

## Chapter 1

# Modelling Intersections of Differential Risk and ART Coverage

### 1.1 Introduction

Early HIV treatment via antiretroviral therapy (ART) offers numerous individual-level health benefits [1–4], and can prevent transmission in serodiscordant partnerships [5–7]. As such, immediate initiation of ART has been recommended by WHO since 2016 [8]. Alongside expanding ART eligibility, interest has grown in the potential population-level prevention impacts of ART, motivating numerous modelling studies [9–12] and several large community-based trials [13–16] of ART scale-up as “treatment as prevention”, especially within Sub-Saharan Africa. In general, the prevention impacts estimated via these trials have not met expectations from modelling, prompting questions about the potential influence of modelling assumptions on predictions [17].

Within these modelling studies, ART prevention impacts are usually quantified as incidence rate reduction or cumulative infections averted in scenarios with higher cascade attainment vs. scenarios with lower attainment [12]. Modelled populations are often stratified by risk, including key populations like FSW and their clients, to capture important epidemic dynamics related to risk heterogeneity [18–20]. However, these studies almost always assume that cascade attainment (i.e., proportions of PLHIV who are diagnosed, treated, and virally suppressed) or progression (i.e., rates of diagnosis, treatment initiation, and treatment failure/discontinuation) are equal across modelled risk groups (e.g., see § ??). For example, among the modelling studies reviewed in Chapter ??, key populations were usually assumed to have “average” cascade progression, or “above average” progression in some scenarios, but never “below average”.

Yet, there is growing evidence of differential ART cascade across population strata, including age, gender, mobility, and risk [21, 22]. These differences can be driven by unique barriers to engagement in care faced by vulnerable populations, which intersect with drivers of HIV risk [23–25]. Moreover, the lowest cascades likely remain unmeasured [21, 26]. These intersections of risk and cascade heterogeneity could potentially undercut the prevention impacts of ART scale-up anticipated from model-based evidence [17]. Therefore, I sought to examine the following questions in an illustrative modelling analysis:

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

I examined these questions using the Eswatini model from Chapter ??, focusing on differential risk related to sex work. Eswatini has recently achieved outstanding cascade gains, surpassing 95-95-95 (see § ??) [27, 28]. As such, I used observed ART scale-up in Eswatini as a *base case* reflecting evidently attainable scale-up, and explored *counterfactual* scenarios in which scale-up was slower, and where specific risk groups could have been “left behind”.

## 1.2 Methods

This section briefly reviews the transmission model used, and outlines the analyses conducted to answer the research questions outlined above.

### 1.2.1 Model

The complete details of model structure, parameterization, and calibration are given in Chapter ?. The proposed force of infection approach from in Chapter ?? was used throughout. Briefly, the deterministic compartmental model features 8 risk groups, including higher and lower risk FSW and clients, and 4 partnership types, including regular and occasional sex work (Figure ??). Risk heterogeneity is captured through group-level factors, including group sizes, turnover, GUD prevalence, and different numbers/types of partnerships; as well as partnership-level factors, including mixing patterns, partnership durations, frequency of vaginal and anal sex, and levels of condom use. Modelled HIV natural history includes acute infection and stages defined by CD4 count, which determine differences in infectiousness, HIV-attributable mortality, and historical ART eligibility. I obtained  $N_f = 1000$  plausible model fits via calibration.

### 1.2.2 Scenarios & Analyses

#### 1.2.2.1 Objective 1: Influence of cascade differences between risk groups

For Objective 1, I defined the *base case* scenario to reflect observed cascade scale-up in Eswatini, reaching 95-95-95 by 2020 [28]. Next, I defined 4 *counterfactual* scenarios in which overall viral suppression was lower, such that the population overall reached 80-80-90 by 2020, reflecting approximate trends in SSA cascades prior to universal ART [28]. In these counterfactual scenarios, I reduced cascade progression among specific risk groups in different combinations: FSW, clients, and/or the remaining population (“lower risk”). I reduced cascade progression by calibrating and applying a constant relative scaling factor “ $R$ ” to group-specific rates of: diagnosis ( $R_d \in [0, 1]$ ), treatment initiation ( $R_t \in [0, 1]$ ), and treatment failure / discontinuation ( $R_u \in [1, 20]$ ). When FSW and/or clients had reduced cascade, I calibrated their  $R$ s so that these populations achieved approximately 60-40-80 by 2020. By contrast, I calibrated  $R$ s for the lower risk population so that the Swati population *overall* achieved 80-80-90 in all 4 counterfactual scenarios, thus ensuring that a consistent proportion of the population overall experienced reduced viral

Table 1.1: Modelling scenarios for Objective 1 defined by 2020 calibration targets

Scenario	ART cascade in 2020 <sup>a</sup>			Re-scaled cascade rates <sup>b</sup>		
	FSW	Clients	Overall	FSW	Clients	Lower Risk
<i>Base Case</i>	95-95-95	—	95-95-95	—	—	—
<i>Leave Behind: FSW</i>	60-40-80	—	80-80-90	✓	✗	✓
<i>Leave Behind: Clients</i>	—	60-40-80	80-80-90	✗	✓	✓
<i>Leave Behind: FSW &amp; Clients</i>	60-40-80	60-40-80	80-80-90	✓	✓	✓
<i>Leave Behind: Neither</i>	—	—	80-80-90	✗	✗	✓

<sup>a</sup> Cascade: % diagnosed among PLHIV; % on ART among diagnosed; % virally suppressed among on ART; <sup>b</sup> Rates of: diagnosis; ART initiation; treatment failure; Lower Risk: all women and men not involved in sex work; FSW: female sex workers; Clients: of FSW. Figure A.1 plots the modelled cascades over time.

suppression. Table 1.1 summarizes these scenarios, while Figure A.1 plots the modelled cascades over time. When cascade rates among FSW and/or clients were unchanged from the base case, the cascade these groups achieved could be lower than 95-95-95 due to risk group turnover and higher incidence. All cascades continued to increase beyond 2020 due to assumed fixed rates of diagnosis, treatment initiation, and treatment failure / discontinuation thereafter.

I quantified ART prevention impacts via relative cumulative additional infections (CAI) and additional incidence rate (AIR) in the counterfactual scenarios ( $k$ ) vs. the base case ( $o$ ), over multiple time horizons up to 2030, starting from  $t_o = 2000$ :

$$CAI, AIR(t) = \frac{\Omega_k(t) - \Omega_o(t)}{\Omega_o(t)}, \quad \Omega(t) = \begin{cases} \int_{t_o}^t \Lambda(\tau) d\tau & CAI \\ \lambda(t) & AIR \end{cases} \quad (1.1)$$

where:  $\Lambda$  denotes absolute numbers of infections per year, and  $\lambda$  denotes incidence rate per susceptible per year. For each scenario, I computed relative additional infections for each model fit  $j$ , and reported median (95% CI) values across model fits, reflecting uncertainty.

### 1.2.2.2 Objective 2: Conditions under which cascade differences matter most

For Objective 2, I estimated via regression: the effects of lower cascade among certain risk groups on relative CAI and AIR, plus potential effect modification by epidemic conditions. The hypothesized causal effects are illustrated as a directed acyclic graph in Figure 1.1, and the synthetic data generation processes and variable definitions are detailed below.

For this regression analysis, I obtained 10,000 samples as follows. I explored a wider range of counterfactual scenarios vs. Objective 1 by randomly sampling the relative rates for diagnosis and treatment initiation  $R_d, R_t \sim \text{Beta}(\alpha = 3.5, \beta = 1.9)$ , having 95% CI: (0.25, 0.95), and treatment failure  $R_u \sim \text{Gamma}(\alpha = 3.4, \beta = 1.9)$ , having 95% CI: (1.5, 15), for each of: FSW, clients, and the remaining lower risk population (9 total values). Sampling distributions were chosen to obtain cascades in 2020 spanning approximately 60-60-90 through 90-90-95 (Figure A.3). For each of  $N_f = 1000$  model fits, I generated  $N_k = 10$  counterfactual scenarios per fit via random relative rates “ $R$ ” via Latin hypercube sampling, yielding  $N_f N_k = 10,000$  total counterfactual samples for the regression.

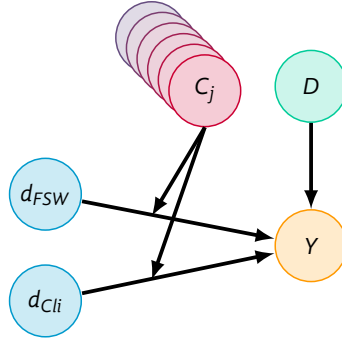


Figure 1.1: Directed acyclic graph (DAG) for inferring the epidemic conditions under which differential viral suppression across risk groups matters most

$Y$ : cumulative additional infections or additional incidence rate by 2030;  $D$ : difference in population-overall viral unsuppression in counterfactual vs. base case scenario;  $d_i$ : difference in group- $i$ -specific viral unsuppression vs. population overall within counterfactual scenario;  $C_j$ : epidemic conditions (effect modifiers of  $d_i$ ).

For each of these 10,000 samples, I defined relative CAI and AIR vs. the base case, as in Objective 1. For each sample, I further defined  $U_{fki}$  for risk groups  $i \in \{1 : \text{FSW}, 2 : \text{clients}, * : \text{overall}\}$  as the proportions virally unsuppressed among people living with HIV by 2020, reflecting a summary measure of ART cascade gaps. Using  $U_{fki}$ , I defined the main regression predictors as:  $D_{fk} = U_{fk*} - U_{fo*} > 0$ , reflecting differences in *population-overall* viral unsuppression in sample  $k \in [1, 10]$  vs. the base case (denoted  $k = 0$ ); and  $d_{fki} = U_{fki} - U_{fk*} \leq 0$ , reflecting differences in *group- $i$ -specific* viral unsuppression in sample  $k$  vs. the population overall in sample  $k$  — i.e., disproportionate unsuppression.

Next, I defined the following measures of epidemic conditions ( $C_{fj}$ ) related to sex work, as hypothesized modifiers of the effect of disproportionate unsuppression on relative CAI and RAI: FSW and client population sizes (% of population overall); average duration (in years) selling sex among FSW and buying sex among clients; and HIV prevalence ratios in the year 2000 among FSW vs. other women, and among clients vs. other men. For these measures, I combined higher and lower risk FSW, and likewise higher and lower risk clients. I used HIV prevalence ratios in 2000 to reflect summary measures of risk heterogeneity prior to ART, as compared to including all modelled risk factors for HIV acquisition and transmission (e.g., Table ??), which could lead to overfitting and improper inference due to effect mediation.

Finally, I defined a general linear model for each outcome (CAI, AIR) as:

$$\text{CAI, AIR} = \beta_0 D + \sum_i \beta_i d_i + \sum_{ij} \beta_{ij} d_i C_j \quad (1.2)$$

such that each outcome is modelled as a sum of the effects of: differential population-level unsuppression in the counterfactual vs. the base scenario ( $D$ ); differential unsuppression among FSW and clients vs. the population overall within the counterfactual scenario ( $d_i$ ); and effect modification of  $d_i$  by epidemic conditions ( $C_j$ ). The model does not include an intercept because if  $D = d_i = 0$ , then we expect  $\text{CAI} = \text{AIR} = 0$ . I fitted this model for each outcome using generalized estimating equations [29] to control for repeated use of each model fit  $f$ . I standardized all model variables ( $D, d_i, C_j$ ) via  $\hat{x} = (x - \text{mean}(x))/\text{SD}(x)$  to avoid issues of different variable scales and collinearity in interaction terms. Note that this standardization does not imply that regression coefficient *magnitudes* can be compared to indicate variable “importance”,

because the standardization applied to each variable is driven by the variance in the variable — in this case reflecting arbitrary ranges ( $D, d_i$ ) or uncertainty in calibration ( $C_j$ ).<sup>1</sup>

## 1.3 Results

Results of model calibration and inferred dynamics of heterosexual HIV transmission in Eswatini are given in § ?? and ?. This section focuses on results of scenarios and analyses outlined in § 1.2.2.

### 1.3.1 Objective 1: Influence of cascade differences between risk groups

Figure A.1 illustrates cascade attainment over time in each of the four counterfactual scenarios (80-80-90 overall by 2020), plus the base case (95-95-95 overall by 2020). Figure 1.2 then illustrates cumulative additional infections (CAI) and additional incidence rate (AIR) in each counterfactual scenario vs. the base case. Leaving behind both FSW and clients resulted the most additional infections: median [IQR] 28.8 [17.5, 46.2] % more than the base case by 2030. By contrast, leaving behind neither FSW nor clients resulted in the fewest additional infections: 13.0 [6.1, 25.6] % more than the base case by 2030 — a 54.2 [30.3, 73.2] % reduction. Leaving behind either FSW or clients resulted in a similar number of additional infections: 21.8 [12.5, 36.7] % and 20.4 [11.8, 34.7] %, respectively. Relative differences were similar for additional incidence rate. Which risk groups acquired additional infections differed across scenarios (Figure A.2c), with more additional infections among clients when FSW were left behind, vs. among lower risk women when clients were left behind. The majority of additional infections were transmitted via casual partnerships in all scenarios (Figure A.2a).

### 1.3.2 Objective 2: Conditions under which cascade differences matter most

Figure 1.3 ...

## 1.4 Discussion

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

Although our analysis only considered Eswatini, our findings are likely generalizable to other epidemic contexts. In fact, HIV prevalence ratios between key populations and the population overall are relatively low in Eswatini versus elsewhere [30, 31]; thus, the transmission impact of cascade gaps among key populations in other contexts would likely be even greater than we found for Eswatini. Moreover, as HIV

<sup>1</sup> I verified that results were qualitatively the same using  $\hat{x} = (x - \text{median}(x))/\text{IQR}(x)$ . For further discussion on interpretation of standardized regression coefficients, see also: [stats.stackexchange.com/questions/29781](https://stats.stackexchange.com/questions/29781) and links therein.

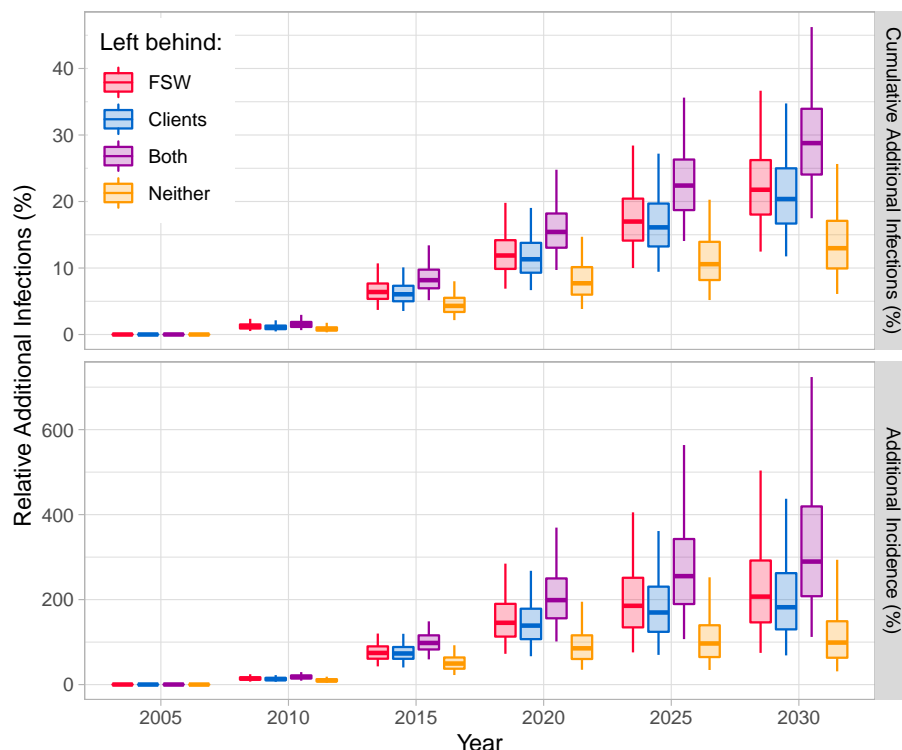


Figure 1.2: Relative additional infections under counterfactual scenarios vs. the base case

Base case: 95-95-95 by 2020; “left behind” counterfactual scenarios: 80-80-90 overall by 2020, with reduced cascade (60-40-80) among FSW, clients of FSW, both, or neither; whiskers, boxes, and midlines: 95% CI, 50% CI, median of model fits.

incidence declines in many settings, epidemics may become re-concentrated among key populations [32, 33], further magnifying the transmission impact of cascade disparities.

To our knowledge, our study is the first to explore the transmission impact of heterogeneity in ART coverage across risk groups, within consistent population-overall coverage. In a previous review of mathematical modelling of ART scale-up in Sub-Saharan Africa, we found that few studies have considered any cascade differences by risk group, but that such differences likely mediate ART prevention impacts [12]. Cascade gaps have been observed among men versus women [22, 34], younger versus older populations [22, 35], key populations versus the population overall [21], and within key populations themselves [36, 37]. Moreover, unmeasured cascades — such as among populations who have not been reached by programs and interventions — are likely lowest [21, 26]. Consistent integration of these data going forward could improve the quality of model-based evidence for HIV resource prioritization.

Global ART scale-up undoubtedly has many benefits, including for individual-level health outcomes [1, 4], prevention in serodiscordant relationships [6], and contributing to population-level incidence declines [38]. However, efforts to maximize cascade coverage should not overlook populations that may be harder to reach, where barriers to engagement in HIV care often intersect with drivers of HIV risk [17, 23–25]. Such populations can be reached effectively through tailored services to meet their unique needs [39], services which can be designed and refined with ongoing community engagement [40–42]. As we have shown, an equity-focused approach to ART scale-up can maximize prevention impacts, and accelerate the end of the HIV epidemic.

Our study has three major strengths. First, drawing on our conceptual framework for risk heterogeneity [12, Table 1] and multiple sources of context-specific data [43–47], we captured several dimensions of risk heterogeneity, including: heterosexual anal sex, four types of sexual partnerships, sub-stratification of FSW and clients into higher and lower risk, and risk group turnover. Second, whereas most modelling studies of ART scale-up project hypothetical future scenarios which may not be achievable, our base case scenario reflects observed scale-up in Eswatini. Finally, our analytic approach to objective ??, in which epidemic conditions are conceptualized as potential effect modifiers, represents a unique methodological contribution to the HIV modelling literature.

Our study has four main limitations. First, we only considered heterosexual HIV transmission in Eswatini, and mainly explored risk heterogeneity related to sex work. However, our findings would likely generalize to other transmission networks and determinants of risk heterogeneity, including risk groups not classically recognized as key populations, such as mobile populations and young women [48, 49]. Second, we did not consider transmitted drug resistance. Drug resistance is more likely to emerge in the context of barriers to viral suppression [50]; thus, cascade gaps among those at higher risk would likely accelerate emergence of transmitted drug resistance, and amplify impacts of such gaps. Third, even among the top 1% of model fits, substantial uncertainty remained in the values of inferred parameters, yielding wide confidence intervals in the outputs of interest (additional infections and incidence). In the absence of additional data, such intervals reflect our true uncertainty in the magnitude of these outputs, but not the trends across scenarios. Finally, our statistical analysis ...

In summary, ...

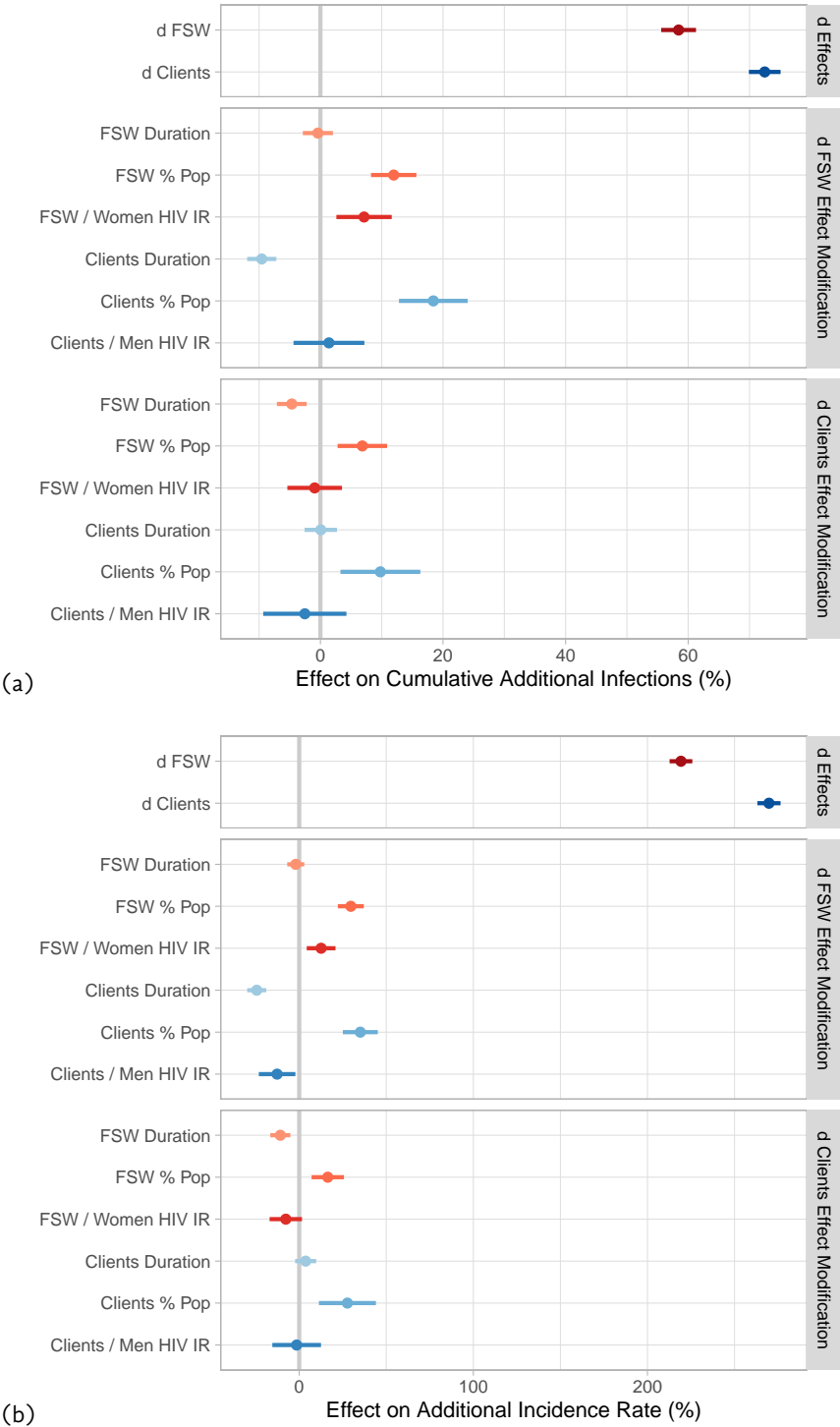


Figure 1.3

points and error bars: mean and 95% CI for each effect.



## References

- [1] 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 (2013), pp. 555–561. <https://doi.org/10.1097/QAI.0b013e3182821821>.
- [2] Gary Maartens, Connie Celum, and Sharon R. Lewin. "HIV infection: Epidemiology, pathogenesis, treatment, and prevention". *The Lancet* 384.9939 (2014), pp. 258–271. [https://doi.org/10.1016/S0140-6736\(14\)60164-1](https://doi.org/10.1016/S0140-6736(14)60164-1).
- [3] TEMPRANO ANRS 12136 Study Group. "A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa". *New England Journal of Medicine* 373.9 (2015), pp. 808–822. <https://doi.org/10.1056/nejmoa1507198>.
- [4] 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>.
- [5] Andrew Anglemyer et al. "Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples". *Cochrane Database of Systematic Reviews* 4 (2013). <https://doi.org/10.1002/14651858.CD009153.pub3>.
- [6] Myron S. Cohen et al. "Antiretroviral Therapy for the Prevention of HIV-1 Transmission". *New England Journal of Medicine* 375.9 (2016), pp. 830–839. <https://doi.org/10.1056/nejmoa1600693>.
- [7] Alison J Rodger et al. "Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study". *The Lancet* 0.0 (2019). <https://linkinghub.elsevier.com/retrieve/pii/S0140673619304180>.
- [8] 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>.
- [9] 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 (2009), pp. 48–57. [https://doi.org/10.1016/S0140-6736\(08\)61697-9](https://doi.org/10.1016/S0140-6736(08)61697-9).
- [10] Jeffrey W. Eaton et al. "HIV treatment as prevention: Systematic comparison of mathematical models of the potential impact of antiretroviral therapy on HIV incidence in South Africa". *PLOS Medicine* 9.7 (2012). Ed. by John Bartlett, e1001245. <https://doi.org/10.1371/journal.pmed.1001245>.
- [11] Jeffrey W Eaton et al. "Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: A combined analysis of 12 mathematical models". *The Lancet Global Health* 2.1 (2014), e23–e34. arXiv: [NIHMS150003](https://arxiv.org/abs/1508.0003). <https://www.sciencedirect.com/science/article/pii/S2214109X13701724>.
- [12] 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>.
- [13] Joseph Makhema et al. "Universal Testing, Expanded Treatment, and Incidence of HIV Infection in Botswana". *New England Journal of Medicine* 381.3 (2019), pp. 230–242. <https://www.nejm.org/doi/10.1056/NEJMoa1812281>.
- [14] Diane V. Havlir et al. "HIV Testing and Treatment with the Use of a Community Health Approach in Rural Africa". *New England Journal of Medicine* 381.3 (2019), pp. 219–229. <https://doi.org/10.1056/nejmoa1809866>.
- [15] Richard J. Hayes et al. "Effect of universal testing and treatment on HIV incidence - HPTN 071 (popart)". *New England Journal of Medicine* 381.3 (2019), pp. 207–218.
- [16] Collins C. Iwuji et al. "Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial". *The Lancet HIV* 5.3 (2018), e116–e125. [http://doi.org/10.1016/S2352-3018\(17\)30205-9](http://doi.org/10.1016/S2352-3018(17)30205-9).
- [17] Stefan Baral et al. "The disconnect between individual-level and population-level HIV prevention benefits of antiretroviral treatment". *The Lancet HIV* 6 (2019), e632–638. [http://doi.org/10.1016/S2352-3018\(19\)30226-7](http://doi.org/10.1016/S2352-3018(19)30226-7).
- [18] Hein Stigum, W. Falck, and P. Magnus. "The core group revisited: The effect of partner mixing and migration on the spread of gonorrhea, chlamydia, and HIV". *Mathematical Biosciences* 120.1 (1994), pp. 1–23. [https://doi.org/10.1016/0025-5564\(94\)90036-1](https://doi.org/10.1016/0025-5564(94)90036-1).
- [19] G. P. Garnett and R. M. Anderson. "Sexually transmitted diseases and sexual behavior: Insights from mathematical models". *Journal of Infectious Diseases* 174.S2 (1996), S150–S161. [https://doi.org/10.1093/infdis/174.Supplement\\_2.S150](https://doi.org/10.1093/infdis/174.Supplement_2.S150).
- [20] Charlotte Watts et al. "Remodelling core group theory: the role of sustaining populations in HIV transmission". *Sexually Transmitted Infections* 86.S3 (2010), pp. iii85–iii92. <https://doi.org/10.1136/sti.2010.044602>.

- [21] Avi Joseph Hakim et al. "Gaps and opportunities: measuring the key population cascade through surveys and services to guide the HIV response". *Journal of the International AIDS Society* 21 (2018), e25119. <http://doi.org/10.1002/jia2.25119>.
- [22] Dylan Green et al. *Evidence of sociodemographic heterogeneity across the HIV treatment cascade and progress towards 90-90-90 in sub-Saharan Africa – a systematic review and meta-analysis*. 2020. <https://doi.org/10.1002/jia2.25470>.
- [23] Rhoda K. Wanyenze et al. "'If you tell people that you had sex with a fellow man, it is hard to be helped and treated': Barriers and opportunities for increasing access to HIV services among men who have sex with men in Uganda". *PLOS ONE* 11.1 (2016). <https://doi.org/10.1371/journal.pone.0151866>.
- [24] Sheree Schwartz et al. "Engagement in the HIV care cascade and barriers to antiretroviral therapy uptake among female sex workers in Port Elizabeth, South Africa: Findings from a respondent-driven sampling study". *Sexually Transmitted Infections* 93.4 (2017), pp. 290–296. <https://sti.bmj.com/content/93/4/290>.
- [25] Megan Schmidt-Sane. "Male partners of female sex workers: The intersectional risk environment of HIV/AIDS in a Kampala informal settlement". *Social Science and Medicine* 298 (2022), p. 114873.
- [26] Makini A. S. Boothe et al. "Low engagement in HIV services and progress through the treatment cascade among key populations living with HIV in Mozambique: alarming gaps in knowledge of status". *BMC Public Health* 21.1 (2021), pp. 1–8. <https://link.springer.com/articles/10.1186/s12889-020-10039-2>.
- [27] Fiona Walsh et al. "Getting to 90–90–90: Experiences from the MaxART Early Access to ART for All (EAAA) Trial in Eswatini". *Current HIV/AIDS Reports* 17.4 (2020), pp. 324–332. <https://europepmc.org/article/med/32474844>.
- [28] UNAIDS. *AIDSinfo*. 2023. <http://aidsinfo.unaids.org>.
- [29] Ulrich Halekoh, Søren Højsgaard, and Jun Yan. "The R Package geepack for Generalized Estimating Equations". *Journal of Statistical Software* 15.2 (2006), pp. 1–11.
- [30] Stefan Baral et al. "Burden of HIV among female sex workers in low-income and middle-income countries: A systematic review and meta-analysis". *The Lancet Infectious Diseases* 12.7 (2012), pp. 538–549. [https://doi.org/10.1016/S1473-3099\(12\)70066-1](https://doi.org/10.1016/S1473-3099(12)70066-1).
- [31] P. H. Septime Hessou et al. "Comparison of the prevalence rates of HIV infection between men who have sex with men (MSM) and men in the general population in sub-Saharan Africa: A systematic review and meta-analysis". *BMC Public Health* 19.1 (2019), pp. 1–10. <https://doi.org/10.1186/s12889-019-8000-x>.
- [32] Tim Brown and Wiwat Peerapatanapokin. "Evolving HIV epidemics: The urgent need to refocus on populations with risk". *Current Opinion in HIV and AIDS* 14.5 (2019), pp. 337–353. <https://doi.org/10.1097/COH.0000000000000571>.
- [33] Geoff P. Garnett. "Reductions in HIV incidence are likely to increase the importance of key population programmes for HIV control in sub-Saharan Africa". *Journal of the International AIDS Society* 24.S3 (2021), e25727. <https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25727>.
- [34] Caitlin Quinn et al. "Who are the missing men? Characterising men who never tested for HIV from population-based surveys in six sub-Saharan African countries". *Journal of the International AIDS Society* 22.10 (2019), e25398. <https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25398>.
- [35] Refeletswe Lebelonyane et al. "To achieve 95-95-95 targets we must reach men and youth: High level of knowledge of HIV status, ART coverage, and viral suppression in the Botswana Combination Prevention Project through universal test and treat approach." *PLOS ONE* 16.8 (2021), e0255227. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0255227>.
- [36] Yunia Mayanja et al. "'Test and Treat' Among Women at High Risk for HIV-infection in Kampala, Uganda: Antiretroviral Therapy Initiation and Associated Factors". *AIDS and Behavior* 22.3 (2018), pp. 1053–1061. <https://doi.org/10.1007/s10461-017-1973-5>.
- [37] Maya Jaffer et al. "The HIV Cascade of Care and Service Utilisation at Sex Work Programmes Among Female Sex Workers in South Africa". *AIDS and Behavior* 26.9 (2022), pp. 2907–2919. <https://link.springer.com/article/10.1007/s10461-022-03616-6>.

- [38] Diane Havlir et al. *What do the Universal Test and Treat trials tell us about the path to HIV epidemic control?* 2020. <https://doi.org/10.1002/jia2.25455>.
- [39] Peter Ehrenkranz, Anna Grimsrud, and Miriam Rabkin. *Differentiated service delivery: Navigating the path to scale*. 2019. <https://doi.org/10.1097/COH.0000000000000509>.
- [40] Chido D. Chikwari, Stefanie Dringus, and Rashida A. Ferrand. “Barriers to, and emerging strategies for, HIV testing among adolescents in sub-Saharan Africa”. *Current Opinion in HIV and AIDS* 13.3 (2018), pp. 257–264.
- [41] Charmaine Khudzie Mlambo et al. “Experiences from a community advisory Board in the Implementation of early access to ART for all in Eswatini: A qualitative study”. *BMC Medical Ethics* 20.1 (2019), pp. 1–11. <https://bmcmethics.biomedcentral.com/articles/10.1186/s12910-019-0384-8>.
- [42] Carly A. Comins et al. “Opportunities and considerations for the design of decentralized delivery of antiretroviral therapy for female sex workers living with HIV in South Africa”. *BMC Health Services Research* 2022 22:1 22.1 (2022), pp. 1–10. <https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-022-08506-0>.
- [43] Central Statistical Office Swaziland. *Swaziland Demographic and Health Survey 2006-07*. Mbabane, Swaziland, 2008. <https://dhsprogram.com/>.
- [44] Swaziland Ministry of Health. *Swaziland HIV Incidence Measurement Survey: First Findings Report*. Mbabane, Swaziland, 2012. <http://shims.icap.columbia.edu/>.
- [45] Jessica Justman et al. “Swaziland HIV Incidence Measurement Survey (SHIMS): a prospective national cohort study”. *The Lancet HIV* 4.2 (2016), e83–e92. [https://doi.org/10.1016/S2352-3018\(16\)30190-4](https://doi.org/10.1016/S2352-3018(16)30190-4).
- [46] Stefan Baral et al. “Reconceptualizing the HIV epidemiology and prevention needs of female sex workers (FSW) in Swaziland”. *PLOS ONE* 9.12 (2014), e115465. <http://doi.org/10.1371/journal.pone.0115465>.
- [47] 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*. Mbabane, Swaziland, 2015.
- [48] Frank Tanser et al. “HIV treatment cascade in migrants and mobile populations”. *Current Opinion in HIV and AIDS* 10.6 (2015), pp. 430–438. <http://doi.org/10.1097/COH.0000000000000192>.
- [49] 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 (2020), p. 10. <https://doi.org/10.3389/frph.2020.00007>.
- [50] Quang D. Pham et al. “Global burden of transmitted HIV drug resistance and HIV-exposure categories: A systematic review and meta-analysis”. *AIDS* 28.18 (2014), pp. 2751–2762. <https://doi.org/10.1097/QAD.0000000000000494>.

# Appendix A

## Supplement to Chapter 1

### A.1 Objective 1

#### A.1.1 Scenario Cascades

Figure A.1 illustrates ...

#### A.1.2 Distributions of Additional Infections

As in § ??, Figure A.2 illustrates ...

### A.2 Objective 2

Figure A.3 illustrates ...

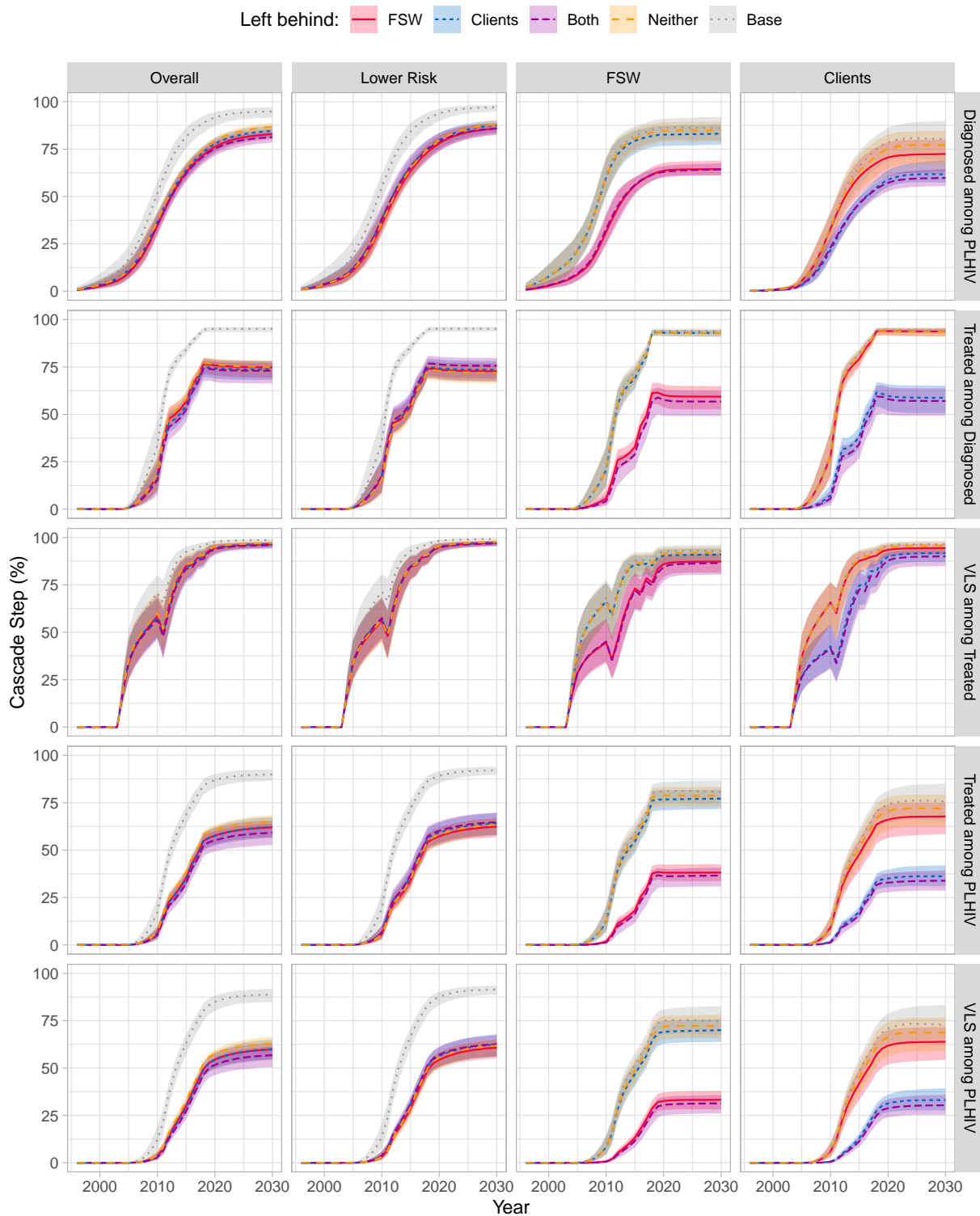


Figure A.1: Cascade attainment over time across scenarios

Lower Risk: all women and men not involved in sex work; FSW: female sex workers; Clients: of FSW; Base case: 95-95-95 by 2020; “left behind” counterfactual scenarios: 80-80-90 overall by 2020, with reduced cascade (60-40-80) among FSW, clients of FSW, both, or neither; ribbon and curve: range and median of model fits.

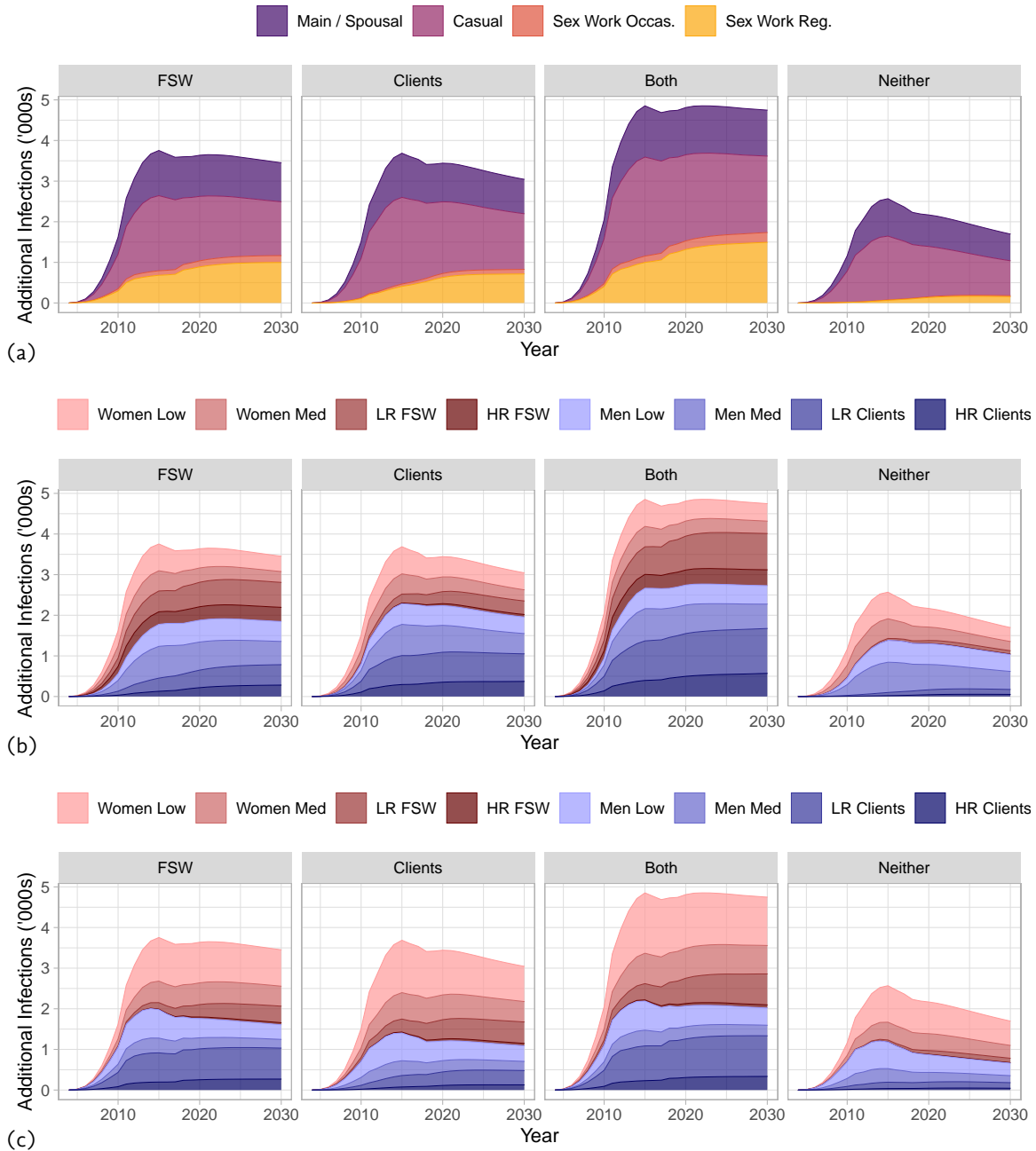


Figure A.2: Additional infections in each “who is left behind” counterfactual scenario vs. the base case, stratified by: (a) partnership type, (b) transmitting group, and (c) acquiring group

Base case: 95-95-95 by 2020; “left behind” counterfactual scenarios: 80-80-90 overall by 2020, with reduced cascade (60-40-80) among FSW, clients of FSW, both, or neither; median numbers of infections across all model fits shown.

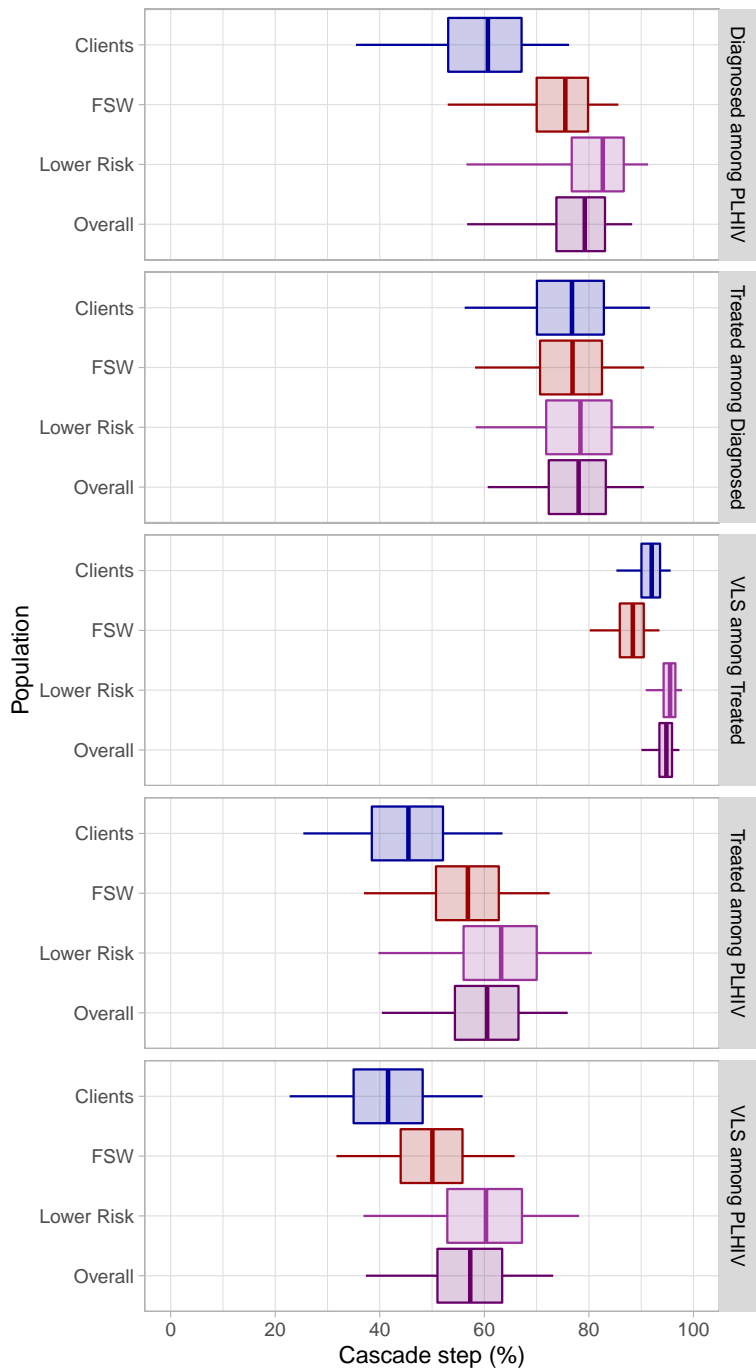


Figure A.3: Cascade attainment by 2020 across samples

Lower Risk: all women and men not involved in sex work; FSW: female sex workers; Clients: of FSW; whiskers, boxes, and midlines: 95% CI, 50% CI, median of model fits.