Cote d'Ivoire/ OR Cote d'Ivoire.mp OR Ivory Coast.mp
G22	46,917	Kenya/ OR Kenya.mp
G23	1,649	Lesotho/ OR Lesotho.mp
G24	4,239	Liberia/ OR Liberia.mp
G25	11,386	Madagascar/ OR Madagascar.mp
G26	16,367	Malawi/ OR Malawi.mp
G27	9,111	Mali/ OR Mali.mp
G28	1,573	Mauritania/ OR Mauritania.mp
G29	2,373	Mauritius/ OR Mauritius.mp
G30	8,502	Mozambique/ OR Mozambique.mp
G31	3,818	Namibia/ OR Namibia.mp
G32	35,455	Niger/ OR Niger.mp
G33	82,192	Nigeria/ OR Nigeria.mp
G34	13,547	Republic of the Congo/ OR Republic of the Congo.mp OR Congo-Brazzaville.mp
G35	1,545	Reunion/
G36	7,597	Rwanda/ OR Rwanda.mp
G37	342	"Sao Tome and Principe"/ OR "Sao Tome and Principe".mp
G38	16,674	Senegal/ OR Senegal.mp
G39	1,566	Seychelles/ OR Seychelles.mp
G40	5,456	Sierra Leone/ OR Sierra Leone.mp
G41	4,667	Somalia/ OR Somalia.mp
G42	114,536	South Africa/ OR South Africa.mp
G43	1,193	South Sudan/ OR South Sudan.mp
G44	21,680	Sudan/ OR Sudan.mp
G45	2,409	Swaziland/ OR Swaziland.mp OR Eswatini/ OR Eswatini.mp
G46	32,442	Tanzania/ OR Tanzania.mp
G47	3,749	Togo/ OR Togo.mp
G48	37,399	Uganda/ OR Uganda.mp
G49	13,506	Zambia/ OR Zambia.mp
G50	15,755	Zimbabwe/ OR Zimbabwe.mp
G51	482,060	exp africa south of the sahara/ OR sub-saharan.mp OR south of the sahara.mp
G52	982,505	OR/ G1-G51
X1	2,190	M8 AND H8 AND G52
X2	2,160	X1 NOT animal/
X3	2,155	limit X2 to english language
X4	2,125	limit X3 to yr="1860 - 2019"
X5	1,384	remove duplicates from X4

A.1.2 Inclusion/Exclusion Criteria

Table A.2: Systematic review criteria for inclusion and exclusion

Include	Exclude
Publication Type	
<ul style="list-style-type: none">English languagepublished before 2020peer-reviewed journal article	<ul style="list-style-type: none">non-English languagepublished in or after 2020non-peer-reviewed articlereview article¹textbook, grey literatureopinions, comments, correspondenceconference abstracts and proceedingsmodel comparison study
Mathematical Modelling of HIV Transmission	
<ul style="list-style-type: none">sexual HIV transmission modelnon-linear HIV transmission model²population-level dynamicscompartmental model³	<ul style="list-style-type: none">no sexual HIV transmission modelledHIV transmission model is linearonly within-host/cellular/protein modellingindividual-based model
Context & Objectives	
<ul style="list-style-type: none">any region in Sub-Saharan Africa (SSA)⁴assess prevention impact of ART scale-up for all⁵	<ul style="list-style-type: none">only regions outside SSA modelledonly theoretical context modelledonly individual-level benefits of ART modelledonly prevention benefits of other interventionsno base-case scenario reflecting status quo[*]only ART-combination interventions[*]only ART intervention targeted to some risk groups[*]only ART prevention impacts reported for some risk groups[*]ART prevention impacts not reported^{5*}

¹ Review articles were included if they also presented new HIV transmission modelling results fitting our criteria. ² We defined a *non-linear model* as one where the number of infections projected at time t is an iterative function of the number of infections previously projected by the model before time t . ³ We defined a *compartmental model* as one where the system variables represent the numbers of individuals in each state, rather than unique individuals. ⁴ SSA was defined based on the countries in the UN regions of East, South, Central, and West Africa, plus South Sudan (see Table A.1 for full country list). Studies were included if the model was parameterized/calibrated to reflect at least one context within SSA. Only model parameters & outcomes for SSA contexts were extracted. ⁵ Articles reporting HIV incidence reduction and/or cumulative HIV infections averted among the whole population due to increased coverage or initiation rate of ART for the whole population. ^{*} Used to define Dataset B only.

A.1.3 Included Studies

A.1.3.1 Dataset B

- [1] 2005 Salomon et al.
- [2] 2006 Abbas, Anderson, and Mellors
- [3] 2009 Granich et al.
- [4] 2009 Hallett et al.
- [5] 2010 Bacaer, Pretorius, and Auvert
- [6] 2010 Pretorius et al.
- [7] 2011 Metzger, Lloyd-Smith, and Weinberger
- [8] 2012 Yusuf and Benyah
- [9] 2012 Andrews et al.
- [10] 2012 Granich et al.
- [11] 2012 Wagner and Blower
- [12] 2013 Abbas et al.
- [13] 2013 Long and Stavert
- [14] 2013 Cremin et al.
- [15] 2013 Alsallaq et al.
- [16] 2014 Nichols et al.
- [17] 2014 Nichols et al.
- [18] 2014 Alistar, Grant, and Bendavid
- [19] 2014 Eaton and Hallett
- [20] 2015 Ying et al.
- [21] 2015 Low et al.
- [22] 2015 Khademi and Moody
- [23] 2015 Gilbert et al.
- [24] 2015 Heaton et al.
- [25] 2016 Rahman, Vaidya, and Zou
- [26] 2016 Gilbert et al.
- [27] 2016 Blaizot et al.
- [28] 2016 Ying et al.
- [29] 2016 Barnighausen, Bloom, and Humair
- [30] 2016 Heffernan et al.
- [31] 2017 Maheu-Giroux et al.
- [32] 2017 Maheu-Giroux et al.
- [33] 2017 Volz et al.
- [34] 2017 Blaizot et al.
- [35] 2018 Mukandavire et al.
- [36] 2018 Guillon
- [37] 2018 Akudibillah, Pandey, and Medlock
- [38] 2018 Stuart et al.
- [39] 2018 Montigny et al.
- [40] 2019 Hauser et al.

A.1.3.2 Dataset A less B

- [41] 2006 Johnson and Dorrington
- [42] 2006 Baggaley, Garnett, and Ferguson
- [43] 2006 Wilson, Kahn, and Blower
- [44] 2008 Bacaer et al.
- [45] 2009 Chigidi and Lungu
- [46] 2010 Williams et al.
- [47] 2011 Nyabadza and Mukandavire
- [48] 2012 Barnighausen, Bloom, and Humair
- [49] 2013 Wagner, Coburn, and Blower
- [50] 2013 Decker et al.
- [51] 2013 Wirtz et al.
- [52] 2014 Shafer et al.
- [53] 2014 Hove-Musekwa et al.
- [54] 2014 Braithwaite et al.
- [55] 2014 Nichols et al.
- [56] 2014 Abu-Raddad and Awad
- [57] 2014 Anderson et al.
- [58] 2014 Alistar et al.
- [59] 2014 Cori et al.
- [60] 2014 Stover et al.
- [61] 2014 Wirtz et al.
- [62] 2015 Korenromp et al.
- [63] 2015 Knight et al.
- [64] 2015 Kerr et al.
- [65] 2015 Fraser et al.
- [66] 2015 Kassa and Ouhinou
- [67] 2015 Bekker et al.
- [68] 2015 Shannon et al.
- [69] 2015 Blaizot et al.
- [70] 2016 Smith et al.
- [71] 2016 Atun et al.
- [72] 2016 Shattock et al.
- [73] 2016 McGillen et al.
- [74] 2016 Johnson et al.
- [75] 2016 Sharma et al.
- [76] 2017 Akudibillah, Pandey, and Medlock
- [77] 2017 Alsallaq et al.
- [78] 2017 Anderson et al.
- [79] 2017 Chiu et al.
- [80] 2017 Johnson et al.
- [81] 2017 Stuart et al.
- [82] 2017 McGillen et al.
- [83] 2017 Cremin et al.
- [84] 2018 Ross et al.
- [85] 2018 Anderson et al.
- [86] 2018 Anderson et al.
- [87] 2018 Omondi, Mbogo, and Luboobi
- [88] 2018 Woods et al.
- [89] 2018 Stevens et al.
- [90] 2019 Stopard et al.
- [91] 2019 Beacroft and Hallett
- [92] 2019 Reidy et al.
- [93] 2019 Omondi, Mbogo, and Luboobi
- [94] 2019 Maheu-Giroux et al.

A.2 Definitions & Extraction

Data were obtained from (in order of precedence): article text; article tables; article figures; appendix text; appendix tables; appendix figures; and likewise for articles cited like “the model is previously described elsewhere”. Data were assessed from figures with the help of a graphical measurement tool.¹

Fitted Parameters. For the values of fitted parameters, we used the posterior value as reported, including the mean or median of the posterior distribution, or the best fitting value. If the posterior was not reported, we used the mean or median of the prior distribution, including the midpoint of uniform sampling ranges.

A.2.1 Epidemic Context

Let t_0 be the time of ART scale-up/scenario divergence in the model.

HIV Prevalence. As reported in the context overall at t_0 : *Low*: <1%; *Medium*: 1-10%; *High*: >10%.

Epidemic Phase. As projected in the base-case scenario in the context overall between t_0 and roughly $t_0 + 10$ years: *Increasing* (linear or exponential); *Increasing but stabilizing*; *Stable*; *Decreasing but stabilizing*; *Decreasing* (linear or exponential).

Geographic Scale. For studies of one geographic context, scale was defined as one of: *regional*: multiple countries; *national*: one country; *sub-national*: smaller than a country but greater than a city; *city*: one city or less. For studies that consider multiple geographic contexts, scale was defined as *multi-x*, where x is the smallest geographically homogeneous scale considered from the list above.

Country. The countries counted were: *Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Eritrea, eSwatini, Ethiopia, The Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Côte d'Ivoire, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Republic of the Congo, Reunion, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Tanzania, Togo, Uganda, Zambia, Zimbabwe*. See Table A.1 for related search terms. If a study modelled multiple countries at a national scale or smaller, the counter for each country was incremented.

A.2.2 Risk Heterogeneity

A.2.2.1 Key Populations

Female Sex Workers. Any female activity group meeting 3 criteria: representing <5% of the female population; and being $<1/3 \times$ the size of client population or highest non-MSM male activity group; and having $>50 \times$ the partners of the lowest sexually active female activity group [96, 97, 98]. We also noted whether the authors described any activity groups as FSW. If it was not possible to evaluate any criteria due to lack of data, then we assumed the criteria was satisfied.

¹ WebPlotDigitizer: apps.automeris.io/wpd/

Clients of FSW. Any male activity group meeting 2 criteria: described as representing clients of FSW; being $>3 \times$ the size of the FSW population [97]. If group sizes were not reported, then we assumed an activity group described as clients met the size criterion. We also noted whether clients were described as comprising a proportion of another male activity group.

Men who have Sex with Men. Any male activity group(s) described by the authors as MSM.

Transgender People. Any activity group(s) described by the authors as transgender.

People who Inject Drugs. Any activity group(s) described by the authors as PWID.

Prisoners. Any activity group(s) described by the authors as prisoners.

A.2.2.2 Activity Groups

Activity groups were defined as any stratification based on sex/gender and the number and/or types of partnerships formed, including key populations, but excluding stratifications by age.

Count. We counted the number of modelled activity groups in total, and separately for women who have sex with men, men who have sex with women, and MSM.

Highest Risk Group Size. The proportion of men and women in the highest risk group.

Turnover. Turnover refers to movement of individuals between activity groups and/or key populations reflecting sexual life course. We defined four classifications of turnover if activity groups were modelled: *None*: no movement between activity groups; *High-Activity*: only movement between one high activity group or key population and other activity group(s); *Multiple*: movement between multiple pairs of risk groups; *Replacement*: only movement from low to high activity to maintain high activity group size(s) against disproportionate HIV mortality.

A.2.2.3 Partnerships

Approaches. How studies defined partnerships, classified into one of three approaches: *Generic*: all partnerships are equal; *By-Group*: partnership types are defined only by the activity groups involved; *Overlapping*: multiple partnership types can be formed by the same pair of activity groups. Within *By-Group*, we classified how the parameters of the partnership were defined, as based on either: the *susceptible* partner; the *lower activity* partner; the *higher activity* partner; or some consideration of *both partners*.

Characteristics. Whether any of the following varied between different partnership types: *Condom Use*: proportion of sex acts protected; *Total Sex*: total number of sex acts, possibly defined by differences in partnership duration and/or frequency of sex.

Mixing. Mixing by activity group was classified as either: *Proportionate*: proportionate to the total number of partnerships offered by each risk group; *Assortative*: any degree of preferential partnership formation between individuals of the same or similar risk groups.

A.2.2.4 Age Groups

Count. The number of age groups considered in the model.

Risk. Whether age groups differed in any characteristic that conferred transmission risk (binary).

Mixing. We classified whether partnership formation between age groups was assumed to be: *Proportionate*: proportionate to the number of partnerships offered by each age group; *Strictly Assortative*: any degree of preferential partnership formation between individuals of the same or similar age groups that is equal for both sexes. *Off-Diagonal*: any degree of preferential partnership formation between younger women and older men.

A.2.3 HIV Natural History

Count. The number of states of HIV infection considered in the model, excluding stratifications related to treatment. If states were defined by both CD4 and viral load, then the count considers all unique combinations.

Acute Infection. Whether any state represented increased infectiousness associated with acute infection (binary).

Late-Stage Infection. Whether any state(s) considered increased infectiousness associated with late-stage infection (binary).

HIV Morbidity. Whether any state(s) considered decreased sexual activity associated with late-stage disease (binary), and how that decreased was modelled: *Inactive*: complete cessation of sexual activity; *Partners*: decreased rate of partnership formation; *Sex Acts per Partnership*: decreased frequency of sex per partnership; and/or *Generic*: representative decreased probability of transmission.

A.2.4 Antiretroviral Therapy

A.2.4.1 Transmission

Transmission Reduction due to ART. The relative reduction in probability of transmission (0 is perfect prevention, 1 is no effect) among individuals who are virally suppressed; if viral suppression was not explicitly modelled, then the relative reduction among individuals who are on treatment was used.

Transmitted Resistance. Any consideration of 1+ strains of HIV which are transmitted and for which ART had reduced benefits. We did not document the number of resistant strains, or characteristics of resistance and transmissibility.

A.2.4.2 Treatment Cascade States

Forward Cascade. We extracted whether each of the following states were included (binary): *Diagnosed*: aware of their HIV+ status, but have not yet started ART; *Not Yet Virally Suppressed*: started ART, but are not yet virally suppressed; *Virally Suppressed*: on ART and achieved viral suppression; and *Generic On ART*: simplifications of any/all of the above.

Stopping ART. We extracted whether individuals stopped ART, either due to: *Treatment Failure*: ART is no longer efficacious due to resistance; or *ART Cessation*: ART is discontinued for other reasons, such as

barriers to access or side effects. We also extracted whether individuals stopping ART for either reason were tracked separately, or whether they re-entered a generic ART-naïve state, such as “Diagnosed”.

Differential Cascade Transitions. We extracted whether rates of transitioning along the ART cascade, including: rate of *HIV diagnosis*; rate of *ART initiation*; and rate of *ART cessation*, differed by any of the following stratifications: *sex*; *age*; *activity*; and *key populations*. If the study did not mention possible differences in such rates, then we assumed that no differences were modelled.

A.2.4.3 Behaviour Change

HIV Counselling. Whether any sexual behaviour change associated with HIV testing and counselling was applied to individuals in the diagnosed and/or on-ART states (binary), and what changed: *Condom Use*: increased; *Serosorting*: any; *Partners*: decreased rate of partnership formation; *Sex Acts per Partnership*: decreased frequency of sex per partnership; and/or *Generic*: representative decreased probability of transmission due to counselling.

A.2.5 ART Prevention Impact

The following data were extracted per scenario, rather than per-study.

A.2.5.1 Intervention

ART Initiation Criteria. What criteria were used for ART eligibility as part of the intervention: *Symptomatic (AIDS)*; *CD4 < 200*; *CD4 < 350*; *CD4 < 500*; *All individuals*; *Other*.

Intervention Population. Among which population sub-group(s) was the scale-up of ART coverage/initiation applied. Only scenarios with ART intervention for all individuals were included in Dataset B.

Impact Population. Among which population sub-group(s) was the ART prevention impact measured. Only scenarios measuring ART prevention impacts in all individuals were included in Dataset B.

ART Coverage Target. The proportion of people living with HIV in the intervention population who are on ART by the end of ART scale-up.

ART Initiation Rate Target. The rate at which people living with HIV in the intervention population initiate ART by the end of ART scale-up.

Intervention t_0 and t_f . The years at which ART scale-up as part of the intervention started and stopped, respectively. If interventions were modelled as instantaneous, such as increasing ART initiation rate, then we considered $t_0 = t_f$. Impact time horizons were measured relative to t_0 .

A.2.5.2 Impact

For both measures of ART prevention impact, we extracted reported values from the text for any available time horizon, as well as figure data for any of the following time horizons, if available: 5, 10, 15, 20, 30, and 40 years, with the help of a graphical measurement tool. If only absolute values were reported, we

calculated the relative reductions manually. Where reported, we extracted confidence intervals for each outcome.

Relative Incidence Reduction. The relative reduction in overall annual HIV incidence (per 1000 person-years) in the intervention scenario as compared to the baseline scenario, both after an equal number of years since t_0 (time horizon). For example, if the baseline and intervention scenarios predicted overall HIV incidence of 1 and 0.7 per 1000 person-years 5 years after t_0 , then the relative incidence reduction for the 5-year time horizon would be 30%.

Proportion of Infections Averted. The relative reduction in cumulative new HIV infections in the intervention scenario as compared to the baseline scenario, both after an equal number of years since t_0 (time horizon). For example, if the baseline and intervention scenarios predicted 1000 and 700 new infections 5 years after t_0 , then the proportion of infections averted for the 5-year time horizon would be 30%.

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Appendix B

Supplement to Chapter 3

B.1 FSW Data

B.1.1 FSW Risk Factor Variable Distributions

Figures B.1 and B.2.

B.1.2 Duration in Sex Work

Figure B.4.

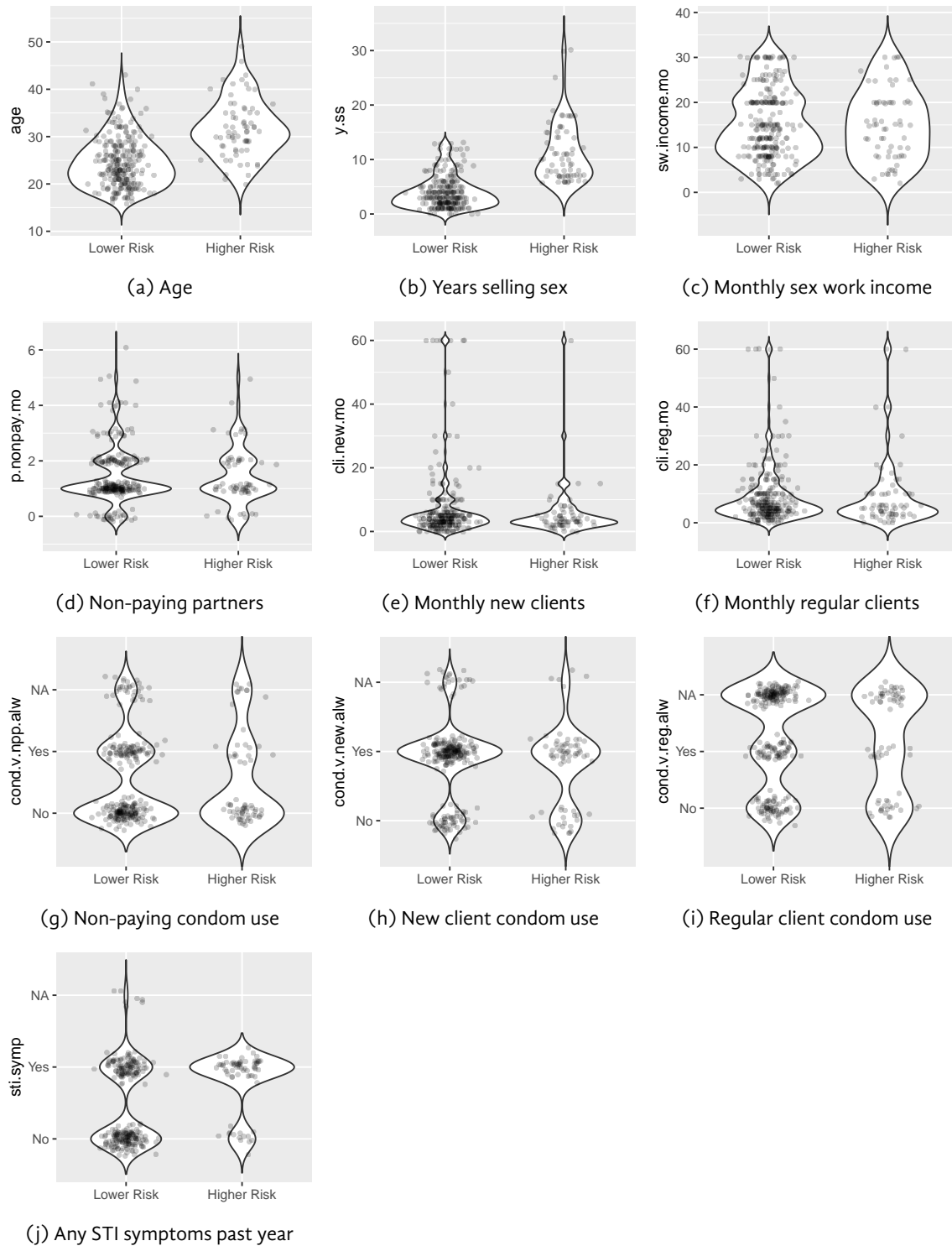


Figure B.1: HIV risk factor variables among higher vs lower risk FSW in eSwatini, as estimated by multivariate logistic regression model for serologic HIV status (2011)

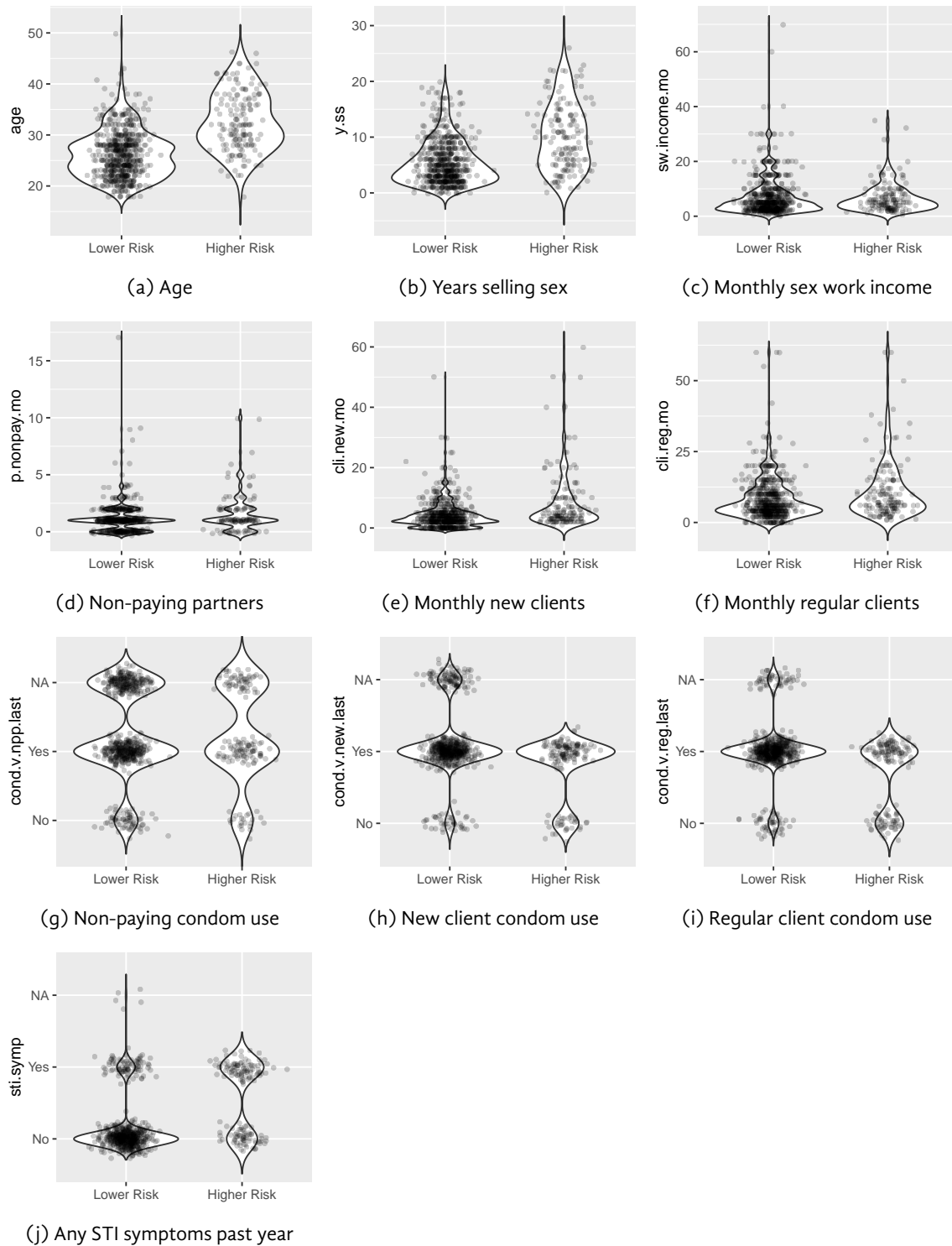


Figure B.2: HIV risk factor variables among higher vs lower risk FSW in eSwatini, as estimated by multivariate logistic regression model for self-reported HIV status (2014)

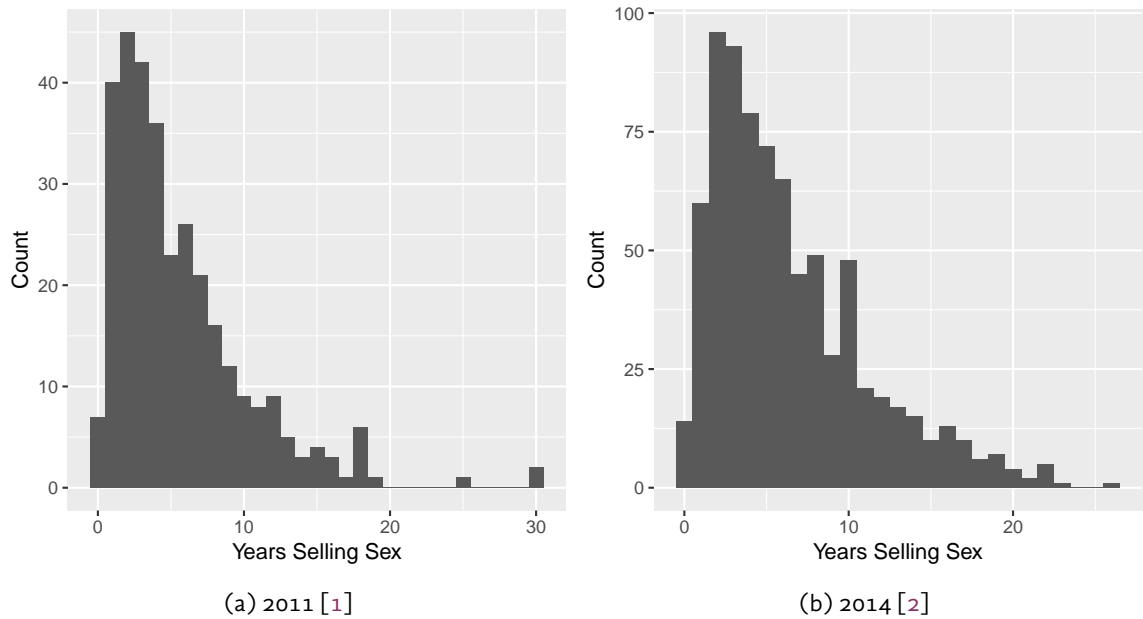


Figure B.3: Years selling sex among FSW in eSwatini (unadjusted)

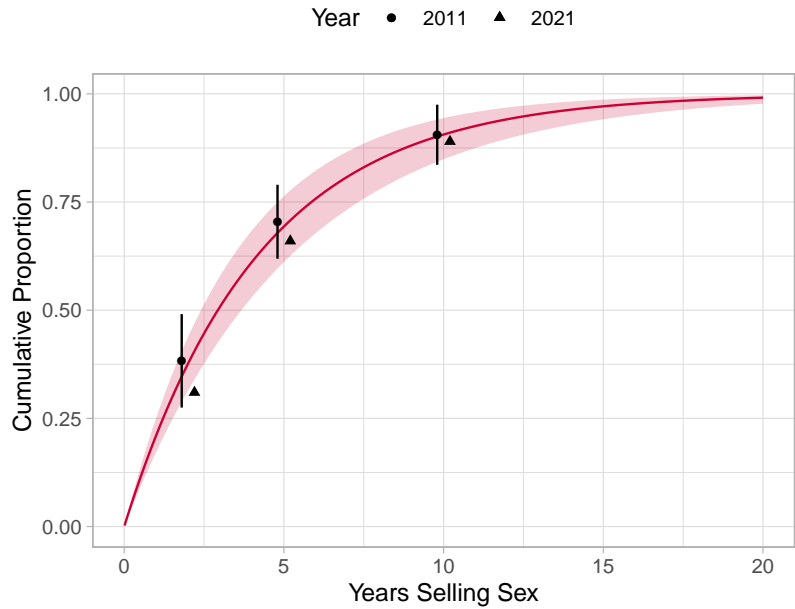


Figure B.4: Cumulative distribution of years selling sex among FSW in eSwatini (RDS-adjusted)

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

B.2 Supporting Mathematics

B.2.1 Distribution Fitting

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:

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

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 $Q(p_i | \theta)$ versus the target quantiles q_i , overlaid on the density distribution $f(x | \theta)$; e.g., Figure B.5.

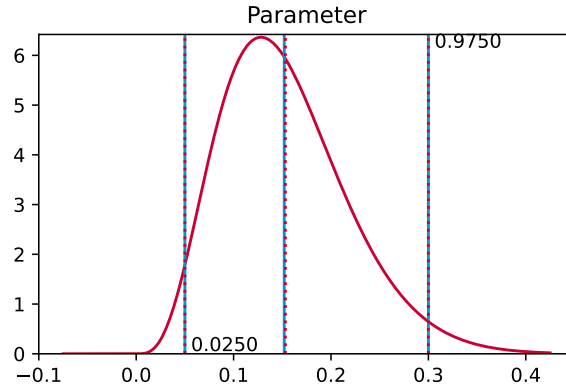


Figure B.5: Example distribution fitting validation plot

Beta 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 $f(x | \theta)$.

B.2.2 Continuous Approximation of the Binomial 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:

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

However, Eq. (B.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

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

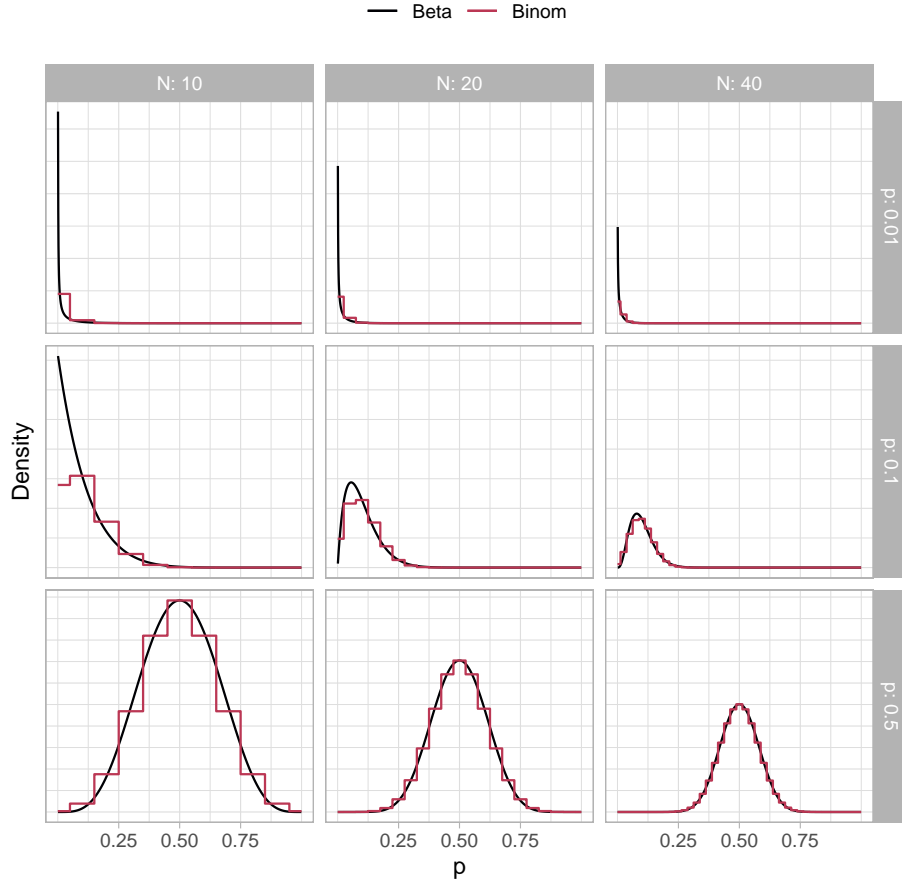


Figure B.6: Approximation of the binomial distribution with the beta distribution

compartmental models can have non-whole-number population sizes. For this purpose, I use a beta approximation of the binomial distribution:

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

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 B.6 illustrates the approximation for $N = \{10, 20, 40\}$ and $\rho = \{0.01, 0.1, 0.5\}$.

B.2.3 Joint Sampling with Relational Constraints

Figure B.7 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 versus 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.

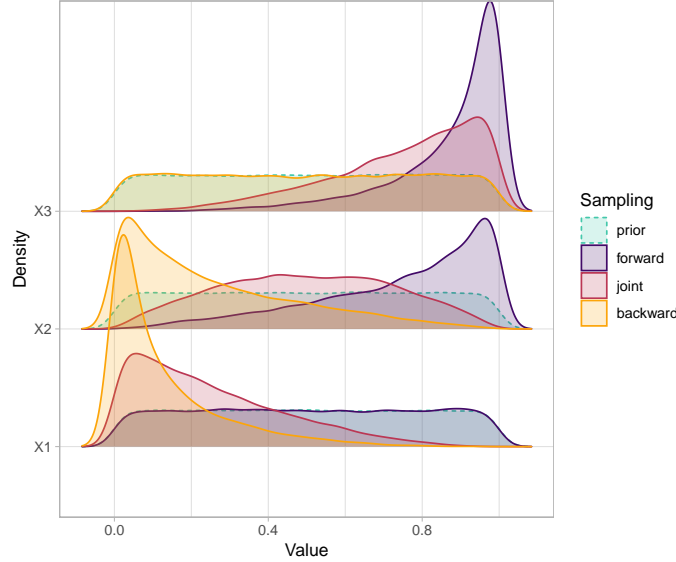


Figure B.7: Illustration of different sampling biases when enforcing $X_1 < X_2 < X_3$

B.2.4 Properties of Compartments with Fixed Exit Rates

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.

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: $1/\lambda_A + 1/\lambda_B$; 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: $\lambda_A + \lambda_B$; thus, the mean duration in AB will be $\delta_{AB} = 1/(\lambda_A + \lambda_B)$.

B.2.5 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,

because respondents will continue selling sex after the survey [4].²

Figure B.8 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 [5]. 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 § B.2.4.

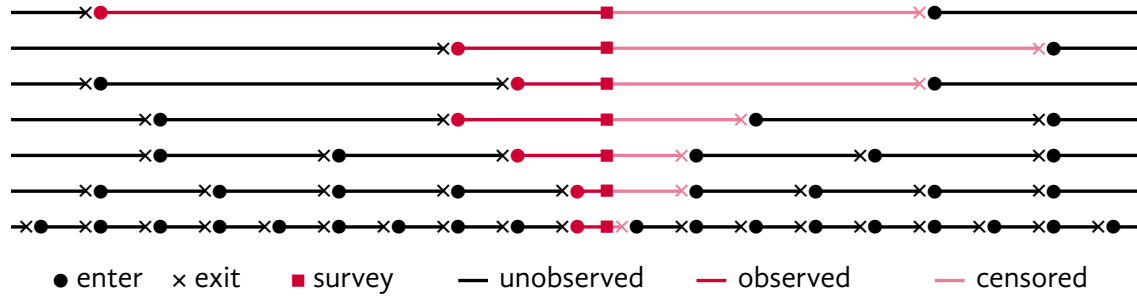


Figure B.8: Illustrative steady-state population of 7 FSW, with varying true durations in sex work δ , versus the observed durations in sex work δ_s via cross-sectional survey.

Another observation we can make from Figure B.8 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 versus 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.

B.3 TODO

B.3.1 TODO

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

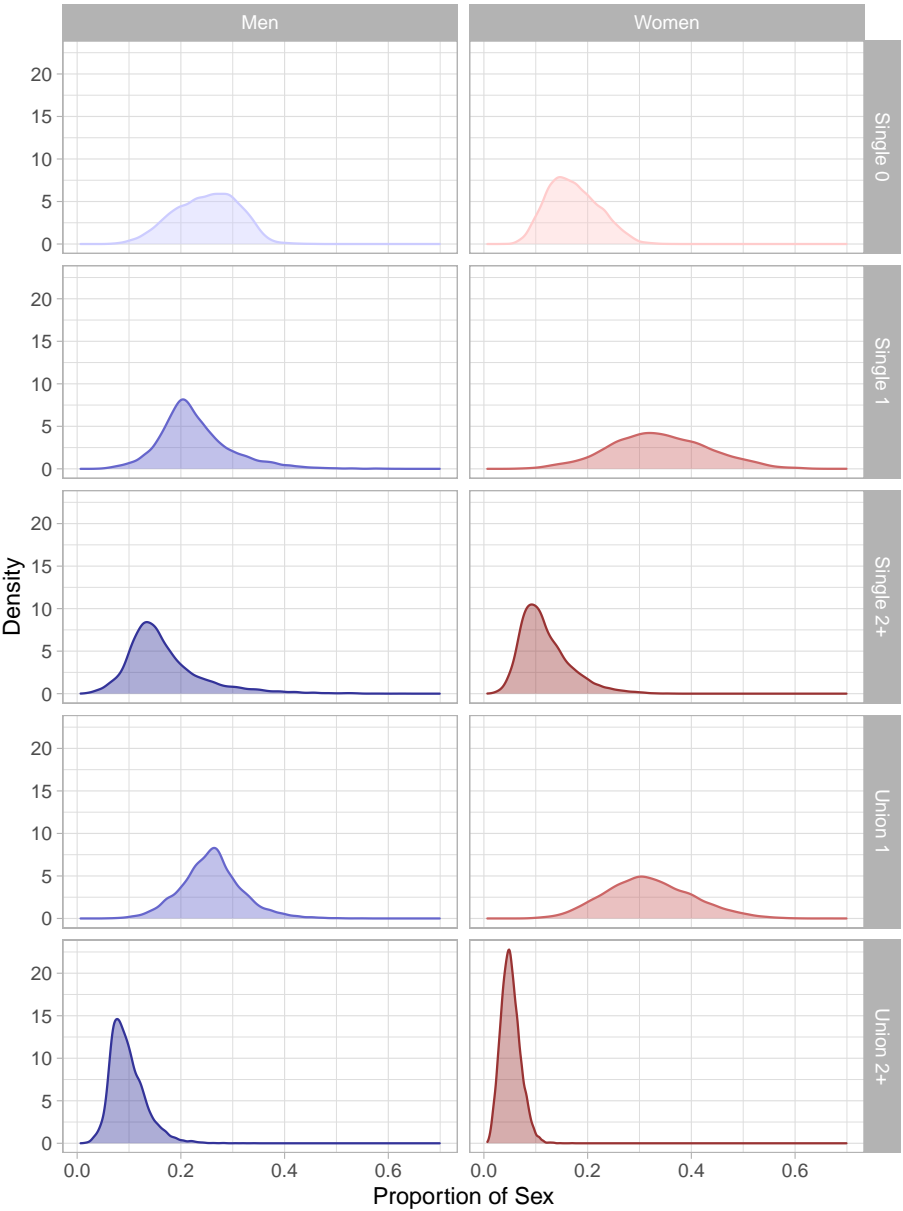


Figure B.9: TODO

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