Reexamining Assumptions in Compartmental Models of Heterosexual HIV Transmission applied to eSwatini

by

Jesse Knight

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Jesse Knight
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Abstract

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Table 1: Acronyms

Acronym	Definition
AGYW	adolescent girls and young women
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
CD4	cluster of differentiation 4 (lymphocyte type)
FSW	female sex worker
GUD	genital ulcer disease
HIV	human immunodeficiency virus
LTFU	lost to follow-up
MSM	men who have sex with men
p12m	past 12 months
PLHIV	people living with HIV
PrEP	pre-exposure prophylaxis
STI	sexually transmitted infection
VMMC	voluntary medical male circumcision
95% CI	95% confidence interval

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Chapter 1

Introduction

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Chapter 2

Systematic Review of Compartmental HIV Transmission Model Structures

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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

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Table 3.1: Overview of model dimensions and stratifications

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

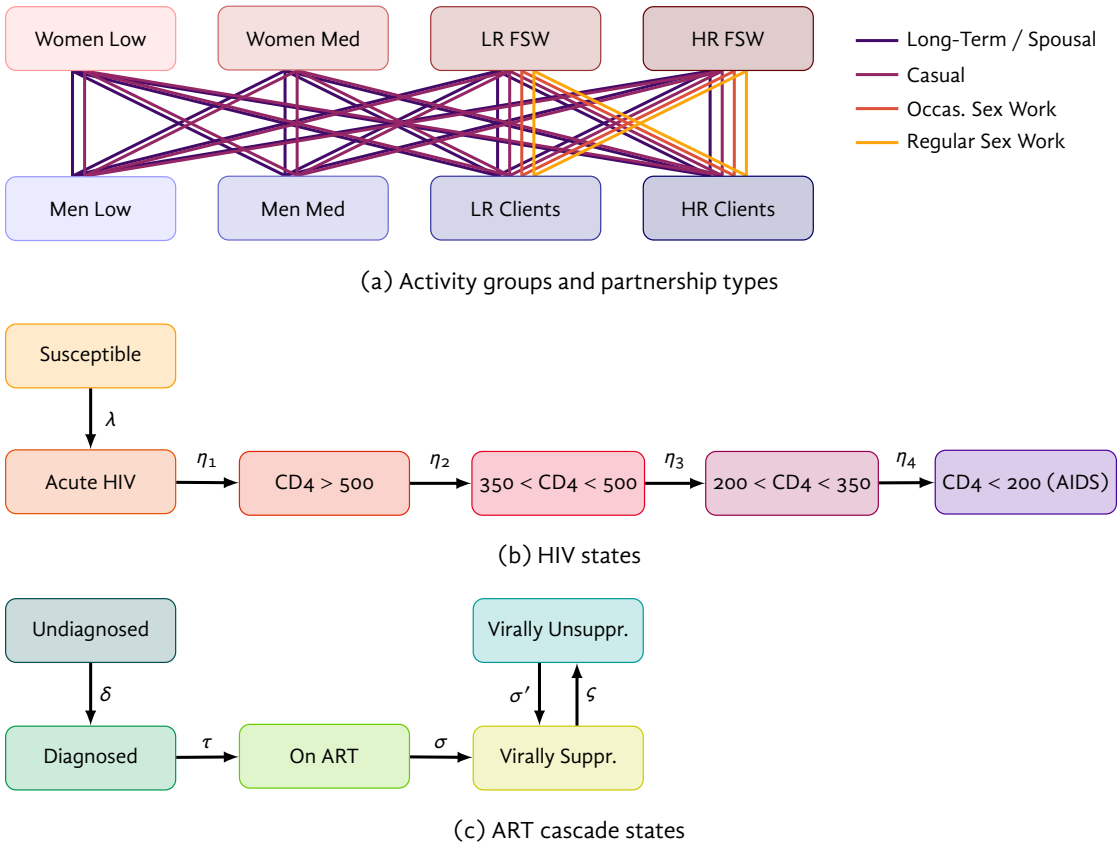
See footnote 4 regarding indices in the code.

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

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

3.1.1 Initialization & Solving

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



(a) Activity groups and partnership types

(b) HIV states

(c) ART cascade states

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 mm^3; Not shown: turnover amongst activity groups in (a).

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

3.2 Parameterization

As described in § **??**, model parameterization involves specification of model parameter values, such as proportions, probabilities, rates, and ratios, including stratified values to reflect heterogeneity, and sampling distributions to reflect uncertainty. Proportions and probabilities were generally modelled using a beta approximation of the binomial distribution (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 [13]. However, I assume that such transmissions have low overall influence on epidemic dynamics.

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

Notation. If X is a parameter stratified by dimensions a, b, c, then $X_{ab_1c_{23}}$ denotes the values of X for a particular but *unspecified* stratum of a, the *specific* stratum $b = 1$, and the *aggregated* strata $c = 2, 3$ (the aggregating operation is context-dependent, e.g., sum for probabilities). Additionally, the indices *sihc* from Table 3.1 denote "self" strata, whereas $s'i'h'c'$ denote "other" strata — i.e., individuals' partners.[4]

3.2.1 Risk Heterogeneity Among FSW

HIV transmission models which include FSW rarely sub-stratify this population, such as to reflect differential HIV risk or distinct typologies of sex work [15, 16]; yet such heterogeneities likely influence transmission dynamics. Among the studies identified in Chapter 2, only three sub-stratified FSW by risk-related factors: Cremin et al. [17] defined three levels of risk via regression analysis, Low et al. [18] distinguished between occasional and full-time FSW, while Shannon et al. [19] sub-stratified FSW by work environment, violence exposure, and context-specific structural factors. Seven other studies, reflecting two unique models [20, 21], employed age stratification of all activity groups, including FSW; these models had several risk-related parameters which varied by age.

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

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

3.2.1.1 FSW Survey Data

Three surveys, in 2011 [33] (N = 325), 2014 [34] (N = 781), and 2021 [35] (N = 676) provide HIV and biobehavioural data on FSW in eSwatini. The 2011 survey employed respondent driven sampling (RDS, details in [36]), as did the 2021 survey. The 2014 survey employed venue-based snowball sampling, based on the Priorities for Local AIDS Control Efforts (PLACE) methodology, which aims to identify areas of higher incidence [37]. I analyzed the individual-level data from 2011 and 2014 (data from 2021 not yet 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 $i \to i - 1$ in the code. Also, the model code reorders states in the ART Cascade dimension for efficiency, with $c = 1$: Undiagnosed; 2: Diagnosed; 3: Virally Un-suppressed; 4: On ART; 5: Virally Suppressed.

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

×: 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%) [33]. Among serologically HIV–, 11% self-reported HIV+ status (false positive), and among serologically HIV+, 26% self-reported HIV– status (false negative or undiagnosed). Overall, self-reported HIV status underestimated HIV prevalence in 2011 by a factor of approximately 0.78 (55 vs 70%). Unadjusted HIV prevalence in 2021 was 58.8%, with 88% (363/411) reporting previous awareness of HIV+ status.

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

3.2.1.3 Risk Factors

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

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

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

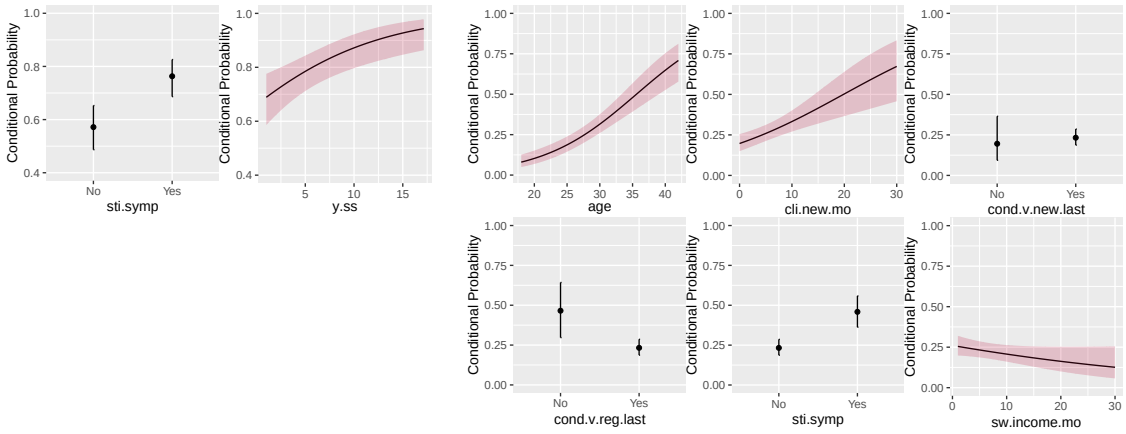
Risk factors were selected based on prior knowledge of plausible mechanistic influence on HIV incidence and/or prevalence. The risk factors explored are summarized in Table 3.2, including univariate and multivariate association under each model. Variable selection for multivariate models was performed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

[5] Logistic regression models were implemented using `lrm` from: cran.r-project.org/package=rms.
Cox proportional hazards models were implemented using `coxaalen` from: cran.r-project.org/package=coxinterval.

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

	2011 LR				2014 LR				2014 CPH			
	Univar		Multivar		Univar		Multivar		Univar		Multivar	
Factor	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.symp: any STI symptoms past year; y.ss: years selling sex; cli.new.mo: monthly new clients; sw.income.mo: monthly sex work income. Conditional probabilities shown for fixed covariates at arbitrary values.

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

	2011 LR		2014 LR		2014 CPH	
Factor	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 [39] 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:

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

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

3.2.2.1 HIV Infection Stage

Boily et al. [11] synthesized per-act transmission probability in the absence of ART from 43 studies in 25 populations. Among 7 studies reporting stage of HIV infection (early, asymptomatic, late), infection stage explained 95% of variance in per-act probability of transmission in [11]. Such differences in transmission are most likely due to differences in viral load, which is associated with HIV stage [40, 41]. The probability of transmission during the middle asymptomatic period, was reported as mean (95% CI) 0.072 (0.053, 0.097)% per act, 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. [11] estimated the relative infectiousness of the first 5 months of infection as 9.2 (4.5, 18.8) times higher than the asymptomatic period. However, both the duration and infectiousness of the acute phase have been long debated [42, 43, 44]. In a recent reanalysis of the Rakai cohort data, Bellan et al. [45] estimate a much smaller contribution of the acute phase to overall infection, summarized as 8.4 (0, 63) "excess hazard-months" (EHM). This excess risk represents the joint uncertainty and collinearity in the estimated duration of 1.7 (.55, 6.8) months and relative infectiousness of 5.3 (.79, 57). Thus, I sampled the duration $\delta_{h=2}$ from a gamma prior with mean (95% CI) 1.7 (.55, 6) months, and relative infectiousness $R_{\beta,h'=2}$ from a gamma prior with 5.3 (1, 15) times the asymptomatic period (confidence intervals were adjusted to fit the gamma distributions, and to ensure $1 < \text{EHM} < 63$).

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

3.2.2.2 Sex Act Types

The model considers vaginal and anal intercourse, further stratified by sex (male-to-female/insertive vs female-to-male/receptive). For vaginal intercourse, evidence for differential risk by sex is mixed, with some studies reporting no difference [46, 47], and others reporting up to 2-times higher male-to-female ($s' = 2, s = 1$) transmission vs female-to-male ($s' = 1, s = 2$) [48, 11]. To reflect this uncertainty, I 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. [49] synthesized the per-act transmission probability for anal intercourse, with most data from MSM studies. Analyses in [49] were not stratified by HIV stage, so I assumed the same relative rates derived in § 3.2.1 applied equally to vaginal and anal intercourse. Overall female-to-male (insertive) per-act transmission probabilities were similar for anal intercourse [50] (without ART): 0.14 (0.04, 0.29)% vs vaginal intercourse [11] (without commercial sex exposure): 0.164 (0.056, 0.481)%; thus I assumed that female-to-male (insertive) transmission probabilities for anal vs vaginal intercourse were equal. By contrast, male-to-female (receptive) per-act transmission probabilities were approximately 10 higher in anal

intercourse [49] (without ART): 1.67 (0.44, 3.67)% vs vaginal intercourse [11] (without commercial sex exposure): 0.143 (0.088, 0.233)%; thus I assumed a fixed 10-fold increase in male-to-female transmission probability for anal vs vaginal intercourse. See § 3.2.10 for sex act frequency within each partnership type.

3.2.2.3 Circumcision

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

3.2.2.4 Condoms

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

3.2.2.5 Genital Ulcer Disease

Genital ulcer disease (GUD) is another another established risk factor for HIV transmission [56, 57]. Some, but not all GUD is associated with sexually transmitted infections (STIs), and some, but not all STIs can cause GUD [57]. GUD is thought to increase both HIV susceptibility and infectiousness through a variety of mechanisms [57, 58, 59], but HIV may also facilitate transmission of various STIs through immunosuppression [60]. The meta-analysis by Boily et al. [11] found that presence of STI alone was not associated with increased HIV transmission: RR 1.11 (0.30, 4.14), but GUD was: RR 5.29 (1.43, 19.6), with most studies examining GUD among the HIV-susceptible partner. One study [61] estimated RR 2.58 (1.03, 5.69) of transmission for GUD among the HIV-positive partner. Most studies defined GUD status as any experience of symptoms during the study period (e.g., past 12 months, p12m), since precise delineation of GUD episodes is challenging. Morover, 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 [62], 30.0% in 2017 [5], and 37% in 2021 [63]. Since VMMC continues to be a key element of eSwatini's HIV response [63], I assumed that coverage could reach and plateau at 50–90% (95% CI) by 2050. There is minimal evidence of differential condom use by circumcision status [62], so I assumed no differences. Similarly, while circumcision differed by union status in [5] (e.g., 22.1% circumcised among men in a union vs 31.7% among men not in a union), differences did not persist after re-stratifying these men into groups with 0-1 vs 2+ partners per year, as described in § **??**. In Zambia, circumcision status was not associated with paying for sex [64].

3.2.3.2 Condom Use

Condom use is typically reported as either categorical for a recent period, usually 30 days, e.g., "*never, rarely, sometimes, often, always*"; or binary for the most recent sex act. Both report types may be subject to reporting bias, but the "last sex" more directly translates into a proportion of sex acts. The direction of reporting bias may vary with social context, with [65] suggesting over-reporting of consom use, and [66] suggesting under-reporting of conddom 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 [69] 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)	[67]	b
		Men	currently	7.3	(5.9, 12.1)	[67]	b
	2002	FSW	last sex	60	—	[68]	cd
			always	45.8	—	[68]	cd
	2006	Women	last sex	36.5	—	[2]	
		Men	last sex	47.2	—	[2]	
	2011	Women	always	30	—	[2]	
		Men	always	34	—	[2]	
		FSW	last sex	51.1	(41.8, 60.4)	[33]	de
			always	20.8	(14.7, 26.9)	[33]	de
	2014	FSW	last sex	80.6	(64.7, 89.6)	[34]	g
	2016	Women	last sex	58.3	—	[5]	
		Men	last sex	53.1	—	[5]	
Casual	2006	Women	last sex	53.5	—	[2]	
		Men	last sex	66.0	—	[2]	
	2016	Women	last sex	64.9	—	[5]	
		Men	last sex	73.7	—	[5]	
Sex Work Unspecified	2002	FSW	last sex	90	—	[68]	d
			always	74.4	—	[68]	d
	2020	FSW	always	50	—	[35]	
New Sex Work	2011	FSW	last sex	84.8	(57.9, 92.4)	[33]	ef
			always	56.7	(47.8, 65.6)	[33]	d
	2014	FSW	last sex	88.5	(54.9, 95.9)	[34]	g
Regular Sex Work	2011	FSW	last sex	82.9	(56.8, 90.0)	[33]	ef
			always	38.6	(29.5, 47.7)	[33]	e
	2014	FSW	last sex	85.6	(47.9, 95.0)	[34]	g

[a] Back-calculated as described in § 3.2.3.2; [b] 95% CI from urban & rural data; [c] Described as "non-paying partners" in the survey; [d] Two major cities only (Manzini & Mbambane); [e] RDS-adjusted; [f] 95% CI lower bound reduced by 25% due to possible reporting bias; [g] 95% CI bounds from regions with lowest and highest reported condom use.

such, I adjusted the lower bound of 95% CI for condom use in sex work partnerships ($p = 3, 4$) as either 75% of the reported lower bound, or the lowest reported region-specific estimate. Estimates for 2002 [68] were obtained from two major cities only (Manzini and Mbambane); since early condom availability was mainly urban, treated these estimates as 95% CI upper-bounds, and defined the lower bound as 20% of the reported values.

Anal Sex. Owen et al. [70] estimate that among FSW globally, condom use in anal sex is approximately 79 (66, 94)% that of condom use in vaginal sex.[8] In eSwatini [33, 34], relative condom use in anal sex vs vaginal sex ranged from 44% among new clients in 2011 to 88% among regular clients in 2014. So, I sampled relative condom use in anal vs vaginal sex from a 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 [67]. I also assume andd 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 [71].

3.2.3.3 Genital Ulcer Disease

Self-reported prevalence of GUD in p12m among sexually active women and men aged 15–49 was approximately 7% in 2006 [2, Table 13.14]; this prevalence was not stratified by numbers of partners, so I assumed it was equal across sexually active individuals in lowest and medium activity groups. However, approximately 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 [72]. 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 [73], Senegal [74] and Zambia [64] have found 2.5–3.7 (95% CI span 1.4–5.0) the odds of STI symptoms during the past 6–12 months among clients 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. [75] estimate median times from seroconversion to CD4 < 500, < 350, and < 200 cells/mm^3, while Mangal [6] directly estimate the rates of progression between CD4 states η_h in a simple compartmental model. Based on these data, I modelled mean durations ($1/\eta_h$) of:[10] 0.142 years in acute infection ($h = 2$, from § 3.2.2.1); 3.35 years in CD4 > 500 ($h = 3$); 3.74 years in 350 < CD4 < 500 ($h = 4$); and 5.26 years in 200 < CD4 < 350 ($h = 5$); plus the remaining time until death in CD4 < 200 ($h = 6$, AIDS). Since the duration in acute infection ($h = 2$) is randomly sampled, the remaining duration in CD4 > 500 ($h = 3$) is adjusted accordingly.

3.2.4.2 HIV Mortality

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

3.2.5 Antiretroviral Therapy

Viral suppression via antiretroviral therapy (ART) influences the probability of HIV transmission, as well as rates of HIV progression and HIV-related mortality. The model considers individuals on ART before ($c = 3$) and after ($c = 4$) achieving full viral load suppression (VLS), as defined by undetectable HIV RNA in blood samples. Among retained patients initiating ART, time to VLS is usually described as "within 6 months" [78]. More specifically, Mujugira et al. [79] estimate the median time to VLS as 3 months, yielding an estimated *mean* duration for $c = 3$ of 4.3 months (see § B.2.4), and thus $\sigma \approx 2.77$ per year.

[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 on ART

All available evidence suggests that viral suppression by ART to undetectable levels prevents HIV transmission, i.e., undetectable = untransmittable ("U=U") [80]. Thus, I assumed zero HIV transmission from individuals with VLS ($c = 4$). However, HIV transmission may still occur during the period between ART initiation to viral suppression ($c = 3$) [79]. Donnell et al. [41] estimate an adjusted incidence ratio of 0.08 (0.0, 0.57) for all individuals on ART. However, in [41] and [81], the 1 and 4 (respectively) genetically linked infections from individuals on ART all occurred within 90 days of ART initiation, suggesting that risk of transmission only persists before viral suppression. Adjusting the incidence denominator (person-time) to 90 days per individual who initiated ART in [41] results in approximately 3.13 times higher estimated incidence ratio: 0.25 for this specific period.[11] Thus, I sampled relative infectiousness on ART but before viral suppression ($c = 3$) from a beta distribution with mean (95% CI) of 0.25 (0.01, 0.67). Finally, I assumed that the virally un-suppressed state ($c = 5$) had half the reduced infectiousness of $c = 3$, yielding 95% CI: (0.50, 0.83).

3.2.5.2 HIV Progression & Mortality on ART

Effective ART stops CD4 cell decline and results in some CD4 recovery [82, 83]. Most CD4 recovery occurs within the first year of treatment [82]. 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 ($c = 3$). Lawn et al. [83] and Gabillard et al. [84] estimate an increase of between 25–39 cells/mm^3 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 $h = 6 \longrightarrow 5 \longrightarrow 4 \longrightarrow 3$ during pre-VLS ART ($c = 3$) as 0.20, 0.20, 0.17 per month, respectively. After initial increases, CD4 recovery is modest and plateaus. Battegay et al. [82] report approximate increases of 22.4 cells/mm^3 per year between years 1 and 5 on ART. Thus, I model rates of movement along $h = 6 \longrightarrow 5 \longrightarrow 4 \longrightarrow 3$ after VLS ($c = 4$) 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 [85]. Lundgren et al. [86] estimated 61% reduction in non-AIDS life-threatening events due to ART. For the same CD4 strata, Gabillard et al. [84] 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 ($c = 4$), and half this (25%) reduction before achieving VLS ($c = 3$).

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

Rates of HIV diagnosis δ, ART initiation τ, viral un-suppression ζ (including treatment failure, discontinuation, or loss to follow-up), and viral re-suppression σ' (Figure 3.1c) were defined to reflect historical trends

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

and ART eligibility for eSwatini. These rates were further calibrated to reproduce observed cascade attainment over time in eSwatini (e.g., proportion on ART among those diagnosed with HIV). Similar to condom use, rates were interpolated between specified years using monotone piecewise cubic interpolation [71].

3.2.6.1 HIV Diagnosis

Multiple eSwatini studies report the proportions of women and men who tested for HIV in the p12m. However, this proportion may not directly reflect the yearly rate of diagnosis, because individuals may test more frequently based on their perceived risk [87]. Indeed, EmaSwati living with HIV were more likely to have previously tested for HIV in 2006 [2, Table 14.9], 2011 [88, Table 5], and 2016 [5, Table 7.3]. Another consideration is that the proportion tested in p12m likely underestimates the *rate* of testing due to repeat testers. Assuming an exponentially-distributed time spent untested in the period under consideration (consistent with inherent compartmental modelling assumptions), the testing rate λ can be calculated from the proportion tested ρ over period T via:

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

HIV diagnosis rates over time δ were then parameterized based on testing rates using non-FSW women as a reference group, with separate time-varying *relative* rates defined for FSW and men. Confidence intervals for relative rates were assumed using a standard deviation of 0.2 for FSW and 0.1 for men (gamma priors).

Early HIV testing in eSwatini was mainly available to pregnant women via antenatal clinics, though a small number of youth and men also accessed HIV testing services [89, 90]. Based on antenatal clinic data [91], I modelled a gradual increase in rates of HIV diagnosis among women from zero to 95% CI (5, 15)% (gamma prior) per year from 1990 to 2002, when the national HIV testing and counselling program was formally introduced [92]. I assumed no initial differeces between FSW and other women, due to the lack of specific key populations prevention programs [93]. I further assumed that HIV diagnosis among men initially occurred at 10% the rate of women.

By 2006, ρ = 21.9 (20.6, 23.3)% of women and 8.9 (7.8, 10.0)% of men had tested for HIV and received the results in p12m [2][12] — relative rate: 0.377 (0.207, 0.597). Further scale-up of HIV testing began in 2006 via provider-initiated testing and improved integration with the general health care system [92]. Between 2007 and 2010, such efforts doubled the number of testing locations (119 to 241) and tripled the number of total yearly tests (53,000 to 154,000) [94, 92]. By 2011, ρ = 50.1% of women, 31.7% of men, and 61.7 (55.6, 67.5)% of FSW had tested for HIV in p12m [88, 33], yielding testing rates of λ = 0.709, 0.384, and 0.962 per year, respectively — relative rate: 0.542 (0.364, 0.755) for men, and 1.365 (1.084, 1.849) for FSW.

Phase 1 of the MaxART program [95] ran from 2011 to 2014, with a primary objective to increase HIV testing. An estimated 284,680 people were reached with 389,658 tests by the end of Phase 1 (2014). By 2016, 57.1% of women and 47.8% of men had tested in p12m [5], yielding testing rates of λ = 0.846 and 0.650 per year, respectively — relative rate: 0.770 (0.587, 0.978) for men. In 2014 [34] and 2020

[12] Unless otherwise noted, "*tested for HIV*" will imply "*and received the results*" throughout this section.

[35] approximately ρ = 75% of FSW had tested in p12m (λ = 1.386) as such, I applied a relative rate of 1.62, (1.29, 2.07) for 2016. I held all rates of HIV diagnosis after 2016 fixed.

3.2.6.2 ART Initiation

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

Eligibility. Historical ART eligibility in eSwatini has generally followed the evolving World Health Organization (WHO) guidelines [96, 97, 98, 99]. Initial eligibility included one of [7]:

- CD4 < 200 cells/mm^3 and any WHO clinical stage
- CD4 < 350 cells/mm^3 and WHO clinical stage III
- any CD4 count and WHO clinical stage IV

Eligibility was revised in 2010 [8] to:

- CD4 < 350 cells/mm^3 and any WHO clinical stage
- any CD4 count and WHO clinical stage III or IV

and again in 2015 [9] to:

- CD4 < 500 cells/mm^3 and any WHO clinical stage
- in a discordant partnership or having a specified illness (any CD4 count or WHO clinical stage)

before adoption of the current "*ART for all*" guidelines in late 2016 (modelled as effectively January 2017) [100, 10]. Phase 2 of MaxART also began in 2015, offering immediate ART via 14 health facilities in a stepped wedge design (6 facilities added per year) [100]. Relative to the 114 total facilities offering ART nationally at this time [101], I assumed this trial had minimal direct impact on population-level ART initiation — notwithstanding valuable insights gained regarding effective implementation [100].

I implemented the CD4-only eligibility criteria directly in the model, which is structured to match these 200, 350, and 500 CD4 cells/mm^3 thresholds (Figure 3.1b). For eligibility by WHO clinical stages (not explicitly modelled), I estimated relative rates of ART initiation based on the following data from South Africa [102, Table 4] and Saudi Arabia [103, Table 2], respectively:

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

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

Availability and Initiation. ART first became available in eSwatini in late 2003 via a one-hospital pilot project [92]. Early ART scale-up was modest, with 31 facilities offering ART by the end of 2009 [104]; however, this number increased rapidly to 110 facilities by the end of 2011 [92]. Phase 1 of MaxART (2011–2014) sought to further increase ART coverage among eligible PLHIV [95], including decentralization

to lower level facilities, bringing the total number of facilities to 170 by 2015 [105]. Finally, national adoption of "*Test and Start*" in 2017 likely further reduced delays in ART initiation, while loss to follow-up was reduced throughout the years of ART scale-up [100].

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

Group Differences. In 2011, conditional ART coverage (among diagnosed) was greater among men versus women (Table 3.9), suggesting greater ART initiation among men versus women. Yet, unconditional ART coverage (among PLHIV, regardless of diagnosis) were approximately equal (31.4 and 33.2%, respectively), and so conditional differences may be explained by the fact that women were more likely to be diagnosed at an earlier HIV stage via antenatal care, and thereafter not yet eligible for ART. Thus, I assumed no differences in ART initiation among men versus women. A similar mechanism could partially explain differences in conditional coverage between FSW versus women overall (36.9 versus 48.0%), as FSW were more slightly likely to know their status (74.1 versus 69.1%). However, FSW face unique barriers to accessing ART related to stigma and material insecurity [106]; as such, I sampled a relative rate for ART initiation among FSW from [0.5, 1] (uniform prior).

3.2.6.3 ART Failure

The modelled virally un-suppressed state ($c = 5$) reflects any combination of treatment failure (i.e., due to resistance mutations), discontinuation, or loss to follow-up (LTFU) after achieving viral suppression. The model does not explicitly simulate emergence and/or transmission of drug resistance, nor multiple unique ART regimens. As of 2016, resistance mutations to at least 1 of 3 drugs in combination regimens were identified in 10% ART-naive PLHIV in eSwatini, and 16% PLHIV with prior ART exposure [107]. However, the extent to which these individual mutations can cause complete treatment failure remains unclear. Additionally, while transmissible resistance mutations could become more prevalent over time, emergence of new drugs (e.g., Dolutegravir) can combat the population-level impacts of this resistance [108].

All available data suggests that retention in ART care — i.e., not discontinued or LTFU — has improved over time in eSwatini [109, 110, 5]. Assuming an exponentially-distributed retention time (consistent with inherent compartmental modelling assumptions), I averaged the available data [110, Table 6] to calculated the effective yearly ART attrition rate as: 16.5% in 2008, 13.8% in 2010, 14.1% in 2012, and 8.3% in 2014. One-year LTFU was reported as 1% in 2016 [5], but it's not clear whether this definition was consistent with the earlier estimates. Many measures of LTFU may also overestimate true LTFU by failing to account for transfers between clinics and deaths [111, 112]; it's not clear whether the reported measures for eSwatini account for transfers or deaths.

LTFU was estimated to be 1.3 times higher among men versus women in South Africa [111], which would be consistent with observed lower viral suppression among men versus women on ART in eSwatini (Table 3.9) [111]. The same study estimated that LTFU did not significantly differ by the modelled CD4-strata [111]. No estimates of LTFU were available for FSW specifically in eSwatini, but among 354

FSW on ART in [35] (2021), 103 knew the results of viral load monitoring in p12m, of whom only 8 self-reported undetectable viral load. Such data may again reflect the unique barriers to accessing ART faced by FSW [106].

Considering all of the above data, I assumed: a yearly rate of viral un-suppression ζ among non-FSW women of 10% until 2010, decreasing to 3% by 2018; plus relative rates for men: [1, 1.5], and FSW: [1, 2] (uniform priors).

3.2.6.4 Viral Re-suppression

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

For treatment failure, viral un-suppression must first be identified. Availability of viral load monitoring in eSwatini was limited until at least 2010 [8], but incorporated into standard of care by 2015 (yearly testing) [9]. Without viral load testing, treatment failure can still be indicated clinically [8]. After suspecting treatment failure, at least three months of additional monitoring is typically required to rule-out issues of adherence [8, 9, 10], before another regimen is started. Moreover, second/third-line regimen options were limited in eSwatini until at least 2014 [101]. Upon switching to an improved regimen, I assume that viral suppression occurs at the same rate as among ART-naive PLHIV (see § 3.2.5).

For LTFU, no data directly indicate the average duration out of care in eSwatini. A recent model-based analysis of Kenyan data [113] suggests an average between 8 months and 2 years. Considering large-scale, multisectorial efforts to improve ART care in eSwatini, it is likely that duration out of care has declined since 2010. Thus, I sampled the initial rate of viral re-suppression σ' from a gamma prior with 95% [0.5, 1.0], which was doubled over 2010–2018. I assumed no differences between groups.

3.2.7 Sex Work: Population Sizes & Partner Numbers

3.2.7.1 Population Sizes

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

Female Sex Workers. The proportion of women who report sex work in national demographic and health surveys is generally considered unreliable due to social desirability bias, particularly if the survey is face-to-face and household-based [114, 115, 116, 117, 66]. Therefore, FSW population size estimates require targeted surveys and unique methodologies [118, 119]. In both [34] and [35], the Swati FSW population size was estimated using a combination of unique object method, service multiplier method, prior survey participation, and network scale-up method (NSUM) [118]. In 2011 [34], regional FSW population size estimates ranged from 0.7% to 6.5% of all women, with overall population-weightedd mean across regions of 2.9%; in 2021 [35], the mean (95% CI) estimates were 2.43 (1.17, 5.02)%. To reflect this uncertainty in the model, a 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 [66]. However, few surveys are designed to reach clients of FSW, and no direct estimates of FSW size exist for eSwatini. So, I use a common approach for inferring the FSW client size [69], similar to the "multiplier method" [120]. 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:

$$\sum_i P_{s_2 i_{34}} = \frac{\sum_{i,p} P_{s_1 i_{34}} C_{p_{34} s_1 i_{34}} F_{p_{34}}}{\sum_{i,p} C_{p_{34} s_2 i_{34}} F_{p_{34}}} \tag{3.3}$$

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

3.2.7.2 Sex Work Partnerships

Female Sex Workers. Table 3.3 summarizes the numbers of numbers of new and regular clients per month reported by Swati FSW, stratified by higher vs lower risk per the analysis in § 3.2.1.3. Based on the survey questions,[13] 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 $C_{p_3 s_1 i_{34}}$. 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) × 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 month. If *N* reflects the numbers of unique clients, then $C_{p_4 s_1 i_{34}}$ should be defined as *N* directly; whereas if *N* reflects the numbers of unique visits, then $C_{p_4 s_1 i_{34}}$ should be defined as $N/(F_{p_4}/12)$. I therefore derived a sampling distribution for $C_{p_4 s_1 i_3}$ 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:

$$C_{p_4 s_1 i_3} \sim (\rho)\, N + (1 - \rho)\, N / (F_{p_4}/12) \tag{3.4}$$

I obtained mean (95%CI): 6.1 (2.7, 9.7) for $C_{p_4 s_1 i_3}$, 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.

[13] The survey questions were: "*In the last 30 days, how many (new/regular) clients have you had sex with?*", or similar.

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 [121]. 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 [122]. Johnson and Dorrington [123] 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 § 3.2.8.4 for numbers of main/spousal and casual partnerships among FSW and clients.

3.2.8 Non-Sex Work: Group Sizes & Partner Numbers

3.2.8.1 Reported Partner Numbers

The 2006-07 DHS [2], 2011 SHIMS [62], and 2016-17 SHIMS2 [5] surveys provide the numbers of respondents who reported 2+ partners in the past 12 months (p12m): 13.5, 18.2, 14.5% among men, and 1.6, 3.8, 4.1% among women, respectively.[14] 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 [114, 124, 116, 66].

Regarding the types of partnerships reported. Both the 2006 DHS [2, Tables 14.6.1 and 14.6.2] and 2016-17 SHIMS [5, Tables 15.4.A and 15.4.B] summarize the numbers of women and men by partners in p12m *and* by marital/union status, although summaries are stratified by each factor separately, not jointly. However, making the following assumptions, I estimated the jointly-stratified proportions of individuals. Let W_{2+}, W_1, and W_0 denote women reporting 2+, 1, and 0 partners, respectively, and likewise with M_{2+}, M_1, M_0 for men (all partners reflect p12m).[15] The assumptions were:

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

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

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 [125, 126], 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. [115] (Zimbabwe), Nnko et al. [127] (Tanzania) and Clark, Kabiru, and Zulu [128] (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 [129, 130]. In fact, a review comparing computer-based tools versus face-to-face interviews for surveying sexual behaviour [131] found that *both* women and men may under-report sexual partners, but women more so. A notable study in Benin [66] found that 7 times as many married women (21 vs 3%) and 3 times as many married men (53 vs 18%) reported any extramarital sex in p12m in a surveys via anonymous polling booth vs face-to-face interview. Similarly, 5 times as many unmarried women (13.5 vs 2.8%) reported exchanging sex for money, gifts or favours in p12m, while 4 times as many unmarried men (62 vs 14%) reported non-transactional sex with a women in p12m. Such findings were similar to those from Zimbabwe (1990s) [115].

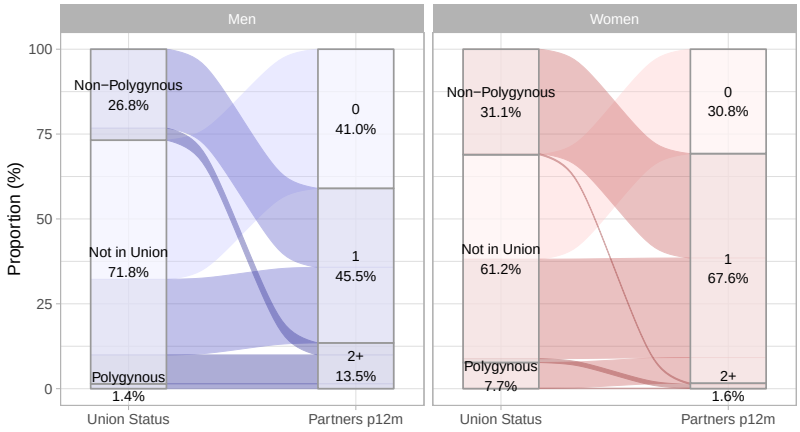
3.2.8.2 Bias Adjustment: Approach

Reflecting these potential reporting biases, I modelled the "true" proportions of Swati women and men in each union/partners in p12m stratum as follows. Let W_{s1} and W_{u1} denote sub-proportions of W_1 who are single and in a union, respectively, and likewise for W_{s2+}, W_{u2+}, M_{s1}, M_{u1}, M_{s2+}, and M_{u2+}. Further, let W_{s1} denote the reported proportion of women (average of 2006-07 and 2016-17), versus W'_{s1} denoting the "true" (adjusted) proportion. I assumed that a faction of W_0 belongs in W'_{s1} — i.e., a fraction of women reporting 0 partners in p12m truly had 1 casual (non-main/spousal) partner. I modelled this relationship through an odds ratio $\varphi_{W,s1:0}$, which is roughly equivalent in interpretation to the proportion ratios estimated by Béhanzin et al. [66]:[16]

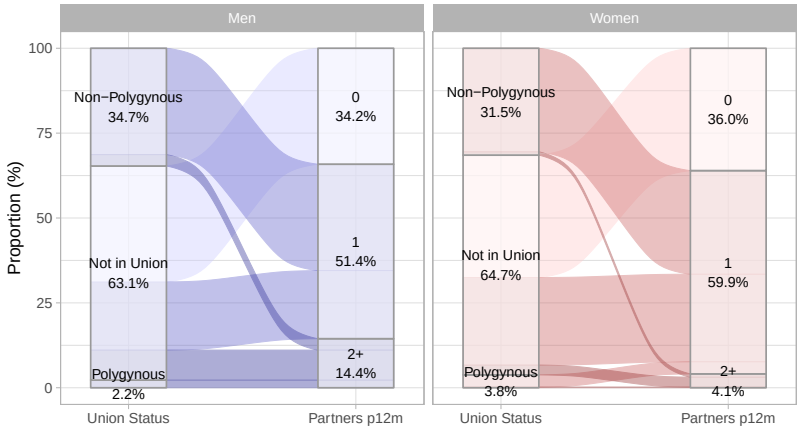
$$\varphi_{Ws1:0} = \frac{W'_{s1}}{W'_0} \Big/ \frac{W_{s1}}{W_0} \tag{3.5}$$

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.

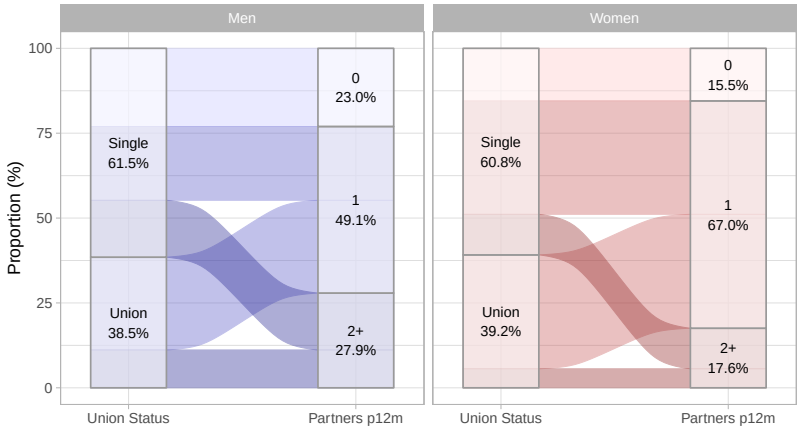
[16] Odds ratios ensure no proportions become greater than one or negative.



(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

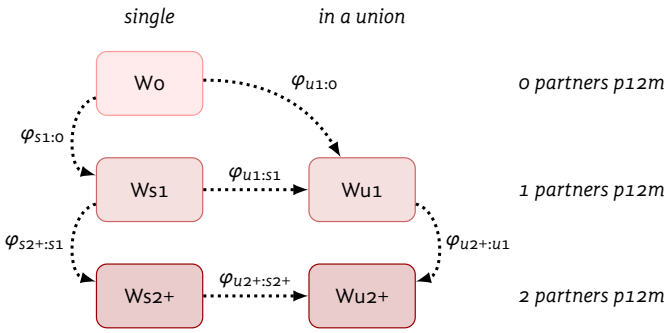


Figure 3.5: Illustration of how women (and equivalently men) are reallocated between union/partners in p12m strata based on odds ratios φ

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.

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 (vertial 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 [66], I assumed that "single" women and men (not married/cohabiting) were less likely to report multiple partners in p12m, but women more so. Thus, I sampled $\varphi_{s2+:s1}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = 4$ for women and $\alpha = 1$ for men, yielding 5.00 (2.09, 9.77) and 2.00 (1.03, 4.69). I made a similar assumption about married/cohabiting women and men, with the same odds for men, but even greater odds of non-reporting among women. I sampled $\varphi_{u2+:u1}$ from $1 + \text{Gamma}(\alpha, \beta = 1)$ with $\alpha = 6$ for women and $\alpha = 1$ for men, yielding 7.00 (3.20, 12.67) and 2.00 (1.03, 4.69).

3.2.8.3 Bias Adjustment: Resulting Group Sizes & Partner Numbers

The mean resulting adjusted proportions W' and M' from solving the system with the assumed odds ratios φ are illustrated in Figure 3.4c, which can be compared to the reported proportions in a and b. Figure 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'_{01} = 38 (21, 57)% women and M'_{u1}/M'_{01} = 35 (23, 50)% men with 0–1 partners in p12m were in a main/spousal partnership
- W'_{s1}/W'_{01} = 41 (19, 65)% women and M'_{s1}/M'_{01} = 31 (15, 55)% men with 0–1 partners in p12m were in a single casual partnership
- W'_{u2+}/W'_{2+} = 32 (9, 55)% women and M'_{u2+}/M'_{2+} = 38 (13, 62)% men with 2+ partners in p12m were in a main/spousal partnership, and the rest had only casual partnerships.

Group Sizes. From these results, I defined the sizes of the modelled lower and medium activity groups, and the average numbers of main/spousal partnerships per person. I assumed that W'_{2+} and M'_{2+} included FSW and client population sizes, respectively (see § 3.2.7.1). Thus, the populations size of medium activity women was defined as $P_{s_1i_2} = W'_{2+} - P_{s_1i_{34}}$. Sampling W'_{2+} from a beta distribution with 95% CI (10, 27)%, the resulting 95% CI for medium activity women $P_{s_1i_2}$ was (6, 25)% of women. The lowest activity women population size was then defined as $1 - P_{s_1i_{234}}$, representing (73, 90)% of women. Since there is greater uncertainty in the client population size, the same approach for the medium activity men population size $P_{s_2i_2}$ could yield negative values. Instead, I sampled $P_{s_2i_2}$ directly from a beta distribution with 95% CI (10, 17)%, yielding 95% CI for $P_{s_2i_{234}}$ of (15, 50)% of men, which is close to (15, 44)% from M_{2+}. The lowest activity men were then then defined as $1 - P_{s_2i_{234}}$, 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 ($C_{p_1s_{12}i_1}$), as well as all women in the median activity group ($C_{p_1s_1i_2}$). Since FSW and clients had fewer main/spousal partnerships (see § 3.2.8.4), I calculated the proportion of men in the medium activity group having main/spousal partnerships $C_{p_1s_2i_2}$ to balance the total number of main/spousal partnerships among women and men.

Casual Partnerships. I similarly defined a common proportion of women and men in the lowest activity groups having casual partnership $C_{p_2s_{12}i_1}$ with 95% CI (20, 55)%. However, the number of casual partnerships among W_{2+} and M_{2+} ramains 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.

3.2.8.4 Main/Spousal & Casual Partnerships among FSW & Clients

Among Swati FSW, the mean number of total non-paying partners in the past month was approximately 1–1.5 (Table 3.3), which may include both main/spousal partners and casual partners. Among FSW in South Africa [132] and Kenya [133], 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., $C_{p_1 s_1 i_{34}} = 0.5$); lower risk FSW had $C_{p_2 s_1 i_3} = 0.5$ casual partners; and higher risk FSW had $C_{p_2 s_1 i_4} = 1.0$ 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 [134, 74]. Non-paying partners of FSW are also often clients of other FSW [133, 135]. Yet, clients of FSW also tend to be younger and more likely to be never/formerly married versus non-client men [134, 136]. So, I assumed that clients had half the numbers of main/spousal partnerships compared to lowest activity men: $C_{p_1 s_2 i_{34}} = 0.5\, C_{p_1 s_2 i_1}$, and 25–100% the numbers of casual partnerships compared to medium activity women (uniform prior).

3.2.9 Turnover

3.2.9.1 Births & Deaths

The modelled population considers ages 15–49, reflecting commonly reported data and the majority of sexual activity. In the absence of mortality, individuals would therefore remain within the modelled "open cohort" population for 35 years. The estimated average yearly mortality rate for these ages was 1.44% around 2006 [2, Table 15.2]. However, this estimate includes HIV/AIDS-attributable mortality, which I model separately (see § 3.2.4.2), accounting for approximately 64% of deaths around that time [137]. Thus, the overall exit rate from the modelled cohort due to reaching age 50 ("aging out") and non-HIV-attributable mortality was: $\mu = 1/35 + (1 - .64)1.44\% = 3.78\%$.

I estimated the rate of entry into the modelled population ν to fit population size of ages 15–49 in eSwatini [14], and approximate population growth rates [138], 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 [138]. Finally, I calculated the population entry rate as $\nu = g + \mu$. These parameter values were informally validated by comparison of model outputs with Swati population sizes for ages 15–49 from [14].

3.2.9.2 Activity Group Turnover

In addition to overall population turnover (entry/exit from the open population), I model movement of individuals between activity groups within the model. Activity group turnover reflects the fact that risk is not constant over sexual life course, and reported duration in higher activity contexts can be short [16]. Previous modelling has shown that activity group turnover (sometimes called "episodic risk") can strongly influence parameter fitting and intervention impact [139, 140]. 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} [141]:

$$D_{si} = \frac{1}{\mu + \sum_{i'} \theta_{sii'}} \tag{3.6}$$

where μ is the overall exit rate from § 3.2.9.1. As shown previously [140], 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 [33] and 5 [3, 9] in 2014 [34], 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 [33] and 2021 [35]. 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 [142]. 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 [143]. Finally, I assumed that higher risk FSW stay in sex work longer by a factor of R_D with 95% CI (1.54, 3.25) (gamma prior, Table 3.3). Thus, durations in sex work among higher risk (D_{HR}) and lower risk (D_{LR}) FSW can be resolved using:

$$\begin{aligned} \bar{D} &= 0.2\,D_{HR} + 0.8\,D_{LR} \\ R_D &= D_{HR}/D_{LR} \end{aligned} \tag{3.7}$$

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. [143] estimated mean durations of 4.6–5.5 years based on studies in Benin [134] and Kenya [121]. Hodgins et al. [144, 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 [125] suggested that sexual activity (proportion sexually active and mean numbers of partners) was approximately stable with age (after sexual debut and 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 [142, 145]. 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 [16, 146], 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)%.

3.2.10 Sex Frequency & Partnership Duration

3.2.10.1 Sex Frequency

The eSwatini general population data sources [2, 62, 5] did not report on frequency of sex. In South Africa, average numbers of sex acts per week per partnership (non-sex work) was reported as mean 2.5 (IQR: 1–3) [147], 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 [148, Figure 3.15], which is roughly consistent with [147], 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" [149]. 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 § 3.2.7.2, 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.

3.2.10.2 Anal Sex

Among eSwatini data sources, only [34] (FSW, 2014) counted sex acts separately for anal and vaginal sex. Among all FSW, the proportion of "average sex acts per week" that were anal (vs vaginal) was 2.9%. However, a previous coital diary study in neighbouring KwaZulu-Natal suggested much higher proportions were anal [150], and face-to-face interview survey design may result in under-reporting [151]. Owen et al. [152] 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.[17] 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)%.

3.2.10.3 Partnership Duration

As explored in Chapter **??**, the durations of sexual partnerships can be key determinants of epidemic dynamics and intervention impact.[18] eSwatini-specific data on partnership duration are lacking. Moreover, accurate estimation of partnership duration remains challenging even when data exist, due to censoring,

[17] "Higher-risk" populations in [152] were defined as: "*STI clinic patients, FSW, their clients, and HIV-infected individuals*".
[18] Chapter **??** also discusses the related phenomenon of partnership concurrency, and how concurrency is represented in compartmental models.

truncation, and sampling biases [153]. 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.[19] 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 [154]; 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 per Eq. (3.2), I defined $\rho \in (0.56, 0.71)$, $t = 52 - 26 = 26$ years, yielding an effective partnership termination rate of $\lambda \in (1.32, 2.23)\%$ per year, and an effective partnership duration of $\delta_{p_1} = \lambda^{-1} \in (45, 76)$ years.

Classically, partnership duration is used to define the total numbers of sex acts per modelled partnership (see § **??**); with this approach, we should therefore use $\delta_{p_1} = \rho\,(49 - 26) \in (14.5, 18.5)$ years, since the modelled population only includes ages 15–49. However, the proposed approach to modelling partnerships introduced in § **??** can make use of the effective termination rate. In fact, the proposed approach uses a partnership *change* rate, which would be even slower than the partnership termination rate, as the change rate would also consider whether and when divorced/separated individuals form *new* main/spousal partnerships. The change rate could even be tied to the modelled baseline and HIV-attributable mortality, given that the majority of unions ended via spousal death (83% of unions among women and 56% among men by age 50–54) [2]. For simplicity, I assumed an effective main/spousal partnership change rate of 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 [155, 156, 157], Rural Tanzania [127], and four cities in Kenya, Zambia, Benin, and Cameroon [158]. 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 [159].

Sex Work Partnerships. As noted in § 3.2.7.2, duration of occasional sex work partnerships is ill defined, but can be defined to comprise a single sex act with $F_{p_3}\delta_{p_3} = 1$. Data on regular sex work partnerships is severely limited, and sometimes regular paying clients later become non-paying emotional partners [133, 160]. Based on [121], 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.

[19] 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).

3.2.11 Mixing

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

3.2.11.1 Classic ϵ Mixing

In many risk/activity-stratified compartmental transmission models, mixing is parameterized via a single parameter $\epsilon \in [0, 1]$, which controls the degree of like-with-like mixing [161]. This approach is often attributed to [162], wherein a key adjustment for imbalanced partner numbers among women vs men was introduced. The approach defines the *probability* of someone from group i forming a *given* type-p partnership with someone from group i' as:

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

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 $M_{pii'} = M_{pi}\, \rho_{pii'}$. 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**].

3.2.11.2 Log-Linear Mixing

A more general approach to mixing is developed in [163]. This "log-linear" approach defines the mixing matrix elements $M_{pii'}$ as follows. The expected total numbers of partnerships between risk groups under random mixing are defined as:

$$\Pi_{pii'} = \frac{M_{pi} M_{pi'}}{\sum_j M_{pj}} \tag{3.9}$$

Next, a matrix $\Phi_{pii'}$ 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) [163]. Then, an initial estimate of $M_{pii'}$ is:

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

However, this estimate changes the total numbers of partnerships formed by each group: $M_{pi}^{(0)} \neq \Pi_{pi}$, where $M_{pi} = \sum_{i'} M_{pii'}$ and $\Pi_{pi} = \sum_{i'} \Pi_{pii'}$. There is no *a priori* definition of $M_{pii'}$ or adjustment to $\Phi_{pii'}$ that can guarantee the numbers of partnerships will not change.[20] However, an iterative proportional fitting procedure [164] can resolve an estimate $M_{pii'}^{(n)}$ that maintains the total numbers of partnerships:

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

Each step of this procedure can be understood as a re-scaling of the current estimate $M_{pii'}^{(n)}$ 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 [165].

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 $M_{pii'}$ 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 $\Phi_{pii'}$.

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 "compromise" parameter θ in [162], 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.

3.2.11.3 Odds of Mixing

Despite the flexibility in the odds of mixing matrix $\Phi_{pii'}$, limited data are available to inform specific elements, especially for eSwatini in particular. In Kenya [133], Benin, Guinea, and Senegal [135], and Uganda [160], 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:

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

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

Taking $\psi \in (0.33,\ 0.70)$ [133, 135] and $\rho \in (5,\ 20)\%$ [144], we obtain $\Phi \in (2,\ 19)$. As noted in § 3.2.8.4, 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 [166], observed like-with-like sexual mixing preferences in numerous other contexts [163, 167, 168], and prior modelling work [169]. I sampled $\Phi_{p_1 i_1 i'_1}$ 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.

3.3 Calibration

The parameters described in § 3.2 represent model inputs, many of which were uncertain. For each uncertain parameter, I specified a prior distribution based on the available data and/or reasonable assumptions. Next, I further refined these distributions through model calibration to "calibration targets": additional data representing model *outputs*. Such data are detailed in § 3.3.2, and include estimates of HIV incidence, prevalence, and the cascade of care for the population overall, and stratified by risk group where possible.

3.3.1 Approach

I use a Bayesian approach for model calibration [170]. Let θ denote the complete set of model parameters, and T the complete set of calibration targets. Our goal is to obtain samples from the posterior distribution of parameters given the targets $p(\theta \mid T)$. This posterior distribution can be defined via Bayes' rule as:

$$p(\theta \mid T) = \frac{p(T \mid \theta)\, p(\theta)}{p(T)} \tag{3.13}$$

Then, the posterior distribution can be characterized empirically via Monte Carlo simulation — i.e., by randomly sampling parameter sets $\theta_s \sim p(\theta)$, and for each set computing the likelihood $p(T \mid \theta_s)$. This likelihood is defined via independent uncertainty distributions for each calibration target T_i. For example, overall HIV prevalence in eSwatini was estimated as 32.1% from a sample of ~ 18,000 individuals in 2011 [3]. Using this information, I define a beta approximation of the binomial distribution, which I use as the likelihood function for this calibration target $p(T_i \mid \theta_s)$. The independent likelihoods are aggregated as:

$$p(T \mid \theta_s) = \prod_i p(T_i \mid \theta_s) \tag{3.14}$$

Although several iterative methods exist to update the sampling distributions based on the likelihoods, and thereby characterize the posterior distribution more efficiently [170], I do not update the sampling distributions. Rather, I simply take the top $f \approx 0.01$ proportion of parameter sets θ_s by likelihood, and assume these are approximately representative of the posterior distribution.

3.3.2 Calibration Targets

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

3.3.2.1 HIV Prevalence

Table 3.5 summarizes the available HIV prevalence data for eSwatini. Uncertainty around each estimate was modelled using a beta approximation of the binomial distribution. I made several adjustments to the estimates as follows.

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

Biased Partner Number Reporting. As discussed in § **??**, I assumed that the proportion of the population reporting 0–1 sexual partners p6m ("lower risk") is overestimated, and the proportion reporting 2+ ("non-lower risk") is underestimated. While overall HIV prevalence estimates would not be affected by this reporting bias, HIV prevalence among the lower risk group would be overestimated. To correct this overestimate, I further assumed that HIV prevalence among "observed" non-lower risk (had 2+ partners p6m, reported 2+) was representative of HIV prevalence among "unobserved" non-lower risk (had 2+, reported 0–1). Thus, HIV prevalence among the "true" lower risk (had 0–1, reported 0–1) can be estimated as:

$$H_{01} = \frac{H - H_{2+} W'_{2+}}{W'_{01}} \tag{3.15}$$

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

Respondent Ages. The 2006 and 2016 surveys provide data for ages 15–49 (the age range intended to be captured by the model) while the 2011 survey was limted to ages 18–49. Since HIV prevalence is much lower among ages 15–17, the 2011 estimates would be biased high; so, I adjusted all 2011 HIV prevalence estimates in as follows. Drawing on age-stratified data in 2006 [2] and 2011 [3], I assumed that HIV prevalence among ages 15–17 was 5% among girls/women, 2% among boys/men, and 3.5% overall. Next, I estimated the fraction of women aged 15–17 among all women aged 15–49 (13.5%), and likewise for men (15.4%) and overall (14.4%) [171]. I then estimated HIV prevalence among women, men, and overall for ages 15–49 using a weighted average of the 15–17 and 18–49 estimates. Finally, I computed the resulting relative reduction in HIV prevalence for women overall, and applied this reduction equally to the HIV prevalence estimates for lower risk and non-lower risk women, and likewise for men and the population overall.

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

Table 3.5: Estimates of HIV prevalence in eSwatini

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

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

Table 3.6: Estimated HIV prevalence ratios in eSwatini

Numerator [a]	Denominator [a]	Year	Ratio	(95% CI)	Used	Ref	Notes
Non-LR Women	LR Women	2006	2.02	(1.84, 2.34)	✓	[2]	
		2011	1.54	(1.47, 1.66)	✓	[3]	
		2016	1.42	(1.37, 1.51)	✓	[5]	
Non-LR Men	LR Men	2006	2.57	(2.16, 5.28)	✓	[2]	
		2011	1.24	(1.20, 1.34)	✓	[3]	
		2016	1.31	(1.34, 1.45)	✓	[5]	
FSW Overall	Women Overall	2011	2.16	(1.87, 2.50)	✓	[33, 3]	
HR FSW	LR FSW	2011	1.46	(1.30, 1.63)	✓	[33]	
		2014	2.30	(1.92, 2.75)	✗	[34]	

[a] LR: lower risk, reporting 0-1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; HR/LR FSW: higher/lower risk FSW, as defined in § 3.2.1; TODO all estimates used the skew normal distribution.

available data, I defined the prevalence ratio targets in Table 3.6. These targets were heavily right skewed.

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

3.3.2.2 HIV Incidence

Population-level incidence was first measured in the 2011 Swaziland HIV Incidence Measurement Survey (SHIMS) via 6-month cohort (gold standard) [62, 4], in which 145 seroconversions were observed among 11,232 re-tested (94.4% follow-up). The follow-up SHIMS2 study in 2016–17 used the HIV-1 Limiting Antigen Enzyme Immunoassay (LAg EIA) "recency test", which detects infections acquired within the past 141 days, 95%CI: (119, 160) [172]; this LAg EIA incidence measure was validated during SHIMS1 [62]. Recency testing was also recently integrated into eSwatini standard of care [63].

Table 3.7 summarizes the available HIV incidence data for eSwatini. Uncertainty around each estimate was modelled using a skew normal distribution. As with prevalence, the 2011 estimates were adjusted for the missing 15–17 age range, this time assuming 2% and 0.4% annual incidence among girls/women and boys/men aged 15–17, respectively. The 2011 estimates for lower risk women and men were also adjusted for biased partner number reporting using the same approach as for HIV prevalence. Several incidence ratios were also defined (Table 3.8).

No study of FSW in eSwatini estimated incidence directly, but the 2021 study [35] reported that 30 of 676 prevalent HIV infections among FSW were identified as recent via LAg EIA per national guidelines [5, 63]. Using Eq. (3.2) with $\rho = 30/676 = 4.44\%$ and $t = 130$ days, I computed an incidence rate of $\lambda = 11.7\%$ per year. I further estimated uncertainty for this rate by combining the 95% CI from $\rho \sim \text{Binom}(p = 4.44\%, N = 676)$ and $t \in (118,\ 140)$, yielding 95% CI for λ of (8.3, 16.9).

Table 3.7: Estimates of HIV incidence in eSwatini

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

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

Table 3.8: Estimated HIV incidence ratios in eSwatini

Numerator [a]	Denominator [a]	Year	Ratio	(95% CI)	Used	Ref	Notes
Non-LR Women	LR Women	2006	2.02	(1.84, 2.34)	✓	[2]	
		2011	1.54	(1.47, 1.66)	✓	[3]	
		2016	1.42	(1.37, 1.51)	✓	[5]	
Non-LR Men	LR Men	2006	2.57	(2.16, 5.28)	✓	[2]	
		2011	1.24	(1.20, 1.34)	✓	[3]	
		2016	1.31	(1.34, 1.45)	✓	[5]	

[a] LR: lower risk, reporting 0-1 partners p6m; Non-LR: lower risk, reporting 2+ partners p6m; FSW: female sex worker; all estimates used the skew normal distribution.

3.3.2.3 HIV Cascade of Care

Table 3.9

Table 3.9: Estimated HIV cascade of care in eSwatini

Step [a]	Population [a]	Year	N	%	(95% CI)	Used	Ref	Notes
Diagnosed among PLHIV	Overall	2011	5,807	62.6	(61.4, 63.8)	✓	[88]	bc
		2016	2,417	86.1	(84.7, 87.6)	✓	[5]	e
	Women overall	2011	3,810	69.1	(67.6, 70.6)	✓	[88]	b
		2016	1,690	90.2	(88.6, 91.8)	✓	[5]	e
	Men overall	2011	1,997	50.1	(47.9, 52.3)	✓	[88]	b
		2016	727	77.3	(74.0, 80.6)	✓	[5]	e
	FSW	2011	313	74.1	(61.7, 89.8)	✓	[173]	d
		2021	411	88.3	(85.1, 91.2)	✓	[35]	bf
On ART among Diagnosed	Overall	2011	3,635	52.1	(50.5, 53.7)	✓	[88]	bcd
		2016	2,113	87.8	(86.0, 89.6)	✓	[5]	e
	Women overall	2011	2,633	48.0	(46.1, 49.9)	✓	[88]	bd
		2016	1,532	87.5	(85.4, 89.6)	✓	[5]	e
	Men overall	2011	1,002	62.7	(59.7, 65.7)	✓	[88]	bd
		2016	581	88.4	(85.2, 91.6)	✓	[5]	e
	FSW	2011	174	36.9	(30.1, 44.2)	✓	[173]	
		2021	363	97.5	(95.7, 98.9)	✓	[35]	bf
On ART among PLHIV	Overall	2011	5,807	31.9	(30.7, 33.1)	✓	[88]	bc
		2016	2,417	75.6	(73.6, 77.5)	✓	[5]	e
	Women overall	2011	3,810	33.2	(31.7, 34.7)	✓	[88]	b
		2016	1,690	78.9	(76.8, 81.1)	✓	[5]	e
	Men overall	2011	1,997	31.4	(29.4, 33.4)	✓	[88]	b
		2016	727	68.3	(64.7, 72.0)	✓	[5]	e
	FSW	2011	313	27.4	(20.9, 35.7)	✓	[173]	d
		2021	411	86.1	(82.6, 89.3)	✓	[35]	bf
VLS among On ART	Overall	2016	1,858	90.3	(89.0, 91.6)	✓	[5]	e
	Women overall	2016	1,342	91.4	(89.9, 92.8)	✓	[5]	e
	Men overall	2016	516	87.6	(84.4, 90.9)	✓	[5]	e
VLS among PLHIV	Overall	2016	2,417	68.2	(66.1, 70.4)	✓	[5]	e
	Women overall	2016	1,690	72.1	(69.7, 74.5)	✓	[5]	e
	Men overall	2016	727	59.9	(56.1, 63.7)	✓	[5]	e

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

References

[1] S. Gill. "A process for the step-by-step integration of differential equations in an automatic digital computing machine". *Mathematical Proceedings of the Cambridge Philosophical Society* 47.1 (1951), pp. 96–108. https://doi.org/10.1017/S0305004100026414.

[2] Central Statistical Office Swaziland. *Swaziland Demographic and Health Survey 2006-07*. Mbabane, Swaziland, 2008. https://dhsprogram.com/.

[3] George T. Bicego et al. "Recent Patterns in Population-Based HIV Prevalence in Swaziland". *PLOS ONE* 8.10 (Oct. 2013), e77101. ISSN: 19326203. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0077101.

[4] Jessica Justman et al. "Swaziland HIV Incidence Measurement Survey (SHIMS): a prospective national cohort study". *The Lancet HIV* 4.2 (Feb. 2016), e83–e92. ISSN: 23523018. arXiv: 15334406. https://www.sciencedirect.com/science/article/pii/S2352301816301904.

[5] Eswatini Ministry of Health. *Swaziland HIV Incidence Measurement Survey 2 (SHIMS2) 2016-2017*. Mbabane, Eswatini, 2019.

[6] Tara D. Mangal. "Joint estimation of CD4+ cell progression and survival in untreated individuals with HIV-1 infection". *AIDS* 31.8 (May 2017), pp. 1073–1082. https://doi.org/10.1097/QAD.0000000000001437.

[7] Swaziland Ministry of Health. *National Guidelines for Antiretroviral Treatment and Post Exposure Prophylaxis*. Tech. rep. Mbabane, Swaziland, 2006.

[8] Swaziland Ministry of Health. *The National Guidelines on the Comprehensive HIV Package of Care for Adults and Adolescents in Swaziland*. Tech. rep. Mbabane, Swaziland, 2010.

[9] Swaziland Ministry of Health. *Swaziland Integrated HIV Management Guidelines*. Tech. rep. Mbabane, Swaziland, 2015.

[10] Swaziland Ministry of Health. *Swaziland Integrated HIV Management Guidelines*. Tech. rep. Mbabane, Swaziland, 2018.

[11] Marie Claude Boily et al. "Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies". *The Lancet Infectious Diseases* 9.2 (Feb. 2009), pp. 118–129. https://doi.org/10.1016/S1473-3099(09)70021-0.

[12] Alan Whiteside and Amy Whalley. *Reviewing Emergencies for Swaziland: Shifting the Paradigm in a New Era*. Tech. rep. Mbabane, Swaziland: NERCHA, 2007.

[13] John Iliffe. *The African AIDS Epidemic : A History*. Cape Town, South Africa: Double Storey, 2006.

[14] The World Bank. *World Bank Open Data*. 2020. https://data.worldbank.org.

[15] James F. Blanchard and Stephen Moses. "Female Sex Workers and Their Clients in the Epidemiology and Control of Sexually Transmitted Diseases". *Sexually Transmitted Diseases*. Ed. by King K. Holmes et al. 4th ed. McGraw Hill, 2008. Chap. 12, pp. 187–201. https://openlibrary.org/books/OL9792815M.

[16] Fiona Scorgie et al. "Socio-demographic characteristics and behavioral risk factors of female sex workers in sub-Saharan Africa: A systematic review". *AIDS and Behavior* 16.4 (May 2012), pp. 920–933. https://doi.org/10.1007/s10461-011-9985-z.

[17] Ide Cremin et al. "PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study". *The Lancet HIV* 4.5 (2017), e214–e222. https://doi.org/10.1016/S2352-3018(17)30021-8.

[18] Andrea Low et al. "Potential impact of existing interventions and of antiretroviral use in female sex workers on transmission of HIV in Burkina Faso: A modeling study". *Journal of Acquired Immune Deficiency Syndromes* 68 (Mar. 2015), S180–S188. ISSN: 10779450. https://doi.org/10.1097/QAI.0000000000000441.

[19] Kate Shannon et al. "Global epidemiology of HIV among female sex workers: Influence of structural determinants". *The Lancet* 385.9962 (Jan. 2015), pp. 55–71. https://doi.org/10.1016/S0140-6736(14)60931-4.

[20] Leigh F. Johnson et al. "The effect of changes in condom usage and antiretroviral treatment coverage on human immunodeficiency virus incidence in South Africa: A model-based analysis". *Journal of the Royal Society Interface* 9.72 (July 2012), pp. 1544–1554. ISSN: 17425662. https://royalsocietypublishing.org/doi/abs/10.1098/rsif.2011.0826.

[21] Mathieu Maheu-Giroux et al. "Population-level impact of an accelerated HIV response plan to reach the UNAIDS 90-90-90 target in Côte d'Ivoire: Insights from mathematical modeling". *PLOS Medicine* 14.6 (June 2017). Ed. by Nicola Low, e1002321. ISSN: 15491676. https://doi.org/10.1371/journal.pmed.1002321.

[22] Mathias Aklilu et al. "Factors associated with HIV-1 infection among sex workers of Addis Ababa, Ethiopia". *AIDS* 15.1 (Jan. 2001), pp. 87–96. ISSN: 02699370. https://doi.org/10.1097/00002030-200101050-00013.

[23] K. L. Dunkle et al. "Risk factors for HIV infection among sex workers in Johannesburg, South Africa". *International Journal of STD and AIDS* 16.3 (June 2005), pp. 256–261. ISSN: 09564624. https://doi.org/10.1258/0956462053420220.

[24] Anna Jonas et al. "HIV prevalence, risk factors for infection, and uptake of prevention, testing, and treatment among female sex workers in Namibia". *Journal of Epidemiology and Global Health* 10.4 (Dec. 2020), pp. 351–358. ISSN: 22106014. https://doi.org/10.2991/jegh.k.200603.001.

[25] Charlotte Watts et al. "Remodelling core group theory: the role of sustaining populations in HIV transmission". *Sexually Transmitted Infections* 86.S3 (Dec. 2010), pp. iii85–iii92. https://doi.org/10.1136/sti.2010.044602.

[26] Daphne A. van Wees et al. "Longitudinal Patterns of Sexually Transmitted Infection Risk Based on Psychological Characteristics and Sexual Behavior in Heterosexual Sexually Transmitted Infection Clinic Visitors". *Sexually Transmitted Diseases* 47.3 (Mar. 2020), pp. 171–176. ISSN: 15374521. https://doi.org/10.1097/OLQ.0000000000001110.

[27] Elizabeth Roberts et al. "Low program access despite high burden of sexual, structural, and reproductive health vulnerabilities among young women who sell sex in Mombasa, Kenya". *BMC Public Health* 20.1 (May 2020). ISSN: 14712458. https://doi.org/10.1186/s12889-020-08872-6.

[28] Rachael C. Dellar, Sarah Dlamini, and Quarraisha Abdool Karim. "Adolescent girls and young women: Key populations for HIV epidemic control". *Journal of the International AIDS Society* 18.2 (2015), pp. 64–70. ISSN: 17582652. https://doi.org/10.7448/IAS.18.2.19408.

[29] R. Scott McClelland et al. "HIV-1 acquisition and disease progression are associated with decreased high-risk sexual behaviour among Kenyan female sex workers". *AIDS* 20.15 (Oct. 2006), pp. 1969–1973. ISSN: 02699370. https://journals.lww.com/aidsonline/Fulltext/2006/10030/HIV˙1˙acquisition˙and˙disease˙progression˙are.10.aspx.

[30] Lyle R. McKinnon et al. "Risk Factors for HIV Acquisition in a Prospective Nairobi-Based Female Sex Worker Cohort". *AIDS and Behavior* 19.12 (Dec. 2015), pp. 2204–2213. ISSN: 15733254. https://link.springer.com/article/10.1007/s10461-015-1118-7.

[31] Marcellin N NouamanId et al. "Incidence of HIV infection and associated factors among female sex workers in Côte d'Ivoire, results of the ANRS 12361 PrEP-CI study using recent infection assays". *PLOS ONE* 17.11 (Nov. 2022). Ed. by Hamid Sharifi, e0271988. ISSN: 1932-6203. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0271988.

[32] Frances H. Priddy et al. "Anal sex, vaginal practices, and HIV incidence in female sex workers in Urban Kenya: Implications for the development of intravaginal HIV prevention methods". *AIDS Research and Human Retroviruses* 27.10 (Oct. 2011), pp. 1067–1072. ISSN: 08892229. https://doi.org/10.1089/aid.2010.0362.

[33] Stefan Baral et al. "Reconceptualizing the HIV epidemiology and prevention needs of female sex workers (FSW) in Swaziland". *PLOS ONE* 9.12 (Dec. 2014), e115465. ISSN: 19326203. http://dx.plos.org/10.1371/journal.pone.0115465.

[34] PEPFAR. *Characterizing the HIV Prevention and Treatment Needs among Key Populations, including Men who Have Sex with Men and Female Sex Workers in Swaziland: From Evidence to Action*. Tech. rep. Mbabane, Swaziland, 2015.

[35] Eswatini Ministry of Health. *2020–2021 Integrated Biological-Behavioral Surveillance Survey among Female Sex Workers and Men Who Have sex with Men in Eswatini*. Tech. rep. Mbabane, Eswatini, 2022.

[36] Eileen A. Yam et al. "Association between condom use and use of other contraceptive methods among female sex workers in swaziland: A relationship-level analysis of condom and contraceptive use". *Sexually Transmitted Diseases* 40.5 (May 2013), pp. 406–412. ISSN: 01485717. https://doi.org/10.1097/OLQ.0b013e318283c16d.

[37] Sharon Stucker Weir et al. *Priorities for Local AIDS Control Efforts: A Manual for Implementing the PLACE Method*. Tech. rep. University of North Carolina at Chapel Hill, 2005. https://www.measureevaluation.org/resources/publications/ms-05-13.html.

[38] J. F. Lawless and K. Singhal. "Efficient Screening of Nonnormal Regression Models". *Biometrics* 34.2 (June 1978), p. 318. ISSN: 0006341X.

[39] Ajit C. Tamhane and Brent R. Logan. *Finding the maximum safe dose level for heteroscedastic data*. 2004. https://www.tandfonline.com/doi/abs/10.1081/BIP-200035413.

[40] M. S. Saag et al. *HIV viral load markers in clinical practice*. 1996. https://www.nature.com/articles/nm0696-625.

[41] Deborah Donnell et al. "Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis". *The Lancet* 375.9731 (June 2010), pp. 2092–2098. https://doi.org/10.1016/S0140-6736(10)60705-2.

[42] T. Déirdre Hollingsworth, Roy M. Anderson, and Christophe Fraser. "HIV-1 transmission, by stage of infection". *Journal of Infectious Diseases* 198.5 (Sept. 2008), pp. 687–693. ISSN: 00221899. https://doi.org/10.1086/590501.

[43] Myron S. Cohen et al. "Acute HIV-1 Infection". *New England Journal of Medicine* 364.20 (May 2011), pp. 1943–1954. ISSN: 0028-4793. arXiv: NIHMS150003. https://doi.org/10.1056/NEJMra1011874.

[44] Myron S. Cohen et al. "HIV treatment as prevention: Debate and commentary-will early infection compromise treatment-as-prevention strategies?" *PLOS Medicine* 9.7 (July 2012). Ed. by John Bartlett, e1001232. ISSN: 15491277. https://doi.org/10.1371/journal.pmed.1001232.

[45] Steve E. Bellan et al. "Reassessment of HIV-1 Acute Phase Infectivity: Accounting for Heterogeneity and Study Design with Simulated Cohorts". *PLOS Medicine* 12.3 (Mar. 2015). Ed. by Marie-Louise Newell, e1001801. https://doi.org/10.1371/journal.pmed.1001801.

[46] Maria J. Wawer et al. "Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda". *Journal of Infectious Diseases* 191.9 (May 2005), pp. 1403–1409. https://doi.org/10.1086/429411.

[47] James P. Hughes et al. "Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples". *Journal of Infectious Diseases* 205.3 (Feb. 2012), pp. 358–365. https://doi.org/10.1093/infdis/jir747.

[48] Simon Gregson et al. "Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwe". *Lancet* 359.9321 (June 2002), pp. 1896–1903. ISSN: 01406736. https://doi.org/10.1016/S0140-6736(02)08780-9.

[49] Rebecca F. Baggaley et al. *Does per-act HIV-1 transmission risk through anal sex vary by gender? An updated systematic review and meta-analysis*. Nov. 2018. https://doi.org/10.1111/aji.13039.

[50] Rebecca F. Baggaley et al. "Heterosexual Anal Intercourse: A Neglected Risk Factor for HIV?" *American Journal of Reproductive Immunology* 69.S1 (Feb. 2013), pp. 95–105. ISSN: 10467408. https://doi.org/10.1111/aji.12064.

[51] Pragna Patel et al. "Estimating per-act HIV transmission risk: A systematic review". *AIDS* 28.10 (June 2014), pp. 1509–1519. https://doi.org/10.1097/QAD.0000000000000298.

[52] Charles Shey Wiysonge et al. "Male circumcision for prevention of homosexual acquisition of HIV in men". *Cochrane Database of Systematic Reviews* 6 (June 2011). https://doi.org/10.1002/14651858.cd007496.pub2.

[53] Helen A. Weiss, Catherine A. Hankins, and Kim Dickson. *Male circumcision and risk of HIV infection in women: a systematic review and meta-analysis*. Nov. 2009. https://doi.org/10.1016/S1473-3099(09)70235-X.

[54] Foteini K Giannou et al. "Condom effectiveness in reducing heterosexual HIV transmission: a systematic review and meta-analysis of studies on HIV serodiscordant couples". *Expert Review of Pharmacoeconomics and Outcomes Research* 16.4 (July 2016), pp. 489–499. https://doi.org/10.1586/14737167.2016.1102635.

[55] Dawn K. Smith et al. "Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States". *Journal of Acquired Immune Deficiency Syndromes* 68.3 (Mar. 2015), pp. 337–344. https://doi.org/10.1097/QAI.0000000000000461.

[56] Francis A. Plummer et al. "Cofactors in male-female sexual transmission of human immunodeficiency virus type 1". *Journal of Infectious Diseases* 163.2 (Feb. 1991), pp. 233–239. https://doi.org/10.1093/infdis/163.2.233.

[57] Douglas T. Fleming and Judith N. Wasserheit. *From epidemiological synergy to public health policy and practice: The contribution of other sexually transmitted diseases to sexual transmission of HIV infection*. Feb. 1999. http://doi.org/10.1136/sti.75.1.3.

[58] Jeanne S. Sheffield et al. "Effect of genital ulcer disease on HIV-1 coreceptor expression in the female genital tract". *Journal of Infectious Diseases* 196.10 (Nov. 2007), pp. 1509–1516. ISSN: 00221899. https://academic.oup.com/jid/article/196/10/1509/1076179.

[59] Julie Fox and Sarah Fidler. *Sexual transmission of HIV-1*. Jan. 2010.

[60] Judith N. Wasserhelt. "Epidemiological synergy: Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases". *Sexually Transmitted Diseases* 19.2 (1992), pp. 61–77. ISSN: 15374521. https://pubmed.ncbi.nlm.nih.gov/1595015/.

[61] Ronald H Gray et al. "Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda". *The Lancet* 357.9263 (Apr. 2001), pp. 1149–1153. https://doi.org/10.1016/S0140-6736(00)04331-2.

[62] Swaziland Ministry of Health. *Swaziland HIV Incidence Measurement Survey: First Findings Report*. Mbabane, Swaziland, 2012. http://shims.icap.columbia.edu/.

[63] PEPFAR. *Eswatini Country Operational Plan 2021*. Tech. rep. 2021.

[64] Maria A. Carrasco, Joseph G. Rosen, and Ryan Phelps. "Left behind?: male clients of female sex workers in Zambia". *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV* 32.12 (Dec. 2020), pp. 1498–1505. https://doi.org/10.1080/09540121.2020.1718589.

[65] Julia Cordero-Coma and Richard Breen. "HIV Prevention and Social Desirability: Husband-Wife Discrepancies in Reports of Condom Use". *Journal of Marriage and Family* 74.3 (2012), pp. 601–613. ISSN: 00222445.

[66] Luc Béhanzin et al. "Assessment of HIV-related risky behaviour: A comparative study of face-to-face interviews and polling booth surveys in the general population of Cotonou, Benin". *Sexually Transmitted Infections* 89.7 (Nov. 2013), pp. 595–601. https://doi.org/10.1136/sextrans-2012-050884.

[67] Swaziland Ministry of Health. *Swaziland 1988 Family Health Survey*. Tech. rep. Mbabane, Swaziland, 1990.

[68] Swaziland Ministry of Health. *Swaziland Behavioral Surveillance Survey*. Tech. rep. Mbabane, Swaziland, 2002.

[69] Anne-Mariea; Marie Côté et al. "Transactional sex is the driving force in the dynamics of HIV in Accra, Ghana". *AIDS* 18.6 (2004), pp. 917–925. https://doi.org/10.1097/00002030-200404090-00009.

[70] Branwen Nia Owen et al. *What Proportion of Female Sex Workers Practise anal Intercourse and How Frequently? A Systematic Review and Meta-analysis*. Mar. 2020. https://doi.org/10.1007/s10461-019-02477-w.

[71] F. N. Fritsch and R. E. Carlson. "Monotone Piecewise Cubic Interpolation". *SIAM Journal on Numerical Analysis* 17.2 (July 1980), pp. 238–246. ISSN: 0036-1429. https://doi.org/10.1137/0717021.

[72] Caitlyn L. Jasumback et al. "Point-of-Care testing to guide treatment and estimate risk factors for sexually transmitted infections in adolescents and young people with human immunodeficiency virus in Eswatini". *Open Forum Infectious Diseases* 7.3 (Mar. 2020), pp. 1–9. https://doi.org/10.1093/ofid/ofaa052.

[73] Frances M. Cowan et al. "Is sexual contact with sex workers important in driving the HIV epidemic among men in rural Zimbabwe?" *Journal of Acquired Immune Deficiency Syndromes* 40.3 (Nov. 2005), pp. 371–376. https://doi.org/10.1097/01.qai.0000162420.93243.ff.

[74] M. E. Gomes Do Espirito Santo and G D Etheredge. "Male clients of brothel prostitutes as a bridge for HIV infection between high risk and low risk groups of women in Senegal". *Sexually Transmitted Infections* 81.4 (Aug. 2005), pp. 342–344. ISSN: 13684973. https://sti.bmj.com/content/81/4/342%20https://sti.bmj.com/content/81/4/342.abstract.

[75] Sara Lodi et al. "Time from human immunodeficiency virus seroconversion to reaching CD4+ cell count thresholds ¡200, ¡350, and ¡500 Cells/mm3: Assessment of need following changes in treatment guidelines". *Clinical Infectious Diseases* 53.8 (Oct. 2011), pp. 817–825. http://doi.org/10.1093/cid/cir494.

[76] Motasim Badri, Stephen D. Lawn, and Robin Wood. "Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study". *The Lancet* 368.9543 (Oct. 2006), pp. 1254–1259. https://doi.org/10.1016/S0140-6736(06)69117-4.

[77] Xavier Anglaret et al. "AIDS and non-AIDS morbidity and mortality across the spectrum of CD4 cell counts in HIV-infected adults before starting antiretroviral therapy in Côte d'Ivoire". *Clinical Infectious Diseases* 54.5 (Mar. 2012), pp. 714–723. ISSN: 10584838. http://www.ncbi.nlm.nih.gov/pubmed/22173233%20http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3275759%20https://academic.oup.com/cid/article/54/5/714/325838.

[78] Melanie A. Thompson et al. "Antiretroviral Treatment of Adult HIV Infection: 2012 Recommendations of the International Antiviral Society–USA Panel". *JAMA* 308.4 (July 2012), pp. 387–402. ISSN: 0098-7484. https://jamanetwork.com/journals/jama/fullarticle/1221704.

[79] Andrew Mujugira et al. "HIV transmission risk persists during the first 6 months of antiretroviral therapy". *Journal of Acquired Immune Deficiency Syndromes* 72.5 (Aug. 2016), pp. 579–584. https://doi.org/10.1097/QAI.0000000000001019.

[80] Robert W. Eisinger, Carl W. Dieffenbach, and Anthony S. Fauci. *HIV viral load and transmissibility of HIV infection undetectable equals untransmittable*. Feb. 2019.

[81] Myron S. Cohen et al. "Antiretroviral Therapy for the Prevention of HIV-1 Transmission". *New England Journal of Medicine* 375.9 (Sept. 2016), pp. 830–839. ISSN: 0028-4793. https://doi.org/10.1056/nejmoa1600693.

[82] Manuel Battegay et al. "Immunological recovery and antiretroviral therapy in HIV-1 infection". *The Lancet Infectious Diseases* 6.5 (May 2006), pp. 280–287. ISSN: 14733099.

[83] Stephen D. Lawn et al. "CD4 cell count recovery among HIV-infected patients with very advanced immunodeficiency commencing antiretroviral treatment in sub-Saharan Africa". *BMC Infectious Diseases* 6.1 (Mar. 2006), pp. 1–8. ISSN: 14712334. https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-6-59.

[84] Delphine Gabillard et al. "Mortality, AIDS-morbidity, and loss to follow-up by current CD4 cell count among HIV-1-infected adults receiving antiretroviral therapy in Africa and Asia: Data from the ANRS 12222 collaboration". *Journal of Acquired Immune Deficiency Syndromes* 62.5 (Apr. 2013), pp. 555–561. ISSN: 15254135. https://journals.lww.com/jaids/Fulltext/2013/04150/Mortality,˙AIDS˙Morbidity,˙and˙Loss˙to˙Follow˙up.15.aspx.

[85] Andrew N. Phillips, James Neaton, and Jens D. Lundgren. "The role of HIV in serious diseases other than AIDS". *AIDS* 22.18 (2008), pp. 2409–2418. ISSN: 02699370. https://doi.org/10.1097/QAD.0B013E3283174636.

[86] Jens D Lundgren et al. "Initiation of antiretroviral therapy in early asymptomatic HIV infection." *New England Journal of Medicine* 373.9 (2015), pp. 795–807. https://doi.org/10.1056/NEJMoa1506816.

[87] T. Charles Witzel et al. "Uptake contexts and perceived impacts of HIV testing and counselling among adults in East and Southern Africa: A meta-ethnographic review". *PLOS ONE* 12.2 (Feb. 2017). Ed. by Matthew P Fox, e0170588. ISSN: 19326203. https://dx.plos.org/10.1371/journal.pone.0170588.

[88] Swaziland Ministry of Health. *Swaziland HIV Incidence Measurement Survey (SHIMS): Descriptive Data Tables*. Mbabane, Swaziland, 2014.

[89] Government of Swaziland. *Policy Document on HIV/AIDS and STD Prevention and Control*. Tech. rep. Mbabane, Swaziland, 1998.

[90] Human Sciences Research Council. *An Audit of HIV/AIDS Policies in Botswana, Lesotho, Mozambique, South Africa, and Swaziland*. Ed. by Nompumelelo Zungu-Dirwayi et al. 1st ed. Cape Town, South Africa: HSRC Publishers, 2004.

[91] Nokwazi Mathabela et al. *UNGASS 2010 Swaziland Progress Report*. Tech. rep. Mbabane, Swaziland, 2010.

[92] National Emergency Response Council on HIV and AIDS. *Swaziland Country Report On Monitoring The Political Declaration On Hiv And Aids*. Tech. rep. Mbabane, Swaziland, 2012.

[93] National Emergency Response Council on HIV and AIDS. *The Kingdom of Swaziland National AIDS Spending Assessment 2005/06 and 2006/07*. Tech. rep. Mbabane, Swaziland, 2009.

[94] National Emergency Response Council on HIV and AIDS. *National Multi-sectorial Strategic Framework for HIV and AIDS 2009-2014*. Tech. rep. Mbabane, Swaziland, 2009.

[95] Françoise Jenniskens. *Maximizing ART for Better Health and Zero New HIV Infections*. Tech. rep. Mbabane, Eswatini, 2015.

[96] WHO. *Scaling up antiretroviral therapy in resource-limited settings : treatment guidelines for a public health approach*. Tech. rep. Geneva, Switzerland, 2013.

[97] WHO. *Chronic HIV Care with ARV Therapy and Prevention*. Geneva, Switzerland, 2007.

[98] WHO. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection*. Geneva, Switzerland, 2013.

[99] WHO. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection*. Geneva, Switzerland, 2016. https://www.who.int/hiv/pub/arv/arv-2016.

[100] MaxART Consortium. *MaxART Early Access to ART for All implementation study (2014-2018) Final Report*. Report. Mbabane, Eswatini, 2018.

[101] National Emergency Response Council on HIV and AIDS. *Extended National Multisectorial HIV and AIDS Framework*. Tech. rep. Mbabane, Swaziland, 2014.

[102] Motasim Badri et al. "Initiating highly active antiretroviral therapy in sub-Saharan Africa". *AIDS* 18.8 (2004), pp. 1159–1168. ISSN: 0269-9370. https://journals.lww.com/aidsonline/Fulltext/2004/05210/Adherence˙is˙not˙a˙barrier˙to˙successful.9.aspx.

[103] Jameela Edathodu, Batool Ali, and Abdulrahman A. Alrajhi. "CD4 validation for the World Health Organization classification and clinical staging of HIV/AIDS in a developing country". *International Journal of Infectious Diseases* 13.2 (Mar. 2009), pp. 243–246. ISSN: 12019712. https://doi.org/10.1016/j.ijid.2007.12.017.

[104] US Centers for Disease Control and Prevention. "Differences between HIV-Infected men and women in antiretroviral therapy outcomes - six African countries, 2004-2012." *Morbidity and Mortality Weekly Report report* 62.47 (Nov. 2013), pp. 945–52. ISSN: 1545-861X. /pmc/articles/PMC4585632/%20https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4585632/%20http://www.ncbi.nlm.nih.gov/pubmed/24280913%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4585632.

[105] Swaziland Ministry of Health. *Annual HIV Programs Report*. Tech. rep. Mbabane, Swaziland, 2015.

[106] Kathryn E. Lancaster et al. "HIV care and treatment experiences among female sex workers living with HIV in sub-Saharan Africa: A systematic review". *African Journal of AIDS Research* 15.4 (Dec. 2016), pp. 377–386. ISSN: 17279445. https://www.tandfonline.com/doi/abs/10.2989/16085906.2016.1255652.

[107] WHO. *HIV Drug Resistance Report 2021*. Tech. rep. Geneva, Switzerland, 2021.

[108] Anthony Hauser et al. "Bridging the gap between hiv epidemiology and antiretroviral resistance evolution: Modelling the spread of resistance in south africa". *PLOS Computational Biology* 15.6 (2019), e1007083. https://doi.org/10.1371/journal.pcbi.1007083.

[109] National Emergency Response Council on HIV and AIDS. *Swaziland Global Aids Response Progress Reporting 2014*. Tech. rep. 2014.

[110] National Emergency Response Council on HIV and AIDS. *Extended National Multi-sectoral HIV and AIDS Framework 2014-2018: Final Evaluation Report*. Tech. rep. Mbabane, Eswatini, 2018.

[111] Matthew P. Fox et al. "Estimating retention in HIV care accounting for patient transfers: A national laboratory cohort study in South Africa". *PLoS Medicine* 15.6 (June 2018). ISSN: 15491676. /pmc/articles/PMC5995345/%20/pmc/articles/PMC5995345/?report=abstract%20https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5995345/.

[112] Lynne S. Wilkinson et al. *Self-transfer and mortality amongst adults lost to follow-up in ART programmes in low- and middle-income countries: Systematic review and meta-analysis*. Mar. 2015. https://doi.org/10.1111/tmi.12434.

[113] Giorgos Bakoyannis et al. "A semiparametric method for the analysis of outcomes during a gap in HIV care under incomplete outcome ascertainment". *Statistical Communications in Infectious Diseases* 12.s1 (Sept. 2020). ISSN: 2194-6310. https://doi.org/10.1515/SCID-2019-0013.

[114] Elke Konings et al. "Validating population surveys for the measurement of HIV/STD prevention indicators". *AIDS* 9.4 (Apr. 1995), pp. 375–382. ISSN: 02699370. https://doi.org/10.1097/00002030-199509040-00009.

[115] Simon Gregson et al. "Methods to reduce social desirability bias in sex surveys in low-development settings: Experience in Zimbabwe". *Sexually Transmitted Diseases* 29.10 (2002), pp. 568–575. ISSN: 01485717. https://journals.lww.com/stdjournal/Fulltext/2002/10000/Methods˙to˙Reduce˙Social˙Desirability˙Bias˙in˙Sex.2.aspx?casa˙token=6zS0MjmO4BYAAAAA:7EzCQyMe2-TLr6k5sem730YqF2aC0Bfk04HzrypuAG7Cu4cAR5GZ1w4-v12Ce1-SU0WS7jmufYQcZrRO2E8BLiM-.

[116] S. Gregson et al. "Informal confidential voting interview methods and temporal changes in reported sexual risk behaviour for HIV transmission in sub-Saharan Africa". *Sexually Transmitted Infections*. Vol. 80. S2. The Medical Society for the Study of Venereal Disease, Dec. 2004, pp. ii36–ii42. https://sti.bmj.com/content/80/suppl˙2/ii36%20https://sti.bmj.com/content/80/suppl˙2/ii36.abstract.

[117] Catherine M. Lowndes et al. "Polling booth surveys: A novel approach for reducing social desirability bias in HIV-related behavioural surveys in resource-poor settings". *AIDS and Behavior* 16.4 (May 2012), pp. 1054–1062. https://doi.org/10.1007/s10461-011-0004-1.

[118] UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. *Guidelines on Estimating the Size of Populations Most at Risk to HIV*. Geneva, Switzerland, 2010.

[119] Abu S Abdul-Quader, Andrew L Baughman, and Wolfgang Hladik. *Estimating the size of key populations: Current status and future possibilities*. Mar. 2014. http://doi.org/10.1097/COH.0000000000000041.

[120] L. Morison et al. "Commercial sex and the spread of HIV in four cities in sub-Saharan Africa". *AIDS* 15.S4 (2001), S61–S69. https://doi.org/10.1097/00002030-200108004-00007.

[121] Hélène A.C.M. Voeten et al. "Clients of female sex workers in Nyanza Province, Kenya: A core group in STD/HIV transmission". *Sexually Transmitted Diseases* 29.8 (2002), pp. 444–452. ISSN: 01485717. https://doi.org/10.1097/00007435-200208000-00003.

[122] J. K.B. Matovu and B N Ssebadduka. "Sexual risk behaviours, condom use and sexually transmitted infection treatment-seeking behaviours among female sex workers and truck drivers in Uganda". *International Journal of STD and AIDS* 23.4 (Apr. 2012), pp. 267–273. https://doi.org/10.1258/ijsa.2011.011313.

[123] Leigh F. Johnson and Rob E. Dorrington. *Thembisa version 3.2: A model for evaluating the impact of HIV/AIDS in South Africa*. Tech. rep. University of Cape Town, 2017.

[124] M. L. Plummer et al. ""A bit more truthful": The validity of adolescent sexual behaviour data collected in rural northern Tanzania using five methods". *Sexually Transmitted Infections* 80.S2 (Dec. 2004), pp. ii49–ii56. ISSN: 13684973. https://doi.org/10.1136/sti.2004.011924.

[125] J. Todd et al. "Reported number of sexual partners: Comparison of data from four African longitudinal studies". *Sexually Transmitted Infections* 85.S1 (Apr. 2009), pp. i72–i80. ISSN: 13684973. https://sti.bmj.com/content/85/Suppl˙1/i72%20https://sti.bmj.com/content/85/Suppl˙1/i72.abstract.

[126] Jenny A. Higgins, Susie Hoffman, and Shari L. Dworkin. "Rethinking gender, heterosexual men, and women's vulnerability to HIV/AIDS". *American Journal of Public Health* 100.3 (Mar. 2010), pp. 435–445. ISSN: 00900036. https://doi.org/10.2105/AJPH.2009.159723.

[127] Soori Nnko et al. "Secretive females or swaggering males? An assessment of the quality of sexual partnership reporting in rural Tanzania". *Social Science and Medicine* 59.2 (July 2004), pp. 299–310. https://doi.org/10.1016/j.socscimed.2003.10.031.

[128] Shelley Clark, Caroline Kabiru, and Eliya Zulu. "Do men and women report their sexual partnerships differently? Evidence from Kisumu, Kenya". *International Perspectives on Sexual and Reproductive Health* 37.4 (Dec. 2011), pp. 181–190. ISSN: 19440391.

[129] Allison Ruark et al. "Navigating intimate sexual partnerships in an era of HIV: dimensions of couple relationship quality and satisfaction among adults in Eswatini and linkages to HIV risk". *Sahara J* 16.1 (Jan. 2019), pp. 10–24. https://doi.org/10.1080/17290376.2019.1604254.

[130] J. Pulerwitz et al. ""A man without money getting a sexual partner? It doesn't exist in our community": male partners' perspectives on transactional sexual relationships in Uganda and Eswatini". *Culture, Health and Sexuality* (2021). https://doi.org/10.1080/13691058.2021.1904521.

[131] Lisa F. Langhaug, Lorraine Sherr, and Frances M. Cowan. "How to improve the validity of sexual behaviour reporting: Systematic review of questionnaire delivery modes in developing countries: Systematic Review". *Tropical Medicine and International Health* 15.3 (Mar. 2010), pp. 362–381. https://doi.org/10.1111/j.1365-3156.2009.02464.x.

[132] Cassia Wells et al. "Characterizing the patterns of HIV disclosure to clients among South African female sex workers in Port Elizabeth". *AIDS and Behavior* 22.12 (Jan. 2018), pp. 3924–3932. ISSN: 15733254. https://link.springer.com/article/10.1007/s10461-018-2199-x.

[133] H. A.C.M. Voeten et al. "Female sex workers and unsafe sex in urban and rural Nyanza, Kenya: Regular partners may contribute more to HIV transmission than clients". *Tropical Medicine and International Health* 12.2 (Nov. 2007), pp. 174–182. ISSN: 13602276. http://doi.org/10.1111/j.1365-3156.2006.01776.x.

[134] Catherine M. Lowndes et al. "Management of sexually transmitted diseases and HIV prevention in men at high risk: Targeting clients and nonpaying sexual partners of female sex workers in Benin". *AIDS* 14.16 (2000), pp. 2523–2534. ISSN: 02699370. https://journals.lww.com/aidsonline/fulltext/2000/11100/management˙of˙sexually˙transmitted˙diseases˙and.15.aspx?casa˙token=XfwcuM4zRSEAAAAA:dSoyZMHPnTY84ivzw67˙pymmpKLqcbbN5e1Max0OAVhRKm˙a8ESiQ-˙aeLTBSR1jdwkmKOe-J3eNKNxYtNuSOfMv.

[135] Gaston Godin et al. "Correlates of condom use among sex workers and their boyfriends in three West African countries". *AIDS and Behavior* 12.3 (May 2008), pp. 441–451. ISSN: 10907165. https://doi.org/10.1007/s10461-007-9296-6.

[136] M. Carael et al. "Clients of sex workers in different regions of the world: Hard to count". *Sexually Transmitted Infections* 82.S3 (June 2006), pp. iii26–iii33. ISSN: 13684973.

[137] World Health Organization. *Swaziland, Mortality Country Fact Sheet 2006*. 2006.

[138] United Nations. *World Population Prospects*. Report. 2019. https://population.un.org/wpp.

[139] Christopher J. Henry and James S. Koopman. "Strong influence of behavioral dynamics on the ability of testing and treating HIV to stop transmission". *Scientific Reports* 5.1 (Aug. 2015), p. 9467. http://www.doi.org/10.1038/srep09467.

[140] Jesse Knight et al. "Contribution of high risk groups' unmet needs may be underestimated in epidemic models without risk turnover: A mechanistic modelling analysis". *Infectious Disease Modelling* 5 (Jan. 2020), pp. 549–562. https://doi.org/10.1016/j.idm.2020.07.004.

[141] Mick Roberts et al. "Nine challenges for deterministic epidemic models". *Epidemics* 10 (Mar. 2015), pp. 49–53. ISSN: 18780067. https://www.sciencedirect.com/science/article/pii/S1755436514000553#bib0040.

[142] Eve Cheuk et al. "Transitions: Novel Study Methods to Understand Early HIV Risk Among Adolescent Girls and Young Women in Mombasa, Kenya, and Dnipro, Ukraine". *Frontiers in Reproductive Health* 2 (Sept. 2020), p. 10. https://doi.org/10.3389/frph.2020.00007.

[143] Erika Fazito et al. "Analysis of duration of risk behaviour for key populations: a literature review." *Sexually transmitted infections* 88.S2 (Dec. 2012), pp. i24–i32. ISSN: 14723263. https://sti.bmj.com/content/88/Suppl˙2/i24%20https://sti.bmj.com/content/88/Suppl˙2/i24.abstract.

[144] Caroline Hodgins et al. "Population sizes, HIV prevalence, and HIV prevention among men who paid for sex in sub-Saharan Africa (2000–2020): A meta-analysis of 87 population-based surveys". *PLOS Medicine* 19.1 (Jan. 2022). Ed. by Marie-Louise Newell, e1003861. ISSN: 1549-1676. https://doi.org/10.1371/JOURNAL.PMED.1003861.

[145] Huiting Ma et al. "Venue-Based HIV Testing at Sex Work Hotspots to Reach Adolescent Girls and Young Women Living with HIV: A Cross-sectional Study in Mombasa, Kenya". *Journal of Acquired Immune Deficiency Syndromes* 84.5 (Aug. 2020), pp. 470–479. ISSN: 10779450. https://doi.org/10.1097/QAI.0000000000002363.

[146] Despina Learmonth, Suvi Hakala, and Marike Keller. ""I can't carry on like this": barriers to exiting the street-based sex trade in South Africa". *Health Psychology and Behavioral Medicine* 3.1 (Jan. 2015), pp. 348–365. ISSN: 2164-2850. https://doi.org/10.1080/21642850.2015.1095098.

[147] Wim Delva et al. "Coital frequency and condom use in monogamous and concurrent sexual relationships in Cape Town, South Africa". *Journal of the International AIDS Society* 16.1 (Apr. 2013). https://doi.org/10.7448/IAS.16.1.18034.

[148] Olive Shisana and Leickness Simbayi. *South African national HIV prevalence, HIV incidence, behaviour and communication survey, 2005*. Tech. rep. Cape Town, South Africa, 2005.

[149] Martina Morris, Helen Epstein, and Maria Wawer. "Timing Is Everything: International Variations in Historical Sexual Partnership Concurrency and HIV Prevalence". *PLOS ONE* 5.11 (2010), e14092. ISSN: 19326203. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0014092.

[150] Gita Ramjee, Amy E Weber, and Neetha S Morar. "Recording sexual behavior: Comparison of recall questionnaires with a coital diary". *Sexually Transmitted Diseases* 26.7 (Aug. 1999), pp. 374–380. ISSN: 01485717. https://doi.org/10.1097/00007435-199908000-00002.

[151] Branwen N. Owen et al. "Prevalence and correlates of anal intercourse among female sex workers in eSwatini". *PLOS ONE* 15.2 (Feb. 2020). Ed. by Andrew R. Dalby, e0228849. ISSN: 19326203. https://dx.plos.org/10.1371/journal.pone.0228849.

[152] Branwen N. Owen et al. *How common and frequent is heterosexual anal intercourse among South Africans? A systematic review and meta-analysis*. Jan. 2017. https://doi.org/10.7448/IAS.20.1.21162.

[153] Bart Burington et al. "Estimating duration in partnership studies: Issues, methods and examples". *Sexually Transmitted Infections* 86.2 (Apr. 2010), pp. 84–89. ISSN: 13684973. https://doi.org/10.1136/sti.2009.037960.

[154] Ben Malinga John and Vissého Adjiwanou. "Fertility decline in sub-Saharan Africa: Does remarriage matter?" *Population Studies* 76.2 (2022), pp. 213–233. ISSN: 14774747. https://www.tandfonline.com/doi/abs/10.1080/00324728.2021.1933148.

[155] Abigail Harrison, John Cleland, and Janet Frohlich. "Young people's sexual partnerships in KwaZulu-Natal, South Africa: Patterns, contextual influences, and HIV risk". *Studies in Family Planning* 39.4 (Dec. 2008), pp. 295–308. ISSN: 00393665. https://doi.org/10.1111/j.1728-4465.2008.00176.x.

[156] James R. Hargreaves et al. "Characteristics of sexual partnerships, not just of individuals, are associated with condom use and recent HIV infection in rural South Africa". *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV* 21.8 (Aug. 2009), pp. 1058–1070. ISSN: 09540121.

[157] Nadia L. Nguyen et al. "Sexual partnership patterns among South African adolescent girls enrolled in STI preventions trial network 068: Measurement challenges and implications for HIV/STI transmission". *Sexually Transmitted Diseases* 42.11 (2015), pp. 612–618. ISSN: 15374521. https://doi.org/10.1097/OLQ.0000000000000357.

[158] B. Ferry et al. "Comparison of key parameters of sexual behaviour in four African urban populations with different levels of HIV infection". *AIDS* 15.S4 (2001). ISSN: 02699370. https://pubmed.ncbi.nlm.nih.gov/11686464/.

[159] Leigh F. Johnson et al. "Sexual behaviour patterns in South Africa and their association with the spread of HIV: Insights from a mathematical model". *Demographic Research* 21 (Sept. 2009), pp. 289–340. ISSN: 14359871. https://www.demographic-research.org/volumes/vol21/11/default.htm.

[160] Martin Mbonye, Godfrey Siu, and Janet Seeley. "Marginal men, respectable masculinity and access to HIV services through intimate relationships with female sex workers in Kampala, Uganda". *Social Science & Medicine* 296 (Jan. 2022), p. 114742. ISSN: 02779536.

[161] Annett Nold. "Heterogeneity in disease-transmission modeling". *Mathematical Biosciences* 52.3-4 (Dec. 1980), pp. 227–240. ISSN: 00255564. https://www.sciencedirect.com/science/article/abs/pii/0025556480900693.

[162] Geoffrey P. Garnett and Roy M. Anderson. "Balancing sexual partnerships in an age and activity stratified model of HIV transmission in heterosexual populations". *Mathematical Medicine and Biology* 11.3 (Jan. 1994), pp. 161–192. ISSN: 14778599. https://academic.oup.com/imammb/article-lookup/doi/10.1093/imammb/11.3.161.

[163] M Morris. "A log-linear modeling framework for selective mixing." *Mathematical biosciences* 107.2 (Dec. 1991), pp. 349–77. ISSN: 0025-5564. https://doi.org/10.1016/0025-5564(91)90014-a.

[164] Ludger Ruschendorf. "Convergence of the Iterative Proportional Fitting Procedure". *The Annals of Statistics* 23.4 (1995), pp. 1160–1174. https://doi.org/10.1214/aos/1176324703.

[165] Richard Sinkhorn. "A Relationship Between Arbitrary Positive Matrices and Doubly Stochastic Matrices". *Annals of Mathematical Statistics* 35.2 (1964), pp. 876–879. https:/doi.org/10.1214/aoms/1177703591.

[166] Suzanne Leclerc-Madlala. *Age-disparate and intergenerational sex in southern Africa: The dynamics of hypervulnerability*. 2008. https://doi.org/10.1097/01.aids.0000341774.86500.53.

[167] Geoffrey P Garnett and Roy M Anderson. "Contact tracing and the estimation of sexual mixing patterns: The epidemiology of gonococcal infections". *Sexually Transmitted Diseases* 20.4 (1993), pp. 181–191. ISSN: 15374521. https://doi.org/10.1097/00007435-199307000-00001.

[168] Ryan Admiraal and Mark S. Handcock. "Modeling concurrency and selective mixing in heterosexual partnership networks with applications to sexually transmitted diseases". *Annals of Applied Statistics* 10.4 (Dec. 2016), pp. 2021–2046. ISSN: 19417330. https://doi.org/10.1214/16-AOAS963.

[169] Jesse Knight, Rupert Kaul, and Sharmistha Mishra. "Risk heterogeneity in compartmental HIV transmission models of ART as prevention in Sub-Saharan Africa: A scoping review". *Epidemics* 40 (2022), p. 100608. https://doi.org/10.1016/j.epidem.2022.100608.

[170] Nicolas A Menzies et al. "Bayesian Methods for Calibrating Health Policy Models: A Tutorial". *PharmacoEconomics* 35.6 (2017), pp. 613–624. ISSN: 11792027. https://doi.org/10.1007/s40273-017-0494-4.

[171] The World Bank. *DataBank: World Development Indicators*. 2022. https://databank.worldbank.org/ (visited on 08/23/2018).

[172] Yen T. Duong et al. "Detection of recent HIV-1 infection using a new limiting-antigen avidity assay: Potential for HIV-1 incidence estimates and avidity maturation studies". *PLOS ONE* 7.3 (Mar. 2012), e33328. ISSN: 19326203. https://doi.org/10.1371/journal.pone.0033328.

[173] PEPFAR. *HIV among Female Sex Workers and Men Who Have Sex with Men in Swaziland*. Tech. rep. Mbabane, Swaziland, 2014.

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 immun*deficiency virus OR human immun* deficiency virus).mp`

continued ...

… 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	
• English language • published before 2020 • peer-reviewed journal article	• non-English language • published in or after 2020 • non-peer-reviewed article • review article [1] • textbook, grey literature • opinions, comments, correspondence • conference abstracts and proceedings • model comparison study
Mathematical Modelling of HIV Transmission	
• sexual HIV transmission model • non-linear HIV transmission model [2] • population-level dynamics • compartmental model [3]	• no sexual HIV transmission modelled • HIV transmission model is linear • only within-host/cellular/protein modelling • individual-based model
Context & Objectives	
• any region in Sub-Saharan Africa (SSA) [4] • assess prevention impact of ART scale-up for all [5]	• only regions outside SSA modelled • only theoretical context modelled • only individual-level benefits of ART modelled • only prevention benefits of other interventions • no 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/calirated 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, Anand, and Potts
- [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-naive 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%.

References

[1] Joshua A. Salomon et al. "Integrating HIV prevention and treatment: From slogans to impact". *PLOS Medicine* 2.1 (2005), pp. 0050–0056. https://doi.org/10.1371/journal.pmed.0020016.

[2] Ume L Abbas, Roy M Anderson, and John W Mellors. "Potential impact of antiretroviral therapy on HIV-1 transmission and AIDS mortality in resource-limited settings." *Journal of Acquired Immune Deficiency Syndromes* 41.5 (2006), pp. 632–641. https://doi.org/10.1097/01.qai.0000194234.31078.bf.

[3] Reuben M Granich et al. "Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model". *The Lancet* 373.9657 (Jan. 2009), pp. 48–57. ISSN: 01406736. https://doi.org/10.1016/S0140-6736(08)61697-9.

[4] Timothy B Hallett et al. "The role of testing and counselling for HIV prevention and care in the era of scaling-up antiretroviral therapy". *Epidemics* 1.2 (2009), pp. 77–82. https://doi.org/10.1016/j.epidem.2009.02.001.

[5] Nicolas Bacaer, Carel Pretorius, and Bertran Auvert. "An Age-Structured Model for the Potential Impact of Generalized Access to Antiretrovirals on the South African HIV Epidemic". *Bulletin of Mathematical Biology* 72.8 (2010), pp. 2180–2198. https://doi.org/10.1007/s11538-010-9535-2.

[6] Carel Pretorius et al. "Evaluating the Cost-Effectiveness of Pre-Exposure Prophylaxis (PrEP) and Its Impact on HIV-1 Transmission in South Africa". *PLOS ONE* 5.11 (2010), e13646. http://doi.org/10.1371/journal.pone.0013646.

[7] Vincent T Metzger, James O Lloyd-Smith, and Leor S Weinberger. "Autonomous targeting of infectious superspreaders using engineered transmissible therapies". *PLOS Computational Biology* 7.3 (2011), e1002015. https://doi.org/10.1371/journal.pcbi.1002015.

[8] Tunde T Yusuf and Francis Benyah. "Optimal strategy for controlling the spread of HIV/AIDS disease: A case study of South Africa". *Journal of Biological Dynamics* 6.2 (2012), pp. 475–494. https://doi.org/10.1080/17513758.2011.628700.

[9] Jason R Andrews et al. "Projecting the benefits of antiretroviral therapy for HIV prevention: the impact of population mobility and linkage to care." *The Journal of Infectious Diseases* 206.4 (2012), pp. 543–551. https://doi.org/10.1093/infdis/jis401.

[10] Reuben Granich et al. "Expanding ART for Treatment and Prevention of HIV in South Africa: Estimated Cost and Cost-Effectiveness 2011-2050". *PLOS ONE* 7.2 (2012), e30216. https://doi.org/10.1371/journal.pone.0030216.

[11] Wagner G Wagner and Sally Blower. "Universal Access to HIV Treatment versus Universal 'Test and Treat': Transmission, Drug Resistance & Treatment Costs". *PLOS ONE* 7.9 (2012), e41212. https://doi.org/10.1371/journal.pone.0041212.

[12] Ume L Abbas et al. "Antiretroviral therapy and pre-exposure prophylaxis: Combined impact on HIV transmission and drug resistance in South Africa". *The Journal of Infectious Diseases* 208.2 (2013), pp. 224–234. https://doi.org/10.1093/infdis/jit150.

[13] Elisa F Long and Robert R Stavert. "Portfolios of biomedical HIV interventions in South Africa: A cost-effectiveness analysis". *Journal of General Internal Medicine* 28.10 (2013), pp. 1294–1301. https://doi.org/10.1007/s11606-013-2417-1.

[14] Ide Cremin et al. "The new role of antiretrovirals in combination HIV prevention: A mathematical modelling analysis". *AIDS* 27.3 (Jan. 2013), pp. 447–458. ISSN: 02699370. https://doi.org/10.1097/QAD.0b013e32835ca2dd.

[15] Ramzi A Alsallaq et al. "Understanding the Potential Impact of a Combination HIV Prevention Intervention in a Hyper-Endemic Community". *PLOS ONE* 8.1 (2013), e54575. https://doi.org/10.1371/journal.pone.0054575.

[16] Brooke E Nichols et al. "Cost-effectiveness of PrEP in HIV/AIDS control in Zambia: A stochastic league approach". *Journal of Acquired Immune Deficiency Syndromes* 66.2 (2014), pp. 221–228. https://doi.org/10.1097/QAI.0000000000000145.

[17] Brooke E Nichols et al. "Averted HIV infections due to expanded antiretroviral treatment eligibility offsets risk of transmitted drug resistance: A modeling study". *AIDS* 28.1 (2014), pp. 73–83. https://doi.org/10.1097/01.aids.0000433239.01611.52.

[18] Sabrina S Alistar, Philip M Grant, and Eran Bendavid. "Comparative effectiveness and cost-effectiveness of antiretroviral therapy and pre-exposure prophylaxis for HIV prevention in South Africa". *BMC Medicine* 12.1 (2014), p. 46. https://doi.org/10.1186/1741-7015-12-46.

[19] Jeffrey W. Eaton and Timothy B. Hallett. "Why the proportion of transmission during early-stage HIV infection does not predict the long-term impact of treatment on HIV incidence". *Proceedings of the National Academy of Sciences* 111.45 (Nov. 2014), pp. 16202–16207. ISSN: 0027-8424. https://doi.org/10.1073/pnas.1323007111.

[20] Roger Ying et al. "Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda". *Journal of the International AIDS Society* 18.S3 (2015), p. 20013. http://doi.org/10.7448/IAS.18.4.20013.

[21] Andrea Low et al. "Potential impact of existing interventions and of antiretroviral use in female sex workers on transmission of HIV in Burkina Faso: A modeling study". *Journal of Acquired Immune Deficiency Syndromes* 68 (Mar. 2015), S180–S188. ISSN: 10779450. https://doi.org/10.1097/QAI.0000000000000441.

[22] Amin Khademi, Sunanth Anand, and David Potts. "Measuring the potential impact of combination HIV prevention in sub-Saharan Africa". *Medicine* 94.37 (2015), e1453. http://doi.org/10.1097/MD.0000000000001453.

[23] Jennifer A Gilbert et al. "Integrating community-based interventions to reverse the convergent TB/HIV epidemics in rural South Africa". *PLOS ONE* 10.5 (2015), e0126267. https://doi.org/10.1371/journal.pone.0126267.

[24] Laura M Heaton et al. "Estimating the impact of the US President's Emergency Plan for AIDS Relief on HIV treatment and prevention programmes in Africa". *Sexually Transmitted Infections* 91.8 (2015), pp. 615–620. https://doi.org/10.1136/sextrans-2014-051991.

[25] S M Ashrafur Rahman, Naveen K Vaidya, and Xingfou Zou. "Impact of early treatment programs on HIV epidemics: An immunity-based mathematical model". *Mathematical Biosciences* 280 (2016), pp. 38–49. http://doi.org/10.1016/j.mbs.2016.07.009.

[26] Jennifer A Gilbert et al. "Cost-effectiveness of community-based TB/HIV screening and linkage to care in rural South Africa". *PLOS ONE* 11.12 (2016), e0165614. https://doi.org/10.1371/journal.pone.0165614.

[27] Stephanie Blaizot et al. "Potential impact of multiple interventions on HIV incidence in a hyperendemic region in Western Kenya: A modelling study". *BMC Infectious Diseases* 16.1 (2016), p. 189. https://doi.org/10.1186/s12879-016-1520-4.

[28] Roger Ying et al. "Home testing and counselling to reduce HIV incidence in a generalised epidemic setting: a mathematical modelling analysis". *The Lancet HIV* 3.6 (2016), e275–e282. http://doi.org/10.1016/S2352-3018(16)30009-1.

[29] Till Barnighausen, David E Bloom, and Salal Humair. "Human resources for treating HIV/AIDS: Are the preventive effects of antiretroviral treatment a game changer?" *PLOS ONE* 11.10 (2016), e0163960. https://doi.org/10.1371/journal.pone.0163960.

[30] Alastair Heffernan et al. "Impact and cost-effectiveness of point-of-care CD4 testing on the HIV epidemic in South Africa". *PLOS ONE* 11.7 (2016), e0158303. https://doi.org/10.1371/journal.pone.0158303.

[31] Mathieu Maheu-Giroux et al. "Changing Dynamics of HIV Transmission in Côte d'Ivoire: Modeling Who Acquired and Transmitted Infections and Estimating the Impact of Past HIV Interventions (1976-2015)". *Journal of Acquired Immune Deficiency Syndromes* 75.5 (2017), pp. 517–527. ISSN: 10779450. https://doi.org/10.1097/QAI.0000000000001434.

[32] Mathieu Maheu-Giroux et al. "Population-level impact of an accelerated HIV response plan to reach the UNAIDS 90-90-90 target in Côte d'Ivoire: Insights from mathematical modeling". *PLOS Medicine* 14.6 (June 2017). Ed. by Nicola Low, e1002321. ISSN: 15491676. https://doi.org/10.1371/journal.pmed.1002321.

[33] Erik M Volz et al. "Phylodynamic analysis to inform prevention efforts in mixed HIV epidemics". *Virus Evolution* 3.2 (2017), vex014. http://doi.org/10.1093/ve/vex014.

[34] Stephanie Blaizot et al. "Combined interventions to reduce HIV incidence in KwaZulu-Natal: a modelling study". *BMC Infectious Diseases* 17.1 (2017), p. 522. https://doi.org/10.1186/s12879-017-2612-5.

[35] Christinah Mukandavire et al. "Estimating the contribution of key populations towards the spread of HIV in Dakar, Senegal". *Journal of the International AIDS Society* 21 (July 2018), e25126. ISSN: 17582652. https://doi.org/10.1002/jia2.25126.

[36] Marlene Guillon. "Success factors for universal access to antiretroviral treatments in South Africa". *The International Journal of Health Planning and Management* 33.4 (2018), e1160–e1178. https://doi.org/10.1002/hpm.2602.

[37] Gordon Akudibillah, Abhishek Pandey, and Jan Medlock. "Optimal control for HIV treatment". *Mathematical Biosciences and Engineering* 16.1 (2018), pp. 373–396. https://doi.org/10.3934/mbe.2019018.

[38] Robyn M Stuart et al. "The City of Johannesburg can end AIDS by 2030: Modelling the impact of achieving the Fast-Track targets and what it will take to get there: Modelling". *Journal of the International AIDS Society* 21.1 (2018), e25068. https://doi.org/10.1002/jia2.25068.

[39] Simon de Montigny et al. "Assessing the utility of the tipping point ratio to monitor HIV treatment programmes in the era of universal access to ART". *Infectious Disease Modelling* 3 (2018), pp. 85–96. https://doi.org/10.1016/j.idm.2018.03.005.

[40] Anthony Hauser et al. "Bridging the gap between hiv epidemiology and antiretroviral resistance evolution: Modelling the spread of resistance in south africa". *PLOS Computational Biology* 15.6 (2019), e1007083. https://doi.org/10.1371/journal.pcbi.1007083.

[41] Leigh F. Johnson and Rob E. Dorrington. "Modelling the demographic impact of HIV/AIDS in South Africa and the likely impact of interventions". *Demographic Research* 14.22 (2006), pp. 541–574. https://doi.org/10.4054/DemRes.2006.14.22.

[42] Rebecca F Baggaley, Geoff P Garnett, and Niel M Ferguson. "Modelling the Impact of Antiretroviral Use in Resource-Poor Settings". *PLOS Medicine* 3.4 (2006), pp. 493–504. https://doi.org/10.1371/journal.pmed.0030124.

[43] David P. Wilson, James Kahn, and Sally M. Blower. "Predicting the epidemiological impact of antiretroviral allocation strategies in KwaZulu-Natal: The effect of the urban-rural divide". *Proceedings of the National Academy of Sciences of the United States of America* 103.38 (Sept. 2006), pp. 14228–14233. ISSN: 00278424. https://doi.org/10.1073/pnas.0509689103.

[44] Nicolas Bacaer et al. "Modeling the joint epidemics of TB and HIV in a South African township". *Journal of Mathematical Biology* 57.4 (2008), pp. 557–593. https://doi.org/10.1007/s00285-008-0177-z.

[45] Esther Chigidi and Edward M Lungu. "Hiv model incorporating differential progression for treatment-naive and treatment-experienced infectives". *Mathematical Biosciences and Engineering* 6.3 (2009), pp. 427–450. https://doi.org/10.3934/mbe.2009.6.427.

[46] Brian G Williams et al. "Antiretroviral therapy for tuberculosis control in nine African countries". *Proceedings of the National Academy of Sciences of the United States of America* 107.45 (2010), pp. 19485–19489. https://doi.org/10.1073/pnas.1005660107.

[47] Farai Nyabadza and Zindoga Mukandavire. "Modelling HIV/AIDS in the presence of an HIV testing and screening campaign". *Journal of Theoretical Biology* 280.1 (2011), pp. 167–179. https://doi.org/10.1016/j.jtbi.2011.04.021.

[48] T. Barnighausen, D. E. Bloom, and S. Humair. "Economics of antiretroviral treatment vs. circumcision for HIV prevention". *Proceedings of the National Academy of Sciences* 109.52 (Dec. 2012), pp. 21271–21276. ISSN: 0027-8424. https://doi.org/10.1073/pnas.1209017110.

[49] Bradley G Wagner, Brian J Coburn, and Sally Blower. "Increasing survival time decreases the cost-effectiveness of using "test & treat" to eliminate HIV epidemics". *Mathematical Biosciences and Engineering* 10.5-6 (2013), pp. 1673–1686. https://doi.org/10.3934/mbe.2013.10.1673.

[50] Michele R Decker et al. "Estimating the impact of reducing violence against female sex workers on HIV epidemics in Kenya and Ukraine: a policy modeling exercise." *American Journal of Reproductive Immunology* 69.S1 (2013), pp. 122–132. https://doi.org/10.1111/aji.12063.

[51] Andrea L Wirtz et al. "Modelling the impact of HIV prevention and treatment for men who have sex with men on HIV epidemic trajectories in low- and middle-income countries". *International Journal of STD and AIDS* 24.1 (2013), pp. 18–30. https://doi.org/10.1177/0956462412472291.

[52] Leigh Anne Shafer et al. "The dual impact of antiretroviral therapy and sexual behaviour changes on HIV epidemiologic trends in Uganda: A modelling study". *Sexually Transmitted Infections* 90.5 (2014), pp. 423–429. https://doi.org/10.1136/sextrans-2013-051219.

[53] Senelani D Hove-Musekwa et al. "Cost-Effectiveness Analysis of Hospitalization and Home-Based Care Strategies for People Living with HIV/AIDS: The Case of Zimbabwe." *International Scholarly Research Notices* 2014 (2014), p. 836439. https://doi.org/10.1155/2014/836439.

[54] Ronald Scott Braithwaite et al. "How do different eligibility guidelines for antiretroviral therapy affect the cost–effectiveness of routine viral load testing in sub-Saharan Africa". *AIDS* 28.S1 (2014), S73–S83. https://doi.org/10.1097/QAD.0000000000000110.

[55] Brooke E Nichols et al. "Increasing the use of second-line therapy is a cost-effective approach to prevent the spread of drug-resistant HIV: a mathematical modelling study". *Journal of the International AIDS Society* 17 (2014), p. 19164. https://doi.org/10.7448/IAS.17.1.19164.

[56] Laith J Abu-Raddad and Susanne F Awad. "How does population viral load vary with the evolution of a large HIV epidemic in sub-Saharan Africa?" *AIDS* 28.6 (2014), pp. 927–929. https://doi.org/10.1097/QAD.0000000000000211.

[57] Sarah Jane Anderson et al. "Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: A modelling study". *The Lancet* 384.9939 (July 2014), pp. 249–256. ISSN: 1474547X. https://doi.org/10.1016/S0140-6736(14)61053-9.

[58] Sabina S Alistar et al. "HIV epidemic control-a model for optimal allocation of prevention and treatment resources". *Health Care Management Science* 17.2 (2014), pp. 162–181. https://doi.org/10.1007/s10729-013-9240-4.

[59] Anne Cori et al. "HPTN 071 (PopART): A cluster-randomized trial of the population impact of an HIV combination prevention intervention including universal testing and treatment: Mathematical model". *PLOS ONE* 9.1 (Jan. 2014), e84511. ISSN: 19326203. https://doi.org/10.1371/journal.pone.0084511.

[60] John Stover et al. "How Can We Get Close to Zero? The Potential Contribution of Biomedical Prevention and the Investment Framework towards an Effective Response to HIV". *PLOS ONE* 9.11 (2014), e111956. https://doi.org/10.1371/journal.pone.0111956.

[61] Andrea L Wirtz et al. "Epidemic impacts of a community empowerment intervention for HIV prevention among female sex workers in generalized and concentrated epidemics". *PLOS ONE* 9.2 (2014), e88047. https://doi.org/10.1371/journal.pone.0088047.

[62] Eline L Korenromp et al. "Impact and cost of the HIV/AIDS national strategic plan for Mozambique, 2015-2019-projections with the spectrum/goals model". *PLOS ONE* 10.11 (2015), e0142908. https://doi.org/10.1371/journal.pone.0142908.

[63] Gwenan M Knight et al. "Tuberculosis Prevention in South Africa". *PLOS ONE* 10.4 (2015), e0122514. https://doi.org/10.1371/journal.pone.0122514.

[64] Cliff C. Kerr et al. "Optima: A Model for HIV Epidemic Analysis, Program Prioritization, and Resource Optimization". *Journal of Acquired Immune Deficiency Syndromes* 69.3 (July 2015), pp. 365–376. ISSN: 10779450. https://doi.org/10.1097/QAI.0000000000000605.

[65] Nicole Fraser et al. "Reorienting the HIV response in Niger toward sex work interventions: From better evidence to targeted and expanded practice". *Journal of Acquired Immune Deficiency Syndromes* 68.S2 (2015), S213–S220. https://doi.org/10.1097/QAI.0000000000000456.

[66] Semu Mitiku Kassa and Aziz Ouhinou. "The impact of self-protective measures in the optimal interventions for controlling infectious diseases of human population". *Journal of Mathematical Biology* 70.1-2 (2015), pp. 213–236. https://doi.org/10.1007/s00285-014-0761-3.

[67] Linda Gail Bekker et al. *Combination HIV prevention for female sex workers: What is the evidence?* Jan. 2015.

[68] Kate Shannon et al. "Global epidemiology of HIV among female sex workers: Influence of structural determinants". *The Lancet* 385.9962 (Jan. 2015), pp. 55–71. https://doi.org/10.1016/S0140-6736(14)60931-4.

[69] Stephanie Blaizot et al. "Estimation and short-term prediction of the course of the HIV epidemic using demographic and health survey methodology-like data". *PLOS ONE* 10.6 (2015), e0130387. https://doi.org/10.1371/journal.pone.0130387.

[70] Jennifer A Smith et al. "Maximising HIV prevention by balancing the opportunities of today with the promises of tomorrow: a modelling study". *The Lancet HIV* 3.7 (2016), e289–e296. https://doi.org/10.1016/S2352-3018(16)30036-4.

[71] Rifat Atun et al. "Long-term financing needs for HIV control in sub-Saharan Africa in 2015-2050: a modelling study." *BMJ Open* 6.3 (2016), e009656. https://doi.org/10.1136/bmjopen-2015-009656.

[72] Andrew J Shattock et al. "In the interests of time: Improving HIV allocative efficiency modelling via optimal time-varying allocations". *Journal of the International AIDS Society* 19.1 (2016), p. 20627. https://doi.org/10.7448/IAS.19.1.20627.

[73] Jessica B McGillen et al. "Optimum resource allocation to reduce HIV incidence across sub-Saharan Africa: a mathematical modelling study". *The Lancet HIV* 3.9 (2016), e441–e448. https://doi.org/10.1016/S2352-3018(16)30051-0.

[74] Leigh F. Johnson et al. "Prospects for HIV control in South Africa: a model-based analysis". *Global Health Action* 9.1 (Dec. 2016). ISSN: 16549880. https://doi.org/10.3402/gha.v9.30314.

[75] Monisha Sharma et al. "Modeling the cost-effectiveness of homebased HIV testing and education (HOPE) for pregnant women and their male partners in Nyanza Province, Kenya". *AIDS Research and Human Retroviruses* 32.S1 (2016), p. 300. https://doi.org/10.1097/QAI.0000000000001057.

[76] Gordon Akudibillah, Abhishek Pandey, and Jan Medlock. "Maximizing the benefits of ART and PrEP in resource-limited settings". *Epidemiology and Infection* 145.5 (2017), pp. 942–956. https://doi.org/10.1017/S0950268816002958.

[77] Ramzi A Alsallaq et al. "The potential impact and cost of focusing HIV prevention on young women and men: A modeling analysis in western Kenya". *PLOS ONE* 12.4 (2017), e0175447. https://doi.org/10.1371/journal.pone.0175447.

[78] Sarah-Jane Anderson et al. "HIV prevention where it is needed most: Comparison of strategies for the geographical allocation of interventions: Comparison". *Journal of the International AIDS Society* 20.4 (2017), e25020. https://doi.org/10.1002/jia2.25020.

[79] Calvin Chiu et al. "Designing an optimal HIV programme for South Africa: Does the optimal package change when diminishing returns are considered?" *BMC Public Health* 17.1 (2017), p. 143. https://doi.org/10.1186/s12889-017-4023-3.

[80] Leigh F Johnson et al. "Estimating the impact of antiretroviral treatment on adult mortality trends in South Africa: A mathematical modelling study". *PLOS Medicine* 14.12 (2017), e1002468. https://doi.org/10.1371/journal.pmed.1002468.

[81] Robyn M Stuart et al. "Getting it right when budgets are tight: Using optimal expansion pathways to prioritize responses to concentrated and mixed HIV epidemics". *PLOS ONE* 12.10 (2017), e0185077. https://doi.org/10.1371/journal.pone.0185077.

[82] Jessica B McGillen et al. "Consequences of a changing US strategy in the global HIV investment landscape". *AIDS* 31.18 (2017), F19–F23. https://doi.org/10.1097/QAD.0000000000001669.

[83] Ide Cremin et al. "PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study". *The Lancet HIV* 4.5 (2017), e214–e222. https://doi.org/10.1016/S2352-3018(17)30021-8.

[84] Jennifer M Ross et al. "Modeling HIV disease progression and transmission at population-level: The potential impact of modifying disease progression in HIV treatment programs." *Epidemics* 23 (2018), pp. 34–41. https://doi.org/10.1016/j.epidem.2017.12.001.

[85] Sarah-Jane Anderson et al. "Frontloading HIV financing maximizes the achievable impact of hiv prevention". *Journal of the International AIDS Society* 21.3 (2018), e25087. https://doi.org/10.1002/jia2.25087.

[86] Sarah-Jane Anderson et al. "The importance of local epidemic conditions in monitoring progress towards HIV epidemic control in Kenya: a modelling study". *Journal of the International AIDS Society* 21.11 (2018), e25203. https://doi.org/10.1002/jia2.25203.

[87] Evans Otieno Omondi, Rachel Waema Mbogo, and Livingstone S Luboobi. "Mathematical analysis of sex-structured population model of HIV infection in Kenya". *Letters in Biomathematics* 5.1 (2018), pp. 174–194. https://doi.org/10.1080/23737867.2018.1506712.

[88] Beth Woods et al. "Appraising the value of evidence generation activities: an HIV modelling study." *BMJ Global Health* 3.6 (2018), e000488. https://doi.org/10.1136/bmjgh-2017-000488.

[89] Elizabeth R Stevens et al. "Cost-effectiveness of a combination strategy to enhance the HIV care continuum in Swaziland: Link4health". *PLOS ONE* 13.9 (2018), e0204245. https://doi.org/10.1371/journal.pone.0204245.

[90] Isaac J Stopard et al. "The influence of constraints on the efficient allocation of resources for HIV prevention". *AIDS* 33.7 (2019), pp. 1241–1246. https://doi.org/10.1097/QAD.0000000000002158.

[91] Leo Beacroft and Timothy B Hallett. "The potential impact of a "curative intervention" for HIV: a modelling study." *Global Health Research and Policy* 4 (2019), p. 2. https://doi.org/10.1186/s41256-019-0107-1.

[92] Meghan Reidy et al. "Evaluating the potential impact and cost-effectiveness of dapivirine vaginal ring pre-exposure prophylaxis for HIV prevention". *PLOS ONE* 14.6 (2019), e0218710. https://doi.org/10.1371/journal.pone.0218710.

[93] Evans Otieno Omondi, Rachel Waema Mbogo, and Livingstone S Luboobi. "A mathematical modelling study of HIV infection in two heterosexual age groups in Kenya". *Infectious Disease Modelling* 4 (2019), pp. 83–98. https://doi.org/10.1016/j.idm.2019.04.003.

[94] Mathieu Maheu-Giroux et al. "Cost-Effectiveness of Accelerated HIV Response Scenarios in Cote d'Ivoire". *Journal of Acquired Immune Deficiency Syndromes* 80.5 (2019), pp. 503–512. https://doi.org/10.1097/QAI.0000000000001956.

[95] Jesse Knight, Rupert Kaul, and Sharmistha Mishra. "Risk heterogeneity in compartmental HIV transmission models of ART as prevention in Sub-Saharan Africa: A scoping review". *Epidemics* 40 (2022), p. 100608. https://doi.org/10.1016/j.epidem.2022.100608.

[96] Judith Vandepitte et al. "Estimates of the number of female sex workers in different regions of the world". *Sexually Transmitted Infections* 82.S3 (June 2006). ISSN: 13684973. https://pubmed.ncbi.nlm.nih.gov/16735288/.

[97] M. Carael et al. “Clients of sex workers in different regions of the world: Hard to count”. *Sexually Transmitted Infections* 82.S3 (June 2006), pp. iii26–iii33. ISSN: 13684973.

[98] Fiona Scorgie et al. “Socio-demographic characteristics and behavioral risk factors of female sex workers in sub-Saharan Africa: A systematic review”. *AIDS and Behavior* 16.4 (May 2012), pp. 920–933. https://doi.org/10.1007/s10461-011-9985-z.

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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.

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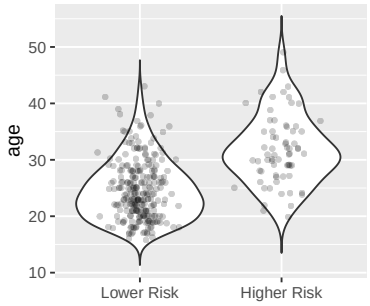
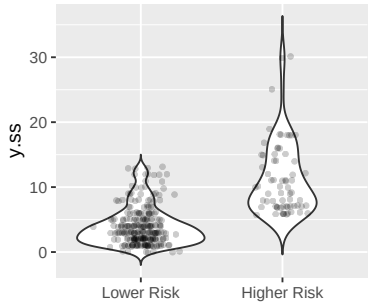
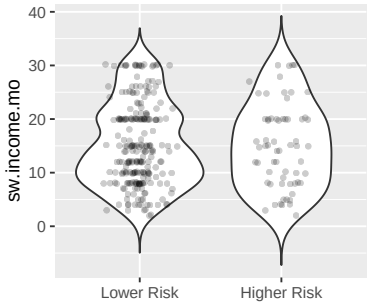


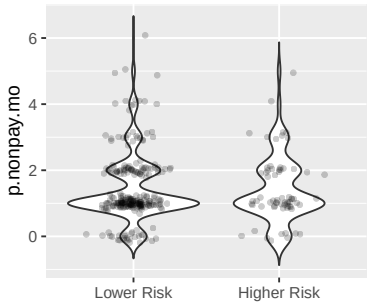
(a) Age



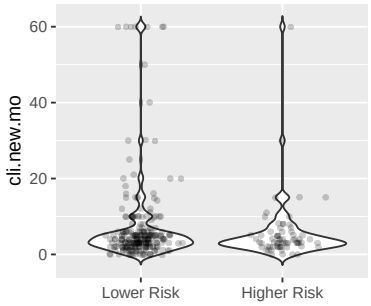
(b) Years selling sex



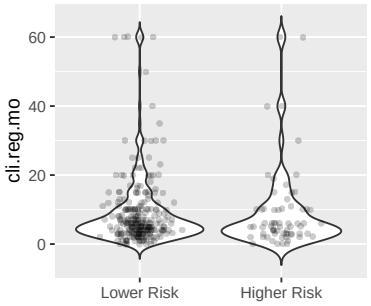
(c) Monthly sex work income



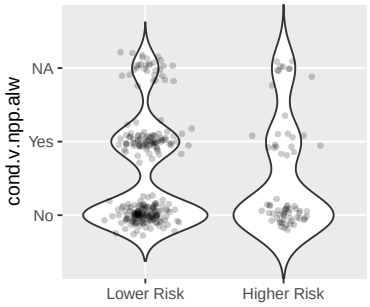
(d) Non-paying partners



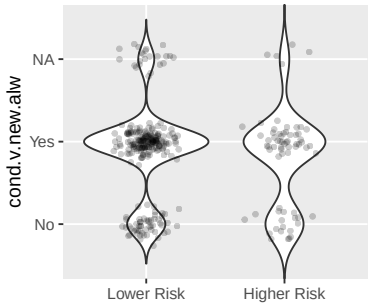
(e) Monthly new clients



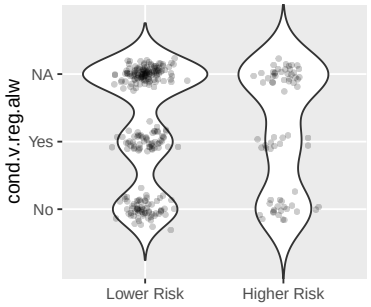
(f) Monthly regular clients



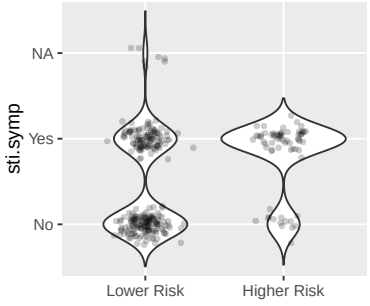
(g) Non-paying condom use



(h) New client condom use

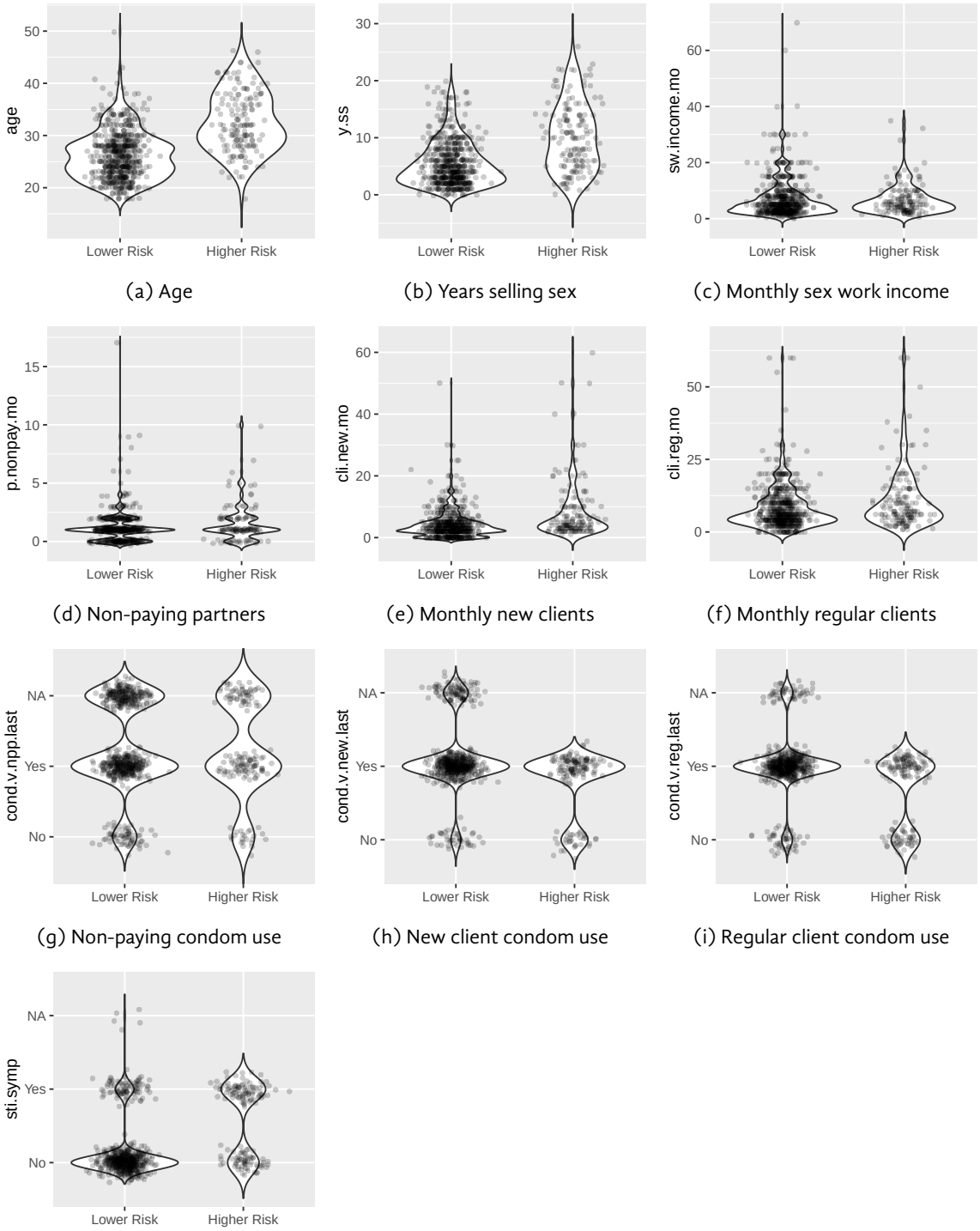


(i) Regular client condom use



(j) Any STI symptoms past year

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)



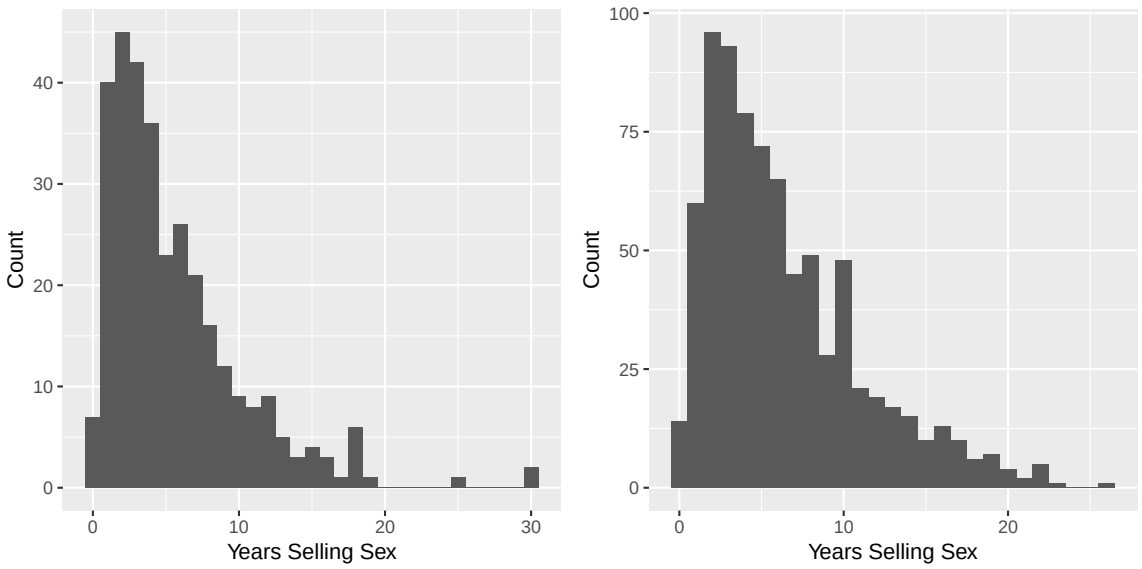
(a) Age (b) Years selling sex (c) Monthly sex work income

(d) Non-paying partners (e) Monthly new clients (f) Monthly regular clients

(g) Non-paying condom use (h) New client condom use (i) Regular client condom use

(j) Any STI symptoms past year

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)



(a) 2011 [1] (b) 2014 [2]

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

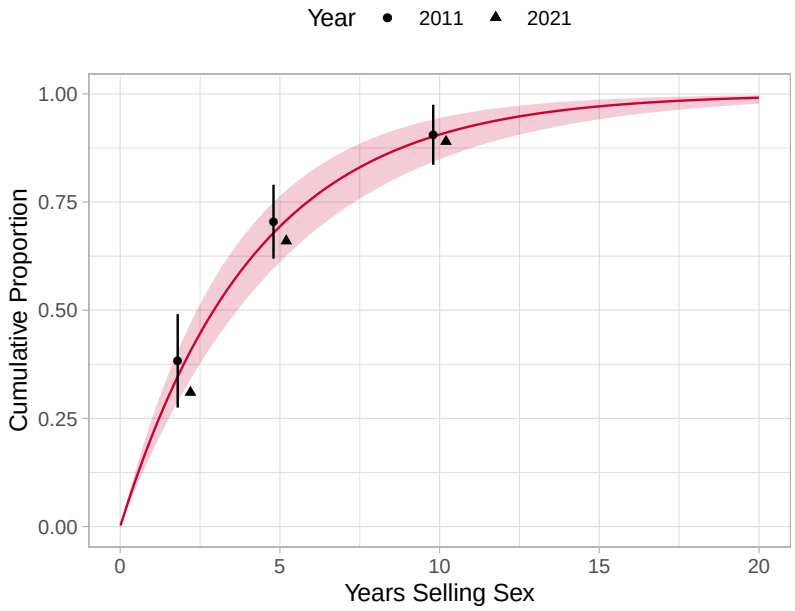


Figure B.4: Cumulative distribution of years selling sex among FSW in eSwatini (RDS-adjusted)

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 $f(x \mid \theta)$ be the probability density function of random variable x (parameter or target) given distribution parameters θ. Then $F(x \mid \theta) = \int_0^x f(\tau)\, d\tau$ is the cumulative distribution function, and $Q(p \mid \theta) = F^{-1}(p \mid \theta)$ 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 minimized[1] the the following error function:

$$J(\theta) = \sum_i \left| q_i - Q(p_i \mid \theta) \right|^\omega \tag{B.1}$$

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

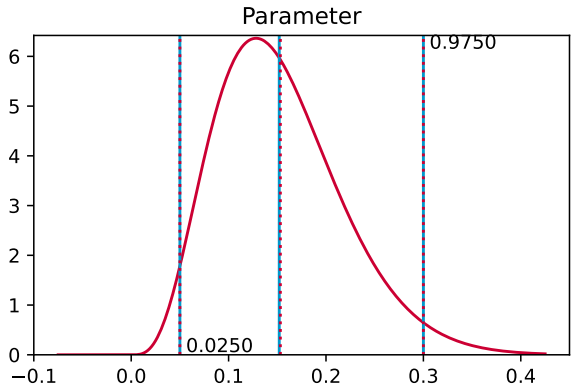


Figure B.5: Example distribution fitting validation plot

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

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:

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

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

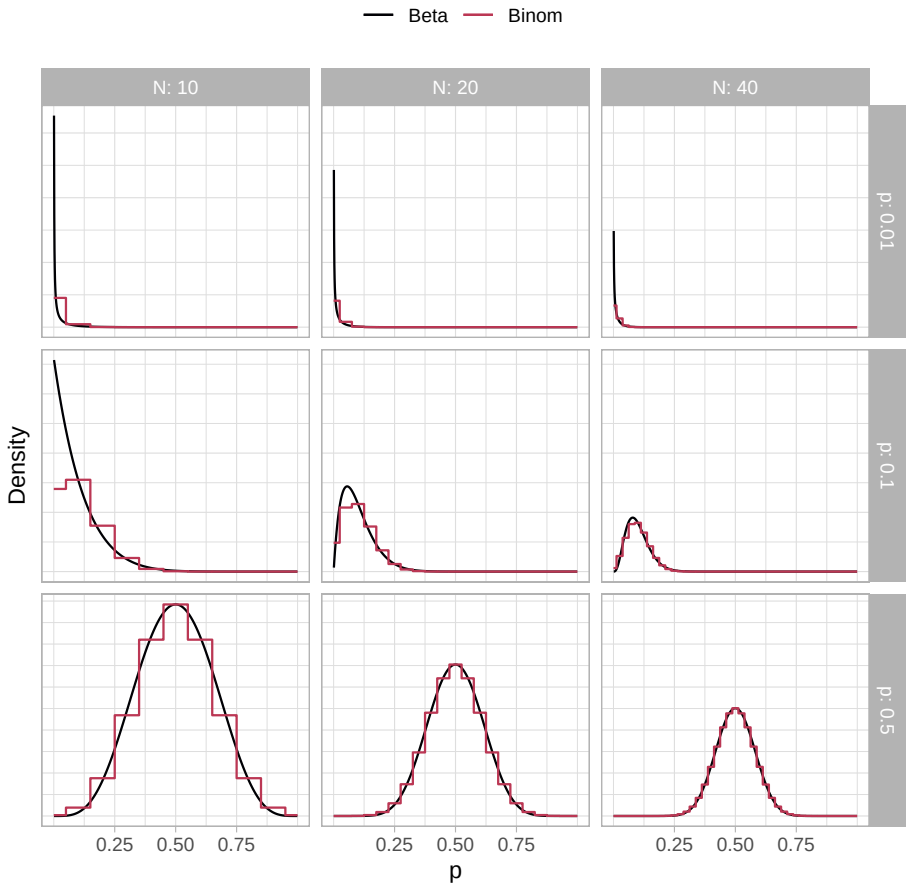


Figure B.6: Approximation of the binomial distribution with the beta distribution

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

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

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 approachs 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.

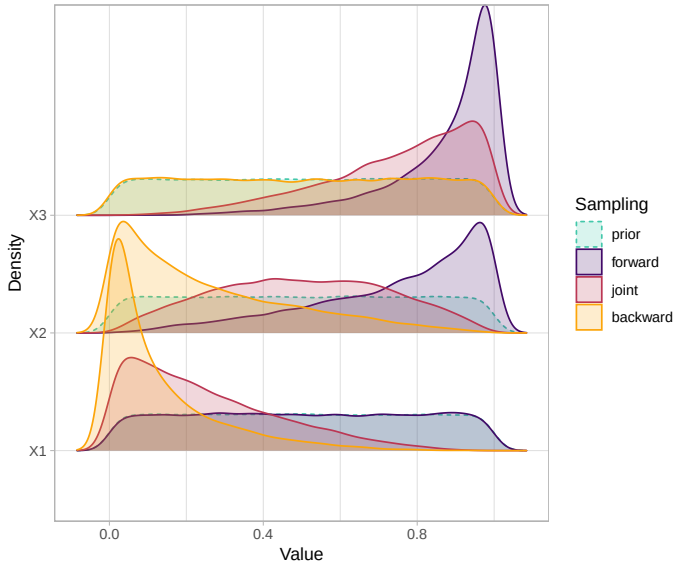


Figure B.7: Illustration of different sampling biases when enforcing $X_1 < X_2 < X_3$

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.

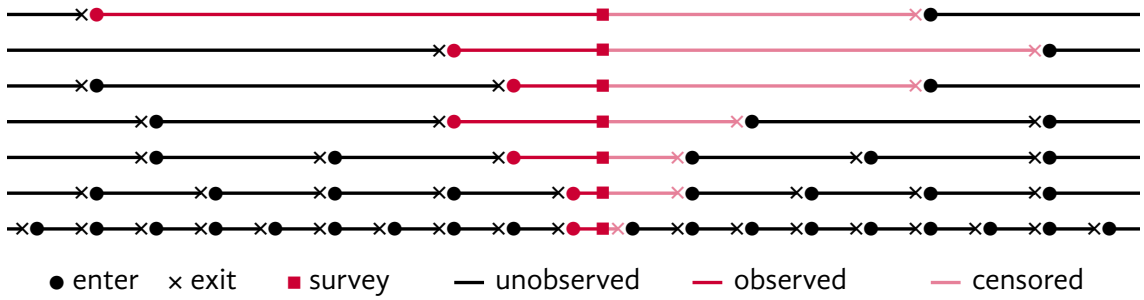


Figure B.8: Illustrative steady-state population of 7 FSW, with varying true durations in sex work δ, versus the observed durations in sex work δ_s via cross-sectional survey.

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 Simcikas and Dr. Jarle Tufto for help identifying and discussing this bias: stats.stackexchange.com/questions/298828.

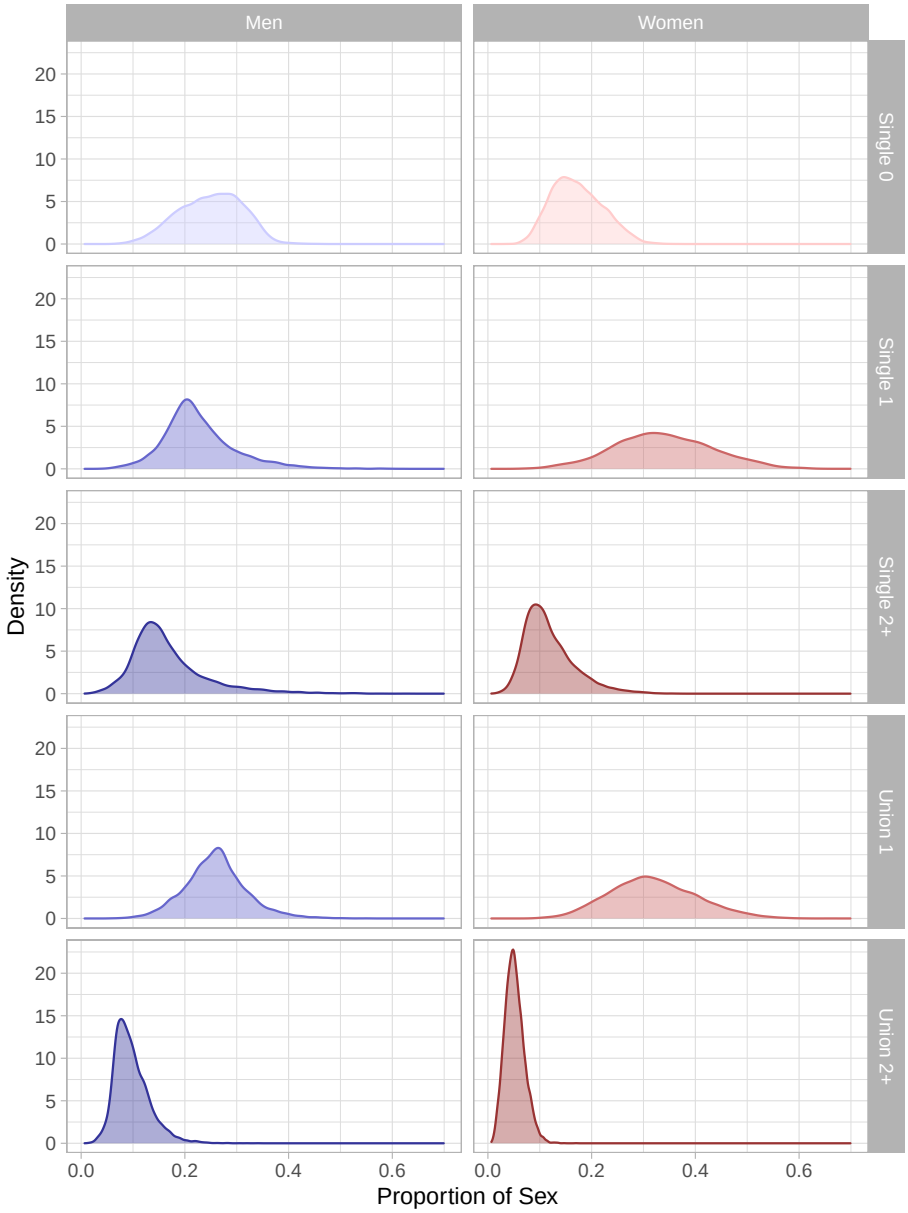


Figure B.9: TODO

References

[1] Stefan Baral et al. "Reconceptualizing the HIV epidemiology and prevention needs of female sex workers (FSW) in Swaziland". *PLOS ONE* 9.12 (Dec. 2014), e115465. ISSN: 19326203. http://dx.plos.org/10.1371/journal.pone.0115465.

[2] PEPFAR. *Characterizing the HIV Prevention and Treatment Needs among Key Populations, including Men who Have Sex with Men and Female Sex Workers in Swaziland: From Evidence to Action*. Tech. rep. Mbabane, Swaziland, 2015.

[3] Eswatini Ministry of Health. *2020–2021 Integrated Biological-Behavioral Surveillance Survey among Female Sex Workers and Men Who Have sex with Men in Eswatini*. Tech. rep. Mbabane, Eswatini, 2022.

[4] Erika Fazito et al. "Analysis of duration of risk behaviour for key populations: a literature review." *Sexually transmitted infections* 88.S2 (Dec. 2012), pp. i24–i32. ISSN: 14723263. https://sti.bmj.com/content/88/Suppl˙2/i24%20https://sti.bmj.com/content/88/Suppl˙2/i24.abstract.

[5] Eve Cheuk et al. "Transitions: Novel Study Methods to Understand Early HIV Risk Among Adolescent Girls and Young Women in Mombasa, Kenya, and Dnipro, Ukraine". *Frontiers in Reproductive Health* 2 (Sept. 2020), p. 10. https://doi.org/10.3389/frph.2020.00007.