Health economic modeling to optimize the HIV care continuum: methods and applications

by

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Abstract

Despite over $20B of annual federal funding directed towards domestic HIV efforts, 38,000 new cases were diagnosed in 2017 in the US. The recently announced “Ending the HIV Epidemic: A Plan for America” initiative set ambitious goals to reduce new HIV infections by 90% within 10 years. Achieving these ambitious goals necessitates a resource-intensive response consisting of targeted, context-specific combination implementation strategies. Economic models play a critical role in informing resource allocations for the care and prevention of HIV/AIDS, providing a unified framework to quantify the health and economic value of different strategies. A diversity of modelling designs and approaches exist, each requiring different forms of data. Input data are rarely known with certainty. This in turn might propagate into result uncertainty and lead to suboptimal decisions. However, presently there is a paucity of standardized guidelines on model structural design, evidence selection and methods to address decision uncertainty. The objective of this thesis is to provide methodological advances in decision-analytic modeling in HIV/AIDS, with a focus on model design, the quality of supporting evidence, calibration, validation and analysis of uncertainty.

The design of a model and input data are two central factors in ensuring credible inferences. We executed a narrative review of a set of dynamic HIV transmission models to comprehensively synthesize and compare the structural design and the quality of evidence used to support each model parameter (Study 1). Model complexity and uncertainty surrounding its inputs can diminish our confidence in a model. We provided a comprehensive description of the calibration and validation of a dynamic HIV transmission model for six US cities with diverse microepidemics, detailing key methodological innovations and efforts to increase rigorousness in the process. The resulting projections will provide a basis for assessing the incremental value of further investments in HIV combination implementation strategies (Study 2). Value of information analysis quantifies the value of collecting more information to reduce decision uncertainty and helps guide efforts for future data collection. Using the developed HIV model, we performed probabilistic sensitivity analysis on the highest-valued combination strategies and applied metamodels to estimate the value of collecting additional information to eliminate decision uncertainty (Study 3).

Findings of this study will make substantial methodological and public health contributions, providing implications for health decision-makers and scientists alike. This methodological approach can serve as a means of optimizing HIV strategies and be applied to diverse settings across North America and internationally.

Keywords: HIV/AIDS; dynamic compartmental transmission model; model calibration and validation; cost-effectiveness analysis; narrative review; value of information analysis

Dedication

This thesis is dedicated to my beloved wife Lijiao who inspired me to pursue PhD.

To my mom Ping who gave me life, love and support.

To my supervisor Bohdan, for without his continuous guidance, support and enthusiasm, none of this would be possible.

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List of Acronyms

ABM	agent-based model
ANN	artificial neural network
ATL	Atlanta
ART	antiretroviral therapy
BAL	Baltimore
BWM	Best-worst method
CBA	cost benefit analysis
CCA	cost consequence analysis
CDC	Centers for Disease Control and Prevention
CEA	cost effectiveness analysis
CMA	cost minimization analysis
CUA	cost utility analysis
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
DALY	disability-adjusted life year
DCM	deterministic compartmental models
EVSI	expected value of sample information
EVPI	expected value of perfect information
EVPPI	expected value of partial perfect information
FSW	female sex workers
GAM	generalized additive model
GoF	goodness-of-fit
HET	heterosexual
IBMM	individual-based microsimulation
ICER	incremental cost-effectiveness ratio
INMB	incremental net monetary benefit
LA	Los Angeles
MIA	Miami
MSM	men who have sex with men
NMB	net monetary benefit
NHBS	National HIV Behavioral Surveillance
NYC	New York City
PLHIV	people living with HIV

PrEP	pre-exposure antiretroviral prophylaxis
PSA	probabilistic sensitivity analysis
pVL	plasma viral load
PWID	people who inject drugs
QALY	quality-adjusted life year
RCT	randomized controlled trial
SAC	Scientific Advisory Committee
SEA	Seattle
SSP	syringe services program
US	United States
USD	United States Dollar
VoI	value of information

Preface

This thesis is formatted using the integrated thesis format (i.e. 'sandwich thesis') that consists of three individual manuscripts, already published or under review by peer-reviewed journals. Chapter 2 has been published in *Pharmacoeconomics*, Chapter 3 is published in *Medical Decision Making*, while Chapter 4 has been submitted to *Value in Health*. As the first author, I was responsible for the study design, data analysis and manuscript preparation in all the three manuscripts. The references and some tables/figures from the original manuscripts have been reformatted to fit this thesis.

Chapters – Manuscript status at time of thesis completion

Chapter 2: Zang X, Krebs E, Wang L, Marshall BD, Granich R, Schackman BR, Montaner JS, Nosyk B, Localized HIV modeling study group. Structural Design and Data Requirements for Simulation Modelling in HIV/AIDS: A Narrative Review. PharmacoEconomics. 2019 37(10):1219-1239.

Chapter 3: Zang X, Krebs E, Min JE, Pandya A, Marshall BD, Schackman BR, Behrends CN, Feaster DJ, Nosyk B. Development and calibration of a dynamic HIV transmission model for 6 US cities. Medical Decision Making. 2020;40(1):3-16.

Chapter 4: Zang X, Jalal H, Krebs E, Pandya A, et al, Prioritizing additional data collection to reduce decision uncertainty in the HIV/AIDS response in 6 US cities: a value of information analysis. 2nd review, Value in Health.

Chapter 1.

Introduction

1.1. Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome

1.1.1. Epidemiology of HIV/AIDS

HIV/AIDS has remained one of the world's major public health issues since the first documented HIV case in 1981. Globally, an estimated 37.9 million (32.7-44.0 million) people were living with HIV in 2018. Among people living with HIV (PLHIV), 19.6 million were residing in East and Southern Africa. In the same year, only 23.3 million (20.5-24.3 million) were accessing antiretroviral therapy (ART) while 770,000 (570,000-1,100,000) died from AIDS-related illness. The number of individuals becoming newly infected in 2018 was estimated to be 1.7 million (1.4-2.3 million), a 40% decline since the peak in 1997 (2.9 million, 2.3-3.8 million)[1]. HIV disproportionately affects key populations at higher risk of contracting HIV, including men who have sex with men (MSM), people who inject drugs (PWID) and sex workers. Canada and the United States (US) feature concentrated HIV epidemics where more than half of the new HIV infections occur in MSM. In Canada, more than 63,000 individuals were estimated to be living with HIV in 2016, with a total of 2,400 new HIV diagnoses reported in 2017. Among Canadian provinces, the rate of reported HIV cases is highest in Saskatchewan, particularly among indigenous people and people from HIV-endemic countries[2].

In the United States (US), approximately 1.1 million people are living with HIV, with over 38,000 people newly infected with HIV each year. HIV has a disproportionate impact across populations and regions, with the Southern states accounting for 50% of new HIV diagnoses in 2017 and male-to-male sexual contact accounting for 68% of all new cases in 2015 (despite gay and bisexual men comprising only about 2% of the US population)[3,4]. Furthermore, the rate of new HIV diagnoses for blacks and Latinos was about 8 times and 3 times that of whites[3]. The US HIV epidemic is a diverse set of

microepidemics dispersed primarily across large urban centres, each with distinct underlying epidemiological and socio-structural features[5].

1.1.2. Treatment and prevention of HIV/AIDS

The decline of new HIV infections from the peak in the 1990s is attributable to many effective prevention and treatment interventions implemented to combat HIV, including behavioural change programs, medical male circumcision, promotion of condom use, HIV testing, blood supply safety, and harm reduction efforts (e.g. syringe service programs, substitution therapies and supervised injection facilities) for PWID[6]. Timely engagement of PLHIV in ART has also been shown to improve individual health outcomes while significantly reducing the risk of transmission (also known as "treatment as prevention")[7]. Pre-exposure antiretroviral prophylaxis (PrEP) is another highly effective HIV prevention strategy that has been recommended for individuals at high risk for HIV infection[8].

National and international governing bodies have mobilized efforts to optimize engagement and retention of PLHIV along the cascade of HIV care, most notably in UNAIDS' targets of 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have achieved viral suppression[9]. However, global data has shown that in 2018, only 79% [67-92%] of PLHIV were aware of their HIV status, 78% [69-82%] were accessing treatment among people who knew their status and 86% [72-92%] of people accessing treatment were virally suppressed. At present, the global public health response has moved toward combination implementation strategies - the application of multiple evidence-based HIV strategies to maximize population-level effects - to combat HIV/AIDS[10-13].

1.1.3. Public health response to HIV/AIDS

Since the discovery of the secondary preventative benefits of ART and introduction of PrEP, the world has witnessed a substantial scale up of investment in the global fight against HIV/AIDS. An estimated US$19.0 billion was invested to combat HIV/AIDS in low- and middle-income countries in 2018, an increase from US$13.7 billion in 2008. However, such enormous spending on HIV/AIDS is still insufficient for the 38 million people living

with HIV, with an estimated financial shortfall of $7.2 billion in 2020[1]. In the US, this investment has grown to $28 billion of federal funding directed towards domestic HIV efforts in 2019[14]. The implementation and expansion of a variety of HIV prevention initiatives, despite being effective, is constrained by the scarcity of resources – both human and financial. Decisions on health resource allocation have thus become the crux of this battle. The main focus of this thesis is to solve complex resource allocation decisions in the context of the US HIV epidemic.

To address its stalled progress in epidemic control, on February 5, 2019 at the State of the Union Address, the US administration announced the intention to end the HIV epidemic in the US by reducing new infections by 75% within 5 years and by 90% within 10 years[15]. To fulfill the goals set by this initiative, key strategies have been identified: 1. **Diagnose** all individuals with HIV as early as possible; 2. **Treat** people with HIV rapidly and effectively to reach sustained viral suppression; 3. **Prevent** new HIV transmissions by using proven interventions, including PrEP and syringe services programs; 4. **Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them[15]. Meanwhile, on June 11, 2019, the US Preventive Services Task Force published new guidelines for HIV screening and PrEP, in which they provided a grade A recommendation for routine, voluntary HIV screening in persons aged 15-65, all individuals at high risk of infection and all pregnant women[16]. They also provided a grade A recommendation for offering PrEP with effective antiretroviral therapy to persons at high risk of HIV acquisition[17].

US HIV epidemic is concentrated primarily in the southern states and other "hotspot" counties[18-20], typically in large urban centers, with fundamental differences in health system infrastructure, funding and HIV-related laws and policies[5]. Our previous study comparing the microepidemics in six US cities identified wide disparities in the prevalence of HIV by race and risk group, and vast differences in access to HIV treatment and prevention services in each city[5]. Achieving the ambitious goals of ending the HIV epidemic thus necessitates targeted, localized strategies to optimize the limited resources available for HIV/AIDS response in each locale.

1.2. Health economic evaluation

Funding allocation decisions in healthcare provision are made in the face of resource scarcity. Health economic evaluation therefore aims to identify decisions representing the best value for money, as every unit of investment spent on one strategy comes at the opportunity cost of the potential benefits gained from funding another. Unlike clinical trials that focus on efficacy or effectiveness of health care interventions, health economic evaluation is a comparative analysis of alternative courses of action in terms of both their costs and health consequences[21]. Health economic evaluation seeks to improve the efficiency of scarce health resources, and can inform decisions about the allocation of resources to implementation strategies that maximize the public health benefits.

Table 1.1 presents a summary of the five most commonly used types of health economic evaluation[21-23].

Table 1.1. Types of health economic evaluation

Types of Analysis	*Costs*	*Consequences*	*Result*
Cost Minimization (CMA)	Dollars	Identical in all aspects	Least cost alternative
Cost Consequence (CCA)	Dollars	Multi-dimensional listing of Outcomes	Costs and consequences listed but no decision rule prescribed
Cost Effectiveness (CEA)	Dollars	Different magnitude of a single effect of interest, common to all alternatives, e.g. life years gained	Cost per unit of consequence, e.g. cost per life year gained
Cost Utility (CUA)	Dollars	Single or multiple effects valued as “utility” e.g. quality-adjusted life year (QALY)	Cost per unit of consequence, e.g. cost per QALY
Cost Benefit (CBA)	Dollars	As for CUA but valued in monetary unit	Net monetary benefit; benefit-cost ratio

Among them, cost-effectiveness analysis (CEA) and cost utility analysis (CUA) are the two most common study designs in the literature. Often, these two terms are used interchangeably; however, they differ in how they treat health consequences, where a utility-based outcome is used for CUA, which is a measure of strength of preference that people have for particular health states[22]. CEA is theoretically grounded in welfare economics[24]. The focus on the incremental cost per utility gained of a new policy, treatment modality or intervention, is considered an ‘extrawelfarist’ approach[25], which identifies health outcomes as the primary focus in maximizing social welfare subject to

funding constraints that occur as governments allocate resources among competing priorities.

The most commonly used metric for utility in economic evaluation is quality-adjusted life years (QALY). The QALY is a measure that defines health in terms of time spent in health states, thus capturing improvements in both morbidity and mortality[26]. The theory underlying the construct of QALY is that individuals move through health states over time and that each health state has a value attached to it ranging usually from zero (i.e., dead) to one (i.e., perfect health). Health, which is the objective decision makers are seeking to maximize, is defined as the value-weighted time—life-years weighted by their quality—accumulated over the relevant time horizon, i.e. QALY. Assessments of value from utility-based cost-effectiveness analyses are easily interpretable, allowing for direct comparison across diseases[27,28], and are consistent with the theoretical basis of health economic evaluation. This practice is deemed preferable by panels in the US, Britain, and the World Health Organization[29]. Our previous study assessed the relative value of different HIV combination interventions in British Columbia, comparing the optimal combination strategies identified using new infections averted versus QALY gained as the health outcomes. Our findings suggested that focusing on averting new HIV infections can lead to sub-optimal decisions as a result of ignoring the health benefits accumulated among the HIV infected population, in particular, undervaluing the full benefits of ART in mitigating disease progression and mortality among this population[29].

In CEA and CUA, the decision criteria are generally expressed as the incremental cost-effectiveness ratio (ICER), which measures the difference in costs, divided by the difference in health effects between the evaluated intervention and the comparison strategy (e.g. status quo). This estimated ICER is then compared to a cost-effectiveness threshold (λ) set by the decision maker: an intervention is cost-effective if its ICER is less than this threshold (i.e. ICER < λ). The cost-effectiveness threshold represents the opportunity cost of health benefits forgone elsewhere from the investment in the new intervention in a healthcare system under resource scarcity[30]. More specifically, the ICER is calculated by:

$$ICER = \frac{Cost_i - Cost_j}{Effect_i - Effect_j}$$

An alternative measure for cost-effectiveness is the incremental net monetary benefit (INMB), which is estimated by the multiplication of incremental effect with the willingness-to-pay threshold less the incremental cost[31]. More specifically, the INMB is calculated by:

$$INMB = \left(Effect_i - Effect_j\right) * \lambda - (Cost_i - Cost_j)$$

Health economic evaluation is usually conducted either alongside clinical trials or using decision-analytical modeling[32]. Under the former framework, all costs and health outcomes relevant to the research question are collected directly alongside a trial and are averaged across all subjects among the different trial arms. The averaged total costs and health outcomes are then compared to estimate the cost-effectiveness of different strategies. Other relevant data such as individuals' preferences can also be collected simultaneously to estimate utility weights for each health state. Health economic evaluation alongside clinical trials provides reliable and less biased estimates for evidence at low marginal cost, as well as individual-level data for more granular studies. However, this form of economic evaluation also has some limitations, including a limited time horizon, comparators, and generalizability to other settings, and more importantly, clinical trials are not always feasible[32,33]. As a result, decision-analytic modeling is increasingly used for health economic evaluation.

1.3. Decision-analytic modeling

Decision-analytical modeling has been widely used in business, natural sciences and health sciences. These models are simplifications of reality to capture the 'essence' of the problem with the minimum level of complexity, synthesizing evidence from multiple sources and extrapolating outcomes that are unavailable, unobservable or unethical to collect. It is a systematic approach to decision making under uncertainty, using mathematical relationships to define a series of possible consequences that would flow from a set of alternative options being evaluated[34]. Therefore, they can provide a critical and unified framework to quantify the clinical and economic impacts of multiple health interventions across disparate settings, accounting for the synergistic effects between different combinations of interventions[35]. Model estimates can provide objective evidence for decision-makers to prioritize expenditures and allocate resources. This is particularly

important for HIV/AIDS, an infectious disease in which interventions implemented today can have far-reaching effects on the epidemic in the future. Generally, with high-quality data, appropriate modeling techniques can clarify, within a causal framework, the relationship between program inputs and effects.

It is important to note, however, that previous studies using disparate model structures have occasionally reached discordant results and conclusions about the same question[20,21], underlining the importance of model design. Models are based on assumptions, and if the required data are sparse or limited, structural designs will be constrained and this uncertainty in inputs will be reflected in the results. Therefore, caution needs to be taken when selecting the appropriate model design and input evidence.

1.3.1. Types of models

A variety of modelling approaches have been developed in decision analysis[36].

Decision Trees are the simplest form of decision-analytic models where alternative options are represented by a series of pathways or branches[32]. An illustrated decision tree includes three types of nodes: decision nodes, chance nodes and terminal nodes. A branch of chance nodes illustrates the probability of a particular pathway occurring and the terminal node represents the average outcome of an event. In health economic evaluation, expected values for the cost and benefits of a particular course of action are derived by summing up the pathway values weighted by pathway probabilities. Although decision trees are valued for their simplicity and transparency, their use is largely limited by their incapability to model time variables and recurring or looping events.

Markov models consist of a set of mutually exclusive health states, each accommodating a proportion of the study population for a chosen time interval. Transitions between these health states are guided by a set of defined transition probabilities[32]. Markov models permit a more straightforward and flexible sequencing of outcomes, including recurring outcomes over a period of time. However, the complexity of Markov models grows exponentially with an increase in the number of health states and they are also sometimes criticized for their memoryless feature (Markovian assumption).

Dynamic compartmental models can be considered as a special case of Markov models applied in infectious disease applications that assume the probability for

susceptible study population to become infected is a function of the size of the infected population, which can change over time[37]. They divide the study population into various compartments according to each individual's characteristics and disease status, representing their average state, and use differential equations to track the rate of transition of individuals between these compartments[38]. Individuals within a single compartment are considered homogeneous. The dynamic transmission probabilities are often determined by a force of infection function, capturing the key drivers of the probability of infection.

Individual-based microsimulation models simulate the study population at the individual level, whereby individuals' transitions are generated using a random process drawn from probability distributions, a process referred to as Monte Carlo simulation[39]. This modelling approach may capture a greater breadth of heterogeneity among subjects and has the capacity to incorporate individual history, allowing greater structural complexity, although it may require more extensive data to populate such models and incur a higher computational burden, particularly when probabilistic sensitivity analysis is also undertaken[40].

Agent-based models are also individual-based, and simulate the behaviours and interactions of autonomous "agents"[41], differing from individual-based microsimulations by allowing interactions between agents. They permit the formation of interactive dynamic networks, and the analysis of the network effects that are difficult to capture in other models. Agents can possess great flexibility and have autonomy in communicating and interacting with each other and the environment governed by specified internal rules. This method may better capture heterogeneity among subjects, though it requires more extensive data to realize its potential benefits and may be constrained from modeling large populations due to computational challenges.

1.3.2. Decision-analytic modeling in HIV

Decision-analytic modeling has been widely used in evaluating a broad spectrum of HIV interventions and programs. The transmission mechanism of HIV involves both biological and social determinants that is important to account for during model development: biological determinants may include characteristics of the pathogen, the host, and biomedical interventions. Further, social determinants may include individual-

level, pairwise processes that affect behaviour and thus the structure and dynamics of the transmission networks[42]. The transmissible nature of HIV requires a dynamic design in modeling such that 'the probability of a susceptible individual becoming infected at any one point in time (the force of infection) is related to the number of infectious individuals in the population, will change over time, and will feed back into the future force of infection'[38]. This is a key feature of HIV modeling that differentiates it from non-communicable disease models.

One of the most prominent examples of HIV modeling was demonstrated in a recent article in the Lancet by Andersen et al[43]. Using a wealth of data on the spatiotemporal course of the HIV epidemic in Kenya to operationalize a dynamic, compartmental model, the authors demonstrated that, with exactly the same investment, a focused strategy for HIV prevention, in which interventions are tailored to specific jurisdictions with disparate HIV epidemics, can be substantially more effective than a strategy in which interventions are rolled out uniformly across the country. Another notable example is the Cost Effectiveness of Preventing AIDS Complications (CEPAC) Model[44-46], a state-transition, Monte Carlo microsimulation model, that has been used in myriad applications evaluating HIV treatment and prevention programs in the US and internationally, as well as in other infectious disease areas such as Tuberculosis. Birger et al. constructed a model of HIV infection including specific care-continuum steps, calibrating to the HIV epidemic in Newark, New Jersey over a 10-year period,[47] whereby a set of four interventions to improve the cascade were tested and compared according solely to their epidemiological impacts. Lasry et al. described a national HIV resource allocation model, designed to inform the Division of HIV/AIDS Prevention at the US CDC on allocation strategies that might improve the effectiveness of HIV prevention efforts[48]. Several other noteworthy modeling and cost-effectiveness studies have provided insights about interventions targeted at specific steps in the HIV care cascade, including screening and ART initiation in Washington DC[49], behavioral interventions for HIV-infected people who inject drugs in addition to opioid agonist therapy (OAT)[50], and home-based testing and linkage to care in South Africa[51]. Furthermore, Marshall et al. developed a stochastic agent-based model to simulate HIV transmission in dynamic networks of MSM in Atlanta[52] and PWID in New York City[53] to examine the effectiveness of long-acting injectable PrEP and combination prevention strategies among the targeted population. Jenness et al.[54,55], focusing on MSM populations, scrutinized key factors relevant to HIV transmission

dynamics using a network-based mathematical model. We also noted several HIV modeling comparison studies by Eaton et al.[56-58], directly comparing projections of different HIV models on a common question. Results were then used to consolidate evidence for the effect of HIV interventions and examine the differences in projection as a result of the underlying evidence used and several structural attributes, such as the construction of transmission behaviours and functions. Their work highlighted the importance of the structural assumptions of HIV simulation models and the quality of supporting evidence inputted into them.

1.4. Handling uncertainty in economic modeling

Health economic models are comprised of complex mathematical relationships and various input data from different evidence sources whose results are inevitably subject to uncertainty. Four types of uncertainty were identified for economic modeling, including stochastic uncertainty (random variability in outcomes between identical simulated individuals), parameter uncertainty (the uncertainty in estimation of the parameter of interest), heterogeneity (the variability between simulated individuals that can be attributed to their characteristics) and structural uncertainty (the assumptions inherent in the decision model)[39]. The value of a model-based analysis lies, not only in generating a precise point estimates for a specific decision, but systematically examining and reporting the uncertainty surrounding the outcome(s) of interest. Handling uncertainty in economic modeling can help assess the robustness of model results in face of uncertainty and enhance our confidence in a chosen course of action. We can also estimate the value of collecting additional information to reduce decision uncertainty[39].

1.4.1. Model calibration

Model calibration refers to the process of matching model outcomes with observed outcomes by adjusting uncertain model parameters and establishing plausible ranges that provide the best fit to available data[59,60]. This process is composed of several stages that each require decisions on the potential methods to be used. No best practice guidelines exist to guide the specific choices at each stage[61], making model calibration a complex task that is often not standardized and may involve subjectivity[62,63]. Vanni et al.[61] provided guidance on the process of model calibration with a seven-step approach: (1) choosing

parameters to include in the calibration; (2) selection of calibration targets; (3) goodness-of-fit (GoF) measures; (4) parameter search strategies/ algorithms; (5) convergence/acceptance criteria; (6) stopping rules; and (7) integrating the results of the calibration and the economic parameters. Previous modeling studies often presented subjective choices at some critical steps along the process of calibration, e.g. the selection of parameters for calibration[61,64], and determination of the summary measure of model fit when multiple targets are used[10,11,36]. This may introduce uncertainty that might poetentially affect model results. In Chapter 3, we provide a more detailed description for each of the seven steps and our justification in choosing the appropriate methods at each step. One notable trend for calibration is the increasing use of Bayesian approaches, which use Bayes' theorem to combine information about the distribution of prior model parameters, structural assumptions of the model and a likelihood function created from the calibration data[65]. The Markov Chain Monte Carlo then estimates a joint set of posterior distributions for the input parameters based on the likelihood function. However, this approach is more often used in models with relatively simple structures, as computational challenges arise in more complex structures.

1.4.2. Sensitivity analysis

It is necessary for a modeling study to include sensitivity analyses on key model parameters. Sensitivity analysis establishes the sensitivity of results to changes in the underlying parameters (parameter uncertainty) and structure (structural uncertainty) of a model. Sensitivity analysis provides information to ascertain the robustness of model results, enabling decision makers to gauge confidence in a decision, and help identify targets for future research/data collection[60]. There are several ways of undertaking sensitivity analysis (depending on the number of parameters to vary at a time), each equipped with different techniques for presenting uncertainty results.

One-way sensitivity analysis is the simplest form of sensitivity analysis that varies the values of one parameter at a time to estimate its impact on the ICER. Tornado diagrams are often used to summarize results from a one-way sensitivity analysis (an example is given in Figure 1.1, figure modified from Zang et al.[66]), in which horizontal bars represent the outcome range associated with the range of the specified parameters (in many cases, the extreme values for the outcome at the upper and lower bound of the uncertainty range for a given parameter) while the vertical axis represents the parameters

to be analyzed. The outcome point estimate corresponding to the base-case values is indicated by a vertical line in the middle as the origin for each horizontal bar. Threshold analysis is another form of one-way sensitivity analysis by estimating the value at which a decision would change. Limitations with one-way sensitivity analysis include implicit assumption of parameter independence and inability to account for the joint effect of multiple parameters.

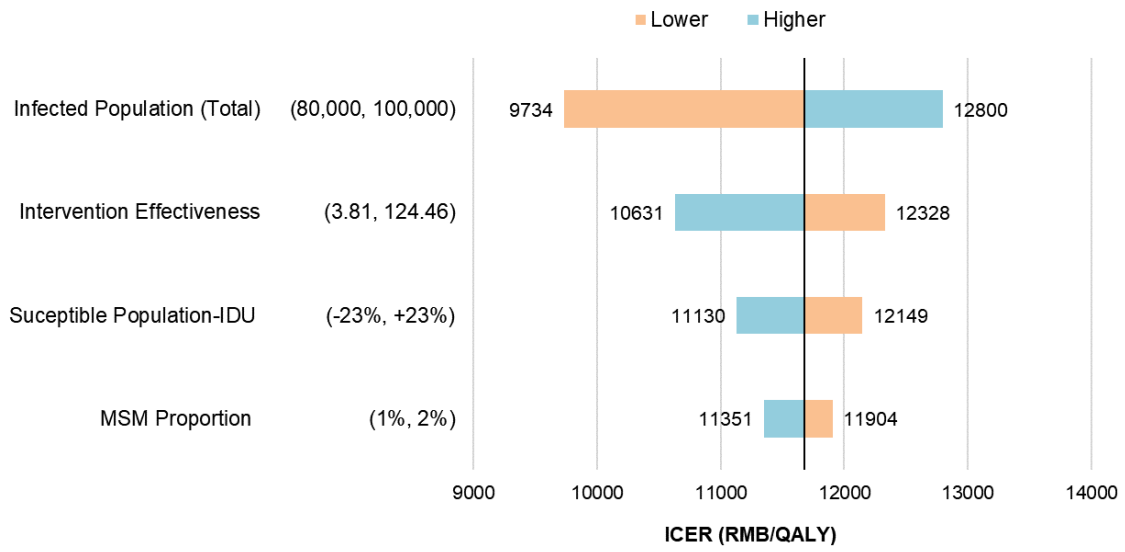


Figure 1.1. Example of a tornado diagram for one-way sensitivity analysis

Multi-way sensitivity analysis is an extension of one-way sensitivity analysis by changing the values of two or more parameters at the same time to estimate their combined effect on results. However, result presentation becomes more sophisticated as the number of parameters involved increases. In performing multi-way sensitivity analysis, sometimes parameter correlations have to be explicitly considered, requiring a joint distribution to be fit where multiple parameters are drawn from. One specific form of multi-way sensitivity analysis is scenario analysis where extreme cases ('best/worst' or 'optimist/pessimistic') are constructed for the selected parameters and simulations will be performed on these sets of extreme values and compared with the base case. Figure 1.2 (figure modified from Krebs et al.[67]) shows an example of a two-way sensitivity analysis on the incremental QALYs, costs and infections averted by varying both the intervention sustainment period and scale of delivery for an ART initiation intervention.

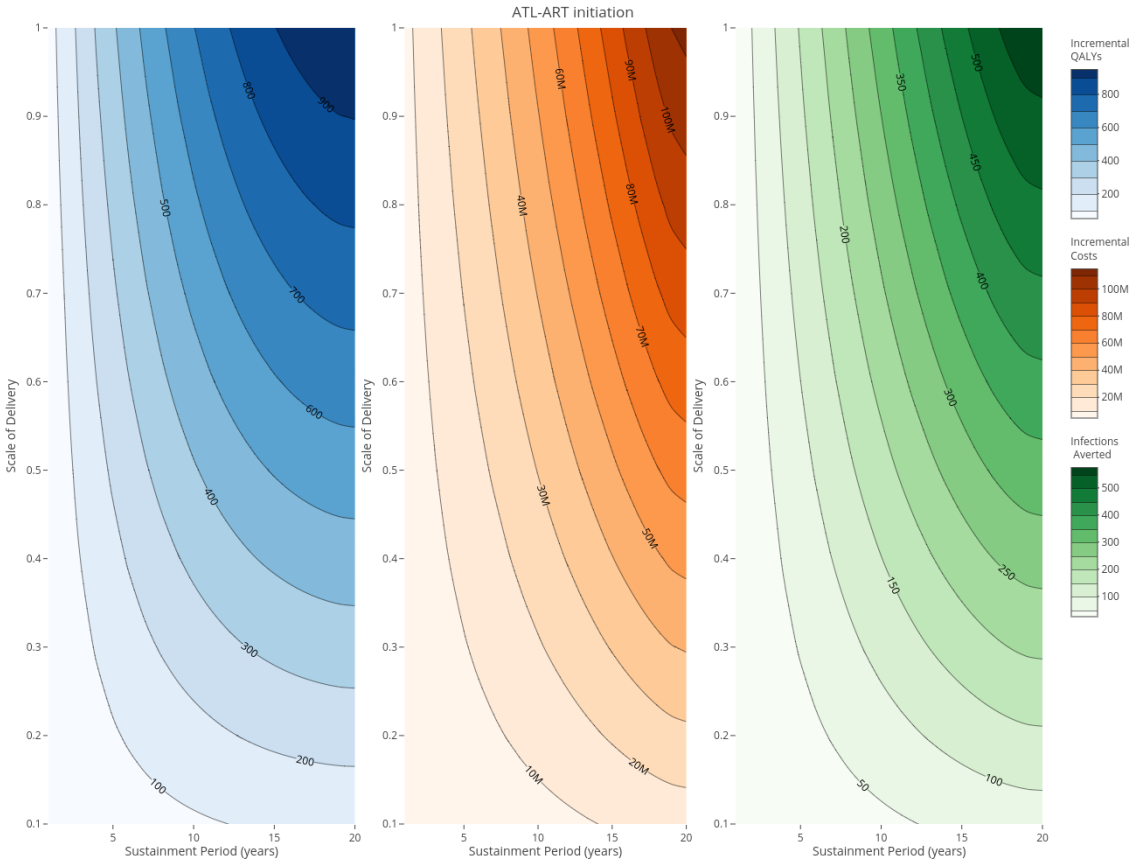


Figure 1.2. Example figure for two-way sensitivity analysis

Probabilistic sensitivity analysis (PSA) involves specifying probability distributions for all input parameters in the model and employing Monte Carlo simulation to randomly sample from these distributions simultaneously, allowing the joint effect of parameter uncertainty to be assessed. This sensitivity analysis method can provide a more complete assessment of the uncertainty associated with all inputs in a model. Cautions need to be taken when performing PSA. For example, the distributions chosen should follow standard statistical methods, e.g. beta distributions for binomial data, gamma or log-normal distributions for positive right-skewed parameters and log-normal distributions for relative risks or hazard ratios. Furthermore, the correlation between parameters should be incorporated if dependencies exist for some parameters. Goldhaber-Fiebert et al. developed a practical method to establish joint uncertainty distributions for potentially correlated parameters from their marginal distributions and the rank ordering within these parameters[68]. The outputs from a PSA may provide several different types of outputs: (1) credible intervals surrounding ICER estimates; (2) cost-effectiveness planes (showing the scatter plots for the distribution of cost and effect of the evaluated intervention in the

analyzed samples), as exemplified in Figure 1.3 (figure modified from Nosyk et al.)[69]; (3) cost-effectiveness acceptability curves (showing the probability of being cost-effective for alternative strategies under different cost-effectiveness thresholds), as exemplified in Figure 1.4 (figure created for illustration purpose only); and (4) value of information analysis, as elaborated upon in Section 1.4.4.

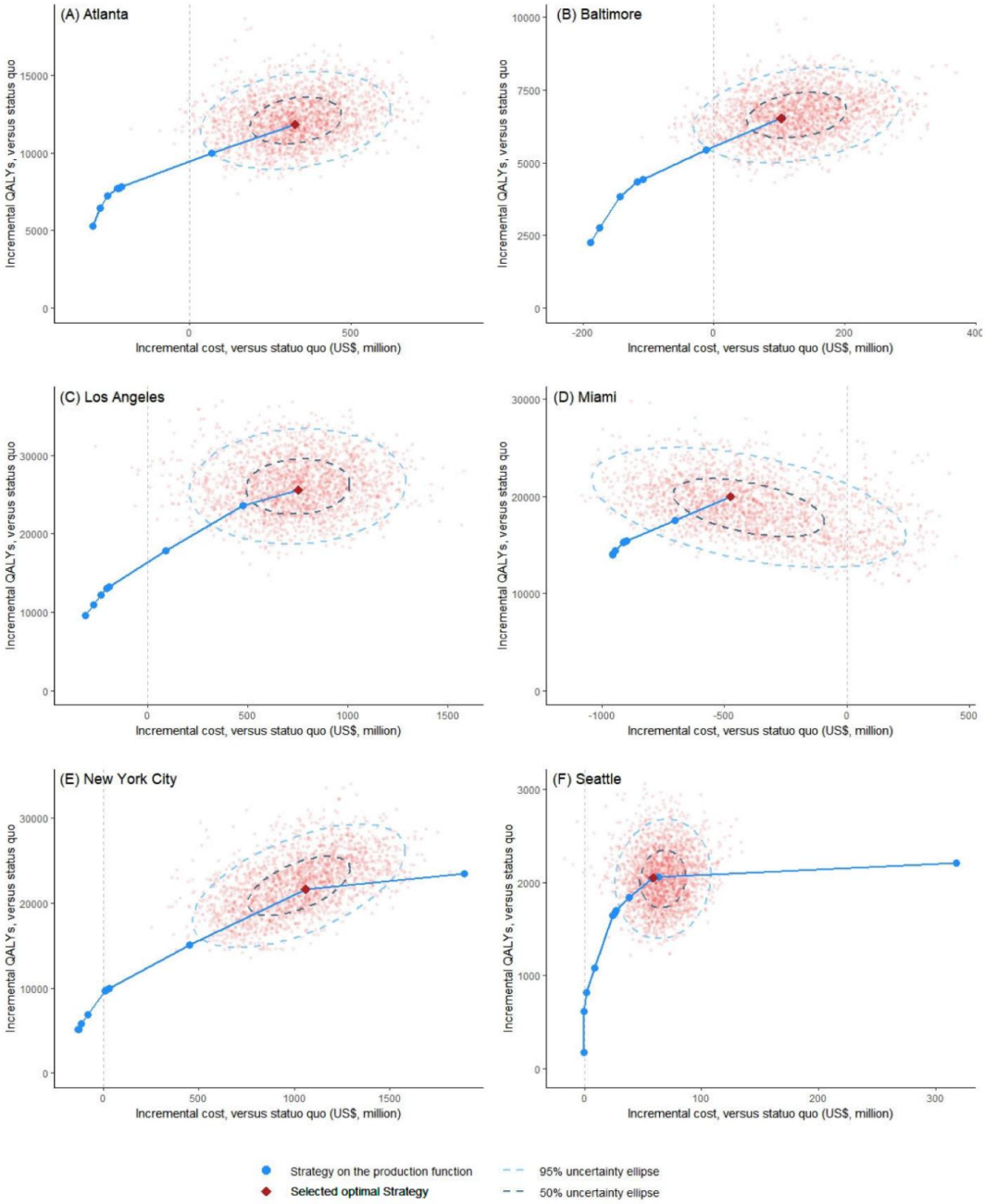


Figure 1.3. Example figure for a cost-effectiveness plane

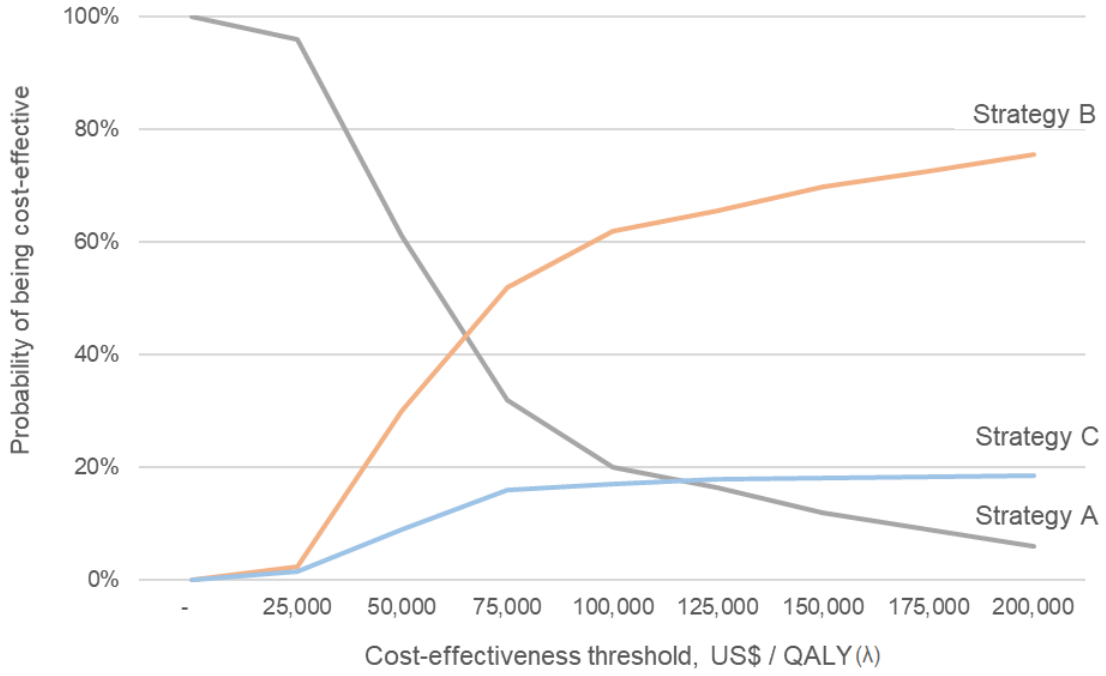


Figure 1.4. Example figure for a cost-effectiveness acceptability curve

1.4.3. Value of information analysis

Value of information (VoI) analysis is another type of uncertainty analysis that quantifies the opportunity cost of making suboptimal decisions due to parameter uncertainty and helps guide efforts to ensure the limited resources available for data collection or future research are focused on the most influential parameters for decision-making[70]. VoI analysis requires PSA outputs generated from Monte Carlo simulation. Decisions in this analysis are made by choosing the strategy with the highest net monetary benefit (NMB), as estimated by:

$$NMB = QALY \times threshold - Cost$$

The expected value of perfect information (**EVPI**) can be interpreted as the cost of decision uncertainty, as measured by the difference between the expected NMB given perfect information and the expected NMB with the current information, placing a upper

bound on the returns to further research[71]. EVPI represents the maximum a decision maker should be willing to pay to eliminate uncertainty from all model parameters. For a decision made between t alternative interventions, with unknown input parameter set θ, Monte Carlo simulation takes K samples from the joint distribution of θ (and K sets of net benefits for each intervention), while the EVPI is calculated by:

$$EVPI = E_\theta \left[\max_t NMB_t(\theta)\right] - \max_t E_\theta[NMB_t(\theta)]$$

Given the existing evidence, the optimal decision is the intervention that generates the maximum expected net-benefit (across the K samples): $\max_t E_\theta[NMB_t(\theta)]$. With perfect information, the optimal decision is the intervention that maximizes the NMB given a particular value of θ: $\max_t NMB_t(\theta)$. However, the true value of θ is unknown and thus the expected value of a decision taken with perfect information is found by averaging the maximum net monetary benefit over the K samples: $E_\theta \left[\max_t NMB_t(\theta)\right]$.

The expected value of partial perfect information (**EVPPI**) provides an estimate of the value of eliminating uncertainty for a specific parameter or group of parameters and is calculated by the difference between the expected NMB with perfect information about the parameters of interest and the expected value with current information[71]. EVPPI reflects the maximum value of additional information on the value of the given (group of) parameter(s) and may help decide whether certain research to find better information on the parameters is worth the cost[72]. EVPPI can help prioritize future research on the subsets of parameters with the highest decision value. Specifically, for a decision made between t alternative interventions, with unknown input parameter set θ that is composed of ϕ (uncertain parameters of our interest) and ψ (other uncertain parameters), a nested Monte Carlo simulation is performed:

- Inner loop: one set of value for ϕ is randomly sampled from pre-defined distribution and held fixed, run PSA on all other uncertain parameters ψ
- Outer loop: after completion, another set of value for ϕ is randomly sampled and held fixed, run PSA on all other uncertain parameters ψ. Repeat this procedure until we have sampled sufficiently from the (joint) distribution of ϕ

The EVPPI is then calculated by:

$$EVPPI(\phi) = E_{\phi}\left[\max_{t} E_{\theta|\phi}[NMB_t(\theta)]\right] - \max_{t} E_{\theta}[NMB_t(\theta)]$$

Given the existing evidence, the optimal decision is the intervention that generates the maximum expected NMB: $\max_{t} E_{\theta}[NMB_t(\theta)]$. With perfect information about ϕ, the optimal decision is the intervention with the maximum expected NMB where the expected NMBs are averaged over the other uncertain parameters ψ: $\max_{t} E_{\theta|\phi}[NMB_t(\theta)]$. The expected value of a decision taken with perfect information for ϕ is found by averaging the maximum expected NMBs over the distribution of ϕ: $E_{\phi}\left[\max_{t} E_{\theta|\phi}[NMB_t(\theta)]\right]$.

The expected value of sample information (**EVSI**) is a measure for the expected value of sample information (imperfect information) from an additional study of a known sample size, which can be used to inform research design. The estimation for EVSI is very similar to EVPPI that also requires a nested Monte Carlo simulation. Assuming X are new potential data from the proposed study for ϕ, EVSI is calculated as the difference between the expected maximum benefit given new potential data X and the maximum benefit with current information:

$$EVSI(\phi) = E_{\phi}\left[\max_{t} E_{\theta|X}[NMB_t(\theta)]\right] - \max_{t} E_{\theta}[NMB_t(\theta)]$$

The major difference from EVPPI is that with sampled information X for ϕ, the expected NMB for each intervention, based on which the optimal decision is made, is informed by a Bayesian update of ϕ given the conditional distribution of $\phi|X$. The uncertainty of ϕ decreases as the sample size of the proposed study increases.

Notwithstanding its importance, VoI analysis to inform research decisions has not been widely used. In addition to the lack of a straightforward interpretation of the VoI results, the major barrier lies in the computational challenges associated with the conventional approach using a nested Monte Carlo procedure, particularly in assessing EVPPI and EVSI for complex models[73]. To address this computational burden, several modern approaches have been developed, including approximation methods, which require further assumptions of the model or are applicable only to single parameters, as well as more recent metamodeling approaches[73].

Metamodels are a model of a model that simplifies and extracts the mathematical relationship between the inputs and outputs of a simulation model[74], which have been increasingly used as an alternative method to expedite the estimation of EVPPI and EVSI. Through directly regressing model outputs on inputs, the fitted metamodel can be used to approximate the input and output functions, as a replacement of the original simulation model, to expedite the VoI estimation. A previous application of the metamodeling approach has substantially shortened the computation time for EVPPI from weeks to minutes, while consistently yielding similar estimates[75]. Various regression approaches have been employed in VoI metamodeling applications to allow for more flexible functions between NMB results and uncertain parameters of interest, such as linear models[76], generalized additive models (GAM)[77] and Gaussian Processes (GP)[78]. This metamodeling approach will help establish a streamlined approach to prioritize future research and data collection efforts based on economic value. However, applications of this method for VoI have rarely been implemented in dynamic transmission models[79], and there is a lack of studies on how this approach can be applied in evaluations involving many competing strategies and parameters with a high level of dimensionality.

1.5. Model validation

Model validation refers to the process of evaluating a model's accuracy in making relevant projections[80]. It entails a comprehensive evaluation of how well the model performs, from the problem construct to the credibility of model results, against a variety of internal and external inputs, including expert opinions, clinical knowledge, and empirical evidence. Four main types of validation are commonly recommended in modeling exercises[81-84]:

Face validation refers to the subjective review of the model evidence, structure, problem formation or results by individuals with clinical and epidemiologic expertise in a given disease area. Evaluation is performed regarding the following questions: whether best available evidence is used; whether key aspects of reality in relating to medical science are explicitly modelled; whether model settings, population, interventions, outcomes, assumptions, etc. correspond to the question of interest; and whether model results match experts' expectations. Face validation ensures the appropriateness of input

evidence, structural design and model specifications, and helps enhance the credibility of model results.

Internal validation investigates and verifies the accuracy and consistency of all mathematical equations and program coding. Commonly used techniques of internal validation may include: (1) documentation of model equations and code; (2) program "walk-throughs" with non-programmers; (3) "double coding" for key model components; (4) extreme scenario analysis or other forms of sensitivity analysis; (5) tracing plots for intermediate results. Internal validation can help avoid errors in computation and program coding.

External validation entails comparison of model projections to external estimates of key clinical and epidemiological data, preferably not used in the model. External validation is the most desired form of validation in literature and provides another tool to enhance model credibility.

Cross validation involves comparing model outputs against other independent modeling results about the same question. This validation can help increase our confidence in a finding or conclusion if similar results are derived from different models, while also providing insights into the differences in model evidence, structure, assumptions, specifications, etc. and their implications if discordant results are found. However, this validation is sometimes limited by the availability of other modeling studies with comparable results.

Despite the importance of model validation for establishing the credibility of model results, this process has not been ubiquitously implemented, or at least reported, in previous modeling studies[85]. Some common challenges may include the unavailability of validation target data and difficulties in establishing explicit criteria for assessing the validity of a model.

1.6. Thesis background

This thesis project is an integrated component of a parent grant entitled "Localized economic modeling to optimize public health strategies for HIV treatment and prevention", funded by National Institute on Drug Abuse (R01-DA041747). This grant aims to develop

a novel economic modeling framework to define an optimized set of HIV care interventions to ensure scarce resources are focused on interventions that can provide the greatest value for money in a given microepidemic. The economic model developed in this thesis has been used to provide public health decision makers at a city level with information about expected returns for incremental investments in interventions to prevent, diagnose and treat HIV/AIDS. To date, 13 related manuscripts have been published (or accepted), with an additional two manuscripts under review (one in 2nd review), and four manuscripts for submission by the end of 2019. These studies included a comprehensive evidence synthesis of available data sources on the spatiotemporal course of the HIV and drug use epidemics in each of the demonstration cities, health resource use of people living with HIV, and evidence on the costs and effectiveness of implementation of interventions in HIV treatment and prevention. Informed by the evidence synthesis and selection of best-available evidence for interventions and implementation modeling, model calibration and validation, city-level HIV microepidemics were replicated with current access to HIV treatment, care and prevention services. We further determined the cost-effectiveness of combinations of HIV treatment and prevention interventions offered at feasible levels of scale and sustainment for each city. Finally, leveraging these data, we projected long-term HIV incidence with city-specific optimal combination implementation strategies, highlighting targeted-context-specific combination implementation strategies are required to 'End the Epidemic' by 2030.

1.7. Thesis aims and objectives

The overall objective of this thesis is to provide methodological advances in decision-analytic modeling in HIV/AIDS, with a focus on model design, the quality of supporting evidence, calibration, validation and analysis of uncertainty. These advances have centered on an applied project designed to inform resource allocation decisions to reduce the economic and public health burden of HIV/AIDS in six US cities[69]. The first objective of the study was to improve model structural design and evidence quality through an in-depth comparative review of HIV transmission models focusing on these two fundamental components. The second objective was to calibrate and validate a dynamic compartmental model of HIV transmission to help solve complex combination implementation decisions within localized microepidemics in six US cities. The third objective of the study was to examine the decision uncertainty underlying the combination

implementation decisions using a value of information analysis to quantify the monetary value of collecting additional information to reduce decision uncertainty.

In this thesis, the scientific aims and general approaches to meeting the thesis aims are outlined below:

Aim 1 – Modeling review: to execute a narrative review to synthesize and compare a selection of peer-reviewed dynamic HIV transmission models used to facilitate healthcare decision making, assessing the structural design and the quality of evidence used to support each model parameter.

Aim 2 – Model calibration/validation: to adapt, calibrate and validate a dynamic compartmental model of HIV transmission for six US cities. Building on the evidence synthesis published separately, this project aims to document the process for model development, a six-step model calibration and an extensive model validation (internal, external and face validation) to maximize its transparency and credibility. The resulting model projections will serve as status quo treatment scenario in each city to identify optimal combination implementation strategies for HIV treatment and prevention.

Aim 3 – Value of information analysis: to quantify the value of gathering additional data to reduce decision uncertainty regarding the cost-effectiveness of HIV combination implementation strategies in 6 US cities. Using a metamodeling approach with advanced regression techniques, this study also aims to identify future data collection priorities through EVPPI analysis on key groups of uncertain parameters.

This thesis is composed of five chapters, addressing each of the aims in order. This first chapter provides a brief introduction to the epidemiology of HIV/AIDS, health economic evaluation, decision-analytical modeling, model calibration and validation, and handling uncertainty in economic models. Chapters two through four provide the contents of the research conducted to fulfill each of the above aims. These chapters, along with appendix A-C, are each stand-alone manuscripts, which have either been published, in press, or under review by a peer-reviewed journal. The final chapter provides a summary of the research findings, limitations of the studies, the unique contributions and implications of the findings of these studies, as well as research plans laid out for future work.

Chapter 2.

Structural Design and Data Requirements for Simulation Modelling in HIV/AIDS: A Narrative Review

Borne out of a necessity for fiscal sustainability, simulation modeling is playing an increasingly prominent role in setting priorities for combination implementation strategies for HIV treatment and prevention globally. The design of a model and the data inputted into it are central factors in ensuring credible inferences. We executed a narrative review of a set of dynamic HIV transmission models to comprehensively synthesize and compare the structural design and the quality of evidence used to support each model. We included nineteen models representing both generalized and concentrated epidemics, classified as compartmental, agent-based, individual-based microsimulation or hybrid in our review. We focused on four structural components (population construction; model entry, exit and HIV care engagement; HIV disease progression; and the force of HIV infection), and two analytical components (model calibration/validation; and health economic evaluation, including uncertainty analysis). While the models we reviewed focused on a variety of individual interventions and their combinations, their structural designs were relatively homogenous across three of the four focal components, with key structural elements influenced by model type and epidemiological context. In contrast, model entry, exit and HIV care engagement tended to differ most across models, with some health system interactions –particularly HIV testing– not modeled explicitly in many contexts. The quality of data used in the models, and the transparency with which the data were presented differed substantially across model components. Representative and high-quality data on health service delivery was most commonly not accessed or unavailable. The structure of an HIV model should ideally fit its epidemiological context and be able to capture all efficacious treatment and prevention services relevant to a robust combination implementation strategy. Developing standardized guidelines on evidence syntheses for health economic evaluation would improve transparency and help prioritize data collection to reduce decision uncertainty.

2.1. Introduction

Despite substantial investments in the global response to HIV, inadequate and plateauing funding levels[86,87] increasingly require decision makers to prioritize the allocation of resources available for HIV treatment and prevention. With a number of efficacious behavioural, biomedical and structural interventions available, a combination implementation strategy (the application of multiple treatment and prevention interventions to maximize population-level impact[88]), has been proposed to reduce the public health burden of HIV/AIDS[11,88]. Simulation models can provide a unified framework to quantify the health and economic value of different strategies to address the HIV/AIDS epidemic while accounting for the synergistic effects of different combinations of public health interventions[34,35,89]. More than ever before, simulation modeling is playing a critical role in priority setting for HIV treatment and prevention[90].

Simulation models are simplifications of reality, designed to capture the 'essence' of a problem with a minimally sufficient level of complexity[81], synthesizing evidence from multiple sources and extrapolating outcomes that may be unavailable, unobservable or unethical to collect[35]. Two key aspects of constructing a model are settling on a structure and gathering evidence to populate it[36,81]. Determining the structure of a model, including the choice of model type (e.g. compartmental model, agent-based model), how the disease process is characterized, and other underlying assumptions should be guided by the decision problem and context[91].

A key challenge in constructing simulation models is the extensive evidence synthesis required to parameterize them. The quality of the evidence used in a model will impact the degree of uncertainty of its outcomes and ultimately the credibility of its inferences. Coyle et al. demonstrated the extent of bias on model outcomes propagated by the use of different underlying data sources within the same modeling framework[92]. HIV simulation models are particularly data intensive due to the need to model both infected and susceptible populations, and the mechanism underlying the force of HIV infection[42,93]. Local epidemiological and structural factors are also critical in capturing the heterogeneity across regional microepidemics, and ultimately assessing targeted, locally-oriented strategies that are essential to allocate resources effectively and efficiently.

Previous model comparison studies or reviews have focused primarily on differences in model outcomes, aiming to examine whether consistent and robust conclusions can be reproduced across models for a given intervention, with limited discussion on structural characteristics and data quality differences as an explanation for variation in outputs[94-98]. Two recent HIV model comparison studies[56,57] have gone beyond simply comparing model predictions, by providing discussion on the differences in several structural attributes that might explain differences in long-term projections. However, as the global public health response moves towards localized combination implementation strategies to combat HIV/AIDS[10-13,99], modellers require more careful consideration of not only the appropriateness of the underlying structural assumptions, but also the quality and context-specificity of the data entering models designed to simulate regional contexts.

We executed a narrative review to synthesize and compare a selection of peer-reviewed dynamic HIV transmission models used to facilitate healthcare decision making. Although systematic reviews are often preferred in generating quantitative answers to specific, often narrow, clinical questions of interest (e.g., comparing modeling studies evaluating a given intervention), narrative reviews are useful for obtaining a broader perspective on a topic[100]. We comprehensively assessed the full breadth of each model's structural design and the quality of evidence used to support each model parameter. We then discuss the implications of the choice in model structure and data quality, with the goal of clarifying the implications of these choices for model developers and informing targets for data collection in the future[70].

2.2. Methods

2.2.1. Selection of relevant articles

We conducted a comprehensive comparison of recently published simulation models to highlight variation in the structural design and quality of data supporting them. Models initially considered for inclusion in our narrative review resulted from a snowball literature search using reference tracking[101] using Eaton et al.[56,57] and Nosyk et al.[102] as seeds. Simulation modeling studies fulfilling the following selection criteria were included in the review: (i) the model focused on HIV/AIDS explicitly—studies characterizing HIV/AIDS as a coinfection were excluded; (ii) the model attempted to reconstruct a real-

world population and was applied in solving real-world health decision problems within a dynamic modeling context (thus excluding methodological studies or those focusing on hypothetical settings and populations), excluding those focusing on subsets of the population, e.g. modeling MSM population exclusively, to ensure the comparability of model structure and evidence requirement; (iii) the model was published in the past 10 years, to ensure the protective benefits of antiretroviral therapy (ART) against HIV transmission were captured in the reviewed models; (iv) the publication provided sufficient detail (in the manuscript or supporting appendix) to capture the majority of the information required for this review. For studies employing the same or similar model, only those with the most comprehensive description of model structure and evidence sources for model parameters were retained for review.

Information pertaining to the structural design, underlying assumptions, and data sources were extracted for each model. We stratified the selected models according to the epidemic context for which the model was developed (generalized or concentrated) and the classification of the dynamic model type (i.e., compartmental, individual-based or agent-based), (Table 2.1). Data extraction for each component was independently performed by at least two reviewers (XZ, EK, and LW) and any differences were resolved with at least one other author.

2.2.2. Assessment of model structure

We extracted information on four structural components (Appendix Fig. A1), representing an exhaustive and mutually exclusive description of the structural elements of any HIV simulation models: (1) the population construction, depicting the complexity of a model in characterizing the heterogeneity within the study population; (2) model entry, exit and HIV care engagement, comprising information about how the transitions into and out of the model or any care or treatment programs and associated adverse events were characterized within the model; (3) HIV disease progression, describing health states pertaining to those infected with HIV/AIDS, and the means by which individuals transition between these states; and (4) the force of HIV infection, describing the route(s) of transmission, any factors influencing infectivity, risk behaviours, mixing patterns and biomedical interventions influencing HIV transmission. We note that for each of the studies assessed we focused exclusively on the underlying structure of the model for the reference

case, or comparator strategy, representing the natural state of an HIV epidemic with current levels of availability of HIV treatment and prevention services[103].

2.2.3. Assessment of analytical components

We also extracted information on two analytical components necessary in adhering to best practices in health economic modeling[81]: (1) model calibration/validation, focusing on the selected calibration and validation targets and the methodological approach used in calibrating and validating the model; (2) health economic evaluation, summarizing information relevant to conducting health economic evaluations, including study perspective, cost and utility estimation, an assessment of reporting quality, and a review of uncertainty analysis, focusing on the forms of sensitivity analysis undertaken (deterministic or probabilistic), analyzed parameters and how alternate scenarios to assess the uncertainty of the results were constructed.

2.2.4. Assessment of quality of supporting evidence

Information relating to the origins of the data used to populate the model was extracted if this information was provided. While explicit guidelines for assessing the quality of evidence in simulation models have not yet been developed[104], we followed Cooper et al.[105], Zechmeister-Koss et al.[106] and Paisley et al.[107,108] in defining evidence categories and potential hierarchies of data sources for decision models. We developed a two-dimensional quality assessment framework for HIV simulation modeling (Table 2.2), with considerations given to the internal and external validity of the input evidence[109]. Model parameters pertinent to the core components were grouped in eight categories according to these previous attempts, with extensions to some domains of evidence specifically for HIV modeling (e.g. HIV risk behaviors).

First, the internal validity of each parameter in each of the eight categories was assessed and ranked differentially on three levels of quality (best, moderate or lowest) on the basis of best possible study design, given the context. Second, for parameters requiring setting-specific evidence, an assessment of the external validity of each parameter was performed by determining whether the evidence was obtained from a representative study setting. More details about the quality ranking criteria can be found in Appendix A, Table A1.

We classified data whose sources were informal or unreported as the lowest quality. In cases where multiple data sources were used for a given parameter, we based our rating on the lowest-quality evidence cited, “as with any model, the results are only as reliable as the model’s poorest data input”[105]. We recognized and acknowledged cases where sources were only used to justify prior ranges/distributions for calibrated parameters, and we noted these cases in the according cell while assessing their quality following the same criteria described above.

2.2.5. Synthesis of model structure and quality of evidence

We then constructed figures for each of the four structural components (listed in section 2.2.2) and two analytical components (list in section 2.2.3), categorizing information in a common format and noting additional assumptions or information in the footnotes. Within these figures, we colour-coded each cell according to the quality of evidence used to inform each design element (Figure 2.1).

2.3. Results

Of the 64 manuscripts (based on 45 HIV simulation models) we identified in our search, 19 met the selection criteria[10,110-127] (see Figure 2.2 for the selection process, results in Table 2.3). Of the 19 models assessed, 3 adopted an agent-based model (ABM) design, 2 employed an individual-based microsimulation (IBMM) design, 13 were deterministic compartmental models (DCM), and 1 was classified as a combination of an IBMM and DCM design (definition in Table 2.1). Most models were constructed to represent generalized HIV epidemics (13/19), as opposed to concentrated epidemic settings (6/19) (definition in Table 2.1). Models representing generalized epidemics seemed to favor individual-based designs (i.e. IBMM and ABM, 6/13), which are better suited to capturing heterogeneity in HIV risk behaviors and differences in demographics across the general population, as opposed to compartmental models, which feature more homogeneous behaviors within specified risk groups and thus better suited to concentrated epidemic settings (6/6).

Furthermore, 10 models supported what could be considered a formal economic evaluation, comparing both costs and health outcomes of alternative strategies[128]. Three framed their analysis as a constrained optimization problem (including one cost-

effectiveness analysis), entailing a decision to be made within budgetary constraints. The remaining were epidemiological models focusing on generating long-term estimates of the epidemiological impact of various public health strategies. The majority of models assessed (15/19) considered at least a 10-year time horizon to capture all meaningful differences in consequences between alternatives considered[81], particularly regarding the long-term benefits of public health interventions (e.g. ART effectiveness in extending the lives of PLHIV and preventing 2nd- and 3rd-order HIV transmission).

Models commonly included three types of comparator strategies: (1) the 'status quo', capturing the observed scale of existing programs using the most recent data on service delivery; (2) the 'standard of care' whereby health services were characterized strictly as being in compliance with current clinical guidelines; and (3) the 'counterfactual' scenario, assuming the absence of a given intervention.

2.3.1. Population construction

***Model structure*:** Among the 19 reviewed models, many explicitly considered heterogeneity by transmission risk group (5/19), behavioral risk levels within a risk group (7/19), gender (16/19), and age (8/19) in their population construction (Figure 2.3). Age was usually only accounted for in models explicitly capturing age-dependent sexual risk behavior among heterosexuals (all in generalized epidemic settings in the reviewed studies)[129-131]. Risk groups were typically determined by routes of HIV transmission. Explicit categories of men who have sex with men (MSM), people who inject drugs (PWID), and female sex workers (FSW), were typically captured in concentrated epidemic settings (5/6). Heterogeneity in risk behaviors within a population subgroup is often characterized by incorporating multiple risk levels (e.g. high- and low-risk). This design feature was adopted only in the reviewed DCMs (n=8). On the contrary, heterogeneity in risk behaviors can, to some extent, be reflected by the stochastic nature of simulating individuals in IBMMs and ABMs[41].

Once infected, PLHIV progressed through stages of acute infection (12/19), HIV diagnosis (10/19), pre-ART care (4/19), and ART (18/19). PLHIV were also differentiated by disease progression states. ABMs/IBMMs often parameterized CD4 and/or plasma viral load (pVL) continuously while DCMs stratified them in discrete levels. Some models

also incorporated separate states pertinent to ART, e.g. multiple regimen types (6/19, more often in ABMs/IBMMs, 3/6), adverse events (8/19), and dropout (2/19).

***Quality of evidence*:** Most of the models assessed used the best-quality evidence on population demographics with good external validity, such as a local census database, but only half of the models applied best-quality and setting-specific evidence to initialize the total population size and its distribution across HIV risk groups. Further, estimates for the initial prevalence of the HIV epidemic were mainly populated with local best-quality evidence (14/19) such as national or regional surveillance databases. However, the initial size or distribution of the infected population across each disease state/compartment was often not explicitly reported by the modellers or derived on the basis of seeded simulation, and therefore rated as the lowest-quality evidence used. The quality of evidence was similar among models characterizing generalized and concentrated epidemic contexts.

2.3.2. Model entry exit and HIV care engagement

Model structure: There was considerably less consensus on how to characterize model entry, exit and HIV care engagement in the selected models (Figure 2.4). Most models (16/19) implemented a dynamic study cohort that allowed the population size to change over time, and population entry/maturation was commonly estimated based on the fraction of individuals who entered or matured out of the defined age group each year or to match the observed population growth or fertility rates. Mortality among the susceptible population was most often dependent on age or gender in ABMs/IBMMs (5/6) and homogeneous in DCMs (7/13).

HIV testing was explicitly captured in 10 models, 3 of which included symptom-based testing in addition to population-based testing, with 6 models also accounting for the decrease in HIV risk behavior following diagnosis. Finally, of the 18 models that explicitly integrated ART, 10 accounted for both the entry (i.e. initiation) and exit (i.e. drop-out) of ART, and 10 also accounted for ART-related adverse events explicitly, among which treatment failure was most frequently cited (9/10). ART drop-out rates were modeled as either constant (4/10), time-dependent (4/10), or dependent on other factors (2/10), and half (5/10) also allowed re-initiation after ART dropout.

Quality of Evidence: Most models based their estimates for cohort entry and exit on the best-quality evidence available locally, such as national or regional census data and life tables, with 2 models not clearly stating the evidence source for this domain. Data on HIV testing rates were primarily obtained from observational studies based on a sample of the target population (moderate-quality), with only 3 models using population-based figures from a health system database, such as health registry/administration database (best-quality). The quality for data on HIV testing effect on risk behaviours was also far from ideal, with half using lowest-quality evidence.

Finally, less than half of the models used ART initiation and drop-out rates derived from what would be considered best-quality data in this context – a local population-level administrative database or registry- with 4 basing their estimates on RCTs or observational studies conducted within the target population. The evidence source was of low-quality for 6/10 studies capturing ART-related adverse events (including failure, resistance and toxicity).

2.3.3. HIV Disease progression

Model structure: HIV disease progression was most commonly measured by CD4 cell count (15/19), followed by pVL (7/19) and disease stage, which generally considered acute, chronic, symptomatic and AIDS as health states (14/19) (Figure 2.5). Although there is no explicit consensus on the superiority of these progression measures, many modellers preferred CD4-based HIV progression since it is in alignment with the CD4-based ART eligibility, entailing more precise characterization of treatment initiation (most models were published before the 2015 World Health Organization (WHO) guidelines recommending ART initiation at diagnosis).

Among the 15 models that incorporated CD4-based disease progression, changes in CD4 counts were characterized mainly by two methods: (i) by fitting some linear or non-linear functions of time or pVL (6/15), as found exclusively in ABMs, IBMMs and DCMs with a stochastic module; or (ii) by calculating the progression rate as reciprocal to the time spent between the previous and subsequent CD4 stratum (7/15). Disease progression by change in pVL used explicitly fitted functions in only one model (1/7), unspecified functional form in two (2/7), and the rest altered pVL status for PLHIV receiving treatment (unsuppressed to suppressed) (4/7).

The effect of ART on improving health was captured in 17/19 models, among which ART was assumed to either reverse (8/17, i.e. CD4 recovery, pVL decrease or suppression), delay (4/17, i.e. longer stage period or reduced transition rate), or stop (8/17, i.e. no change in CD4, VL or stage) disease progression. All models accounted for increased mortality for PLHIV, by either assuming excess mortality varied by CD4, HIV stage, age, opportunistic infections, etc. (10/19) or by assuming increased mortality that was restricted to the final stage of disease (e.g. AIDS) (9/19). The direct effect of ART on mortality was more commonly considered in DCMs (10/13) than in ABMs/IBMMs (2/6).

Quality of evidence: Only half of the models (9/19) used best-quality evidence to characterize HIV disease progression, and one study[132] was consistently cited for evidence on the time spent in each CD4 stratum or HIV stage (6/19). Further, none of the models applied best-quality evidence for characterizing the effect of ART on HIV progression, with many (5/17) deriving this effect from observational studies (moderate-quality), rather than RCTs. Finally, less than half of the models used best-quality evidence for HIV-related mortality and the effect of ART effect on mortality, with sources not clearly stated in 5 models.

2.3.4. The Force of HIV infection

Model structure: First, the infectivity (or susceptibility for the uninfected) was assumed to vary by transmission route (hetero- and homo-sexual, needle/syringe sharing and mother to child) and be influenced by demographic cofactors (age (3/19) and gender (9/19)), biological factors (CD4 (6/19), pVL (3/19), stage (11/19), the presence of sexually transmitted infections other than HIV (4/19)), and other behavioural cofactors (partnership type (4/19)) (Figure 2.6).

Second, HIV transmission was modeled as a function of the number of partners (sexual or injecting) or partner change rate (14/19), contact frequency (12/19), and the probability of condom use during sexual contacts (9/19). Differences in risk behaviours across subgroups were considered in almost all models, commonly by age, gender, risk group or risk level, and partnership type. The effects of several biomedical interventions were also incorporated in the force of infection equations, including ART (18/19), medical male circumcision (MMC, 9/19), pre-exposure prophylaxis (PrEP, 2/19) and condom use (8/19). Finally, all but one model that accounted for partnership mixing (n=16) constructed

preference-based mixing, reflected by a disproportionate likelihood for an individual to select a partner with certain characteristics, such as age (5/16, more in ABMs/IBMMs) and risk group/level (6/16). All ABMs/IBMMs considered more than one partnership type, while additional non-marital, short-term, casual or commercial partnerships were considered in only 4/14 DCMs.

Quality of evidence: The use of best-quality evidence to inform baseline infectivity through different transmission routes was limited. However, the best-quality evidence for biological factors influencing HIV infectivity was more commonly cited, and one longitudinal study[133] was frequently applied to inform the transmission risk by stages of infection (8/19). Although many models used best-quality evidence with good external validity such as population-based behavioural surveillance to populate behavioural parameters, some were obtained strictly through model calibration, where prior ranges were based on assumptions (7/19). Similar categories of evidence sources were used to inform partnership mixing parameters as with other behavioural parameters, whereas the use of lowest-quality evidence was more prevalent. There was also substantial variation in the quality of intervention effect size data: the landmark HTPN-052 study[7] provided best-quality evidence of ART efficacy on reducing transmission risk for most models published afterwards, while none of the assessed models used best-quality evidence to estimate condom efficacy[134].

2.3.5. Model analytical design

Model calibration/validation: Calibrating uncertain inputs to known clinical/epidemiological targets and validating a model against external endpoints provides critical tools to enhance readers' confidence in model outcomes and are both recommended by modeling guidelines[60,80]. Model calibration and validation were both performed only in 2/19 models, while 12 models incorporated calibration only, 2 incorporated validation only, and 3 incorporated neither (Appendix A, Figure A2). Epidemiological endpoints, such as HIV prevalence or incidence, were most often used for setting targets for calibration and validation (14/16), followed by clinical targets (7/16) and demographic targets (4/16). 11/14 models that incorporated calibration reported their calibration methods explicitly, where 4 used a random search (e.g. Latin hypercube sampling), 3 used a directed search (e.g. Nelder-Mead algorithm), 2 adopted a Bayesian

approach, and 1 calibrated parameters manually. We note that model parameters chosen for calibration and their evidence quality were explicated in Figure 2.3-2.6.

Health economic evaluation: As noted earlier, 10/19 reviewed models adopted a formal health economic evaluation, with another 2 constrained optimization models that incorporated costs (Figure 2.7). Among the 12 models incorporating costs, 2/12 adopted the broadest societal perspective, and 7 framed their analysis from the perspective of service provider or public health, scrutinizing costs only borne by the health care system, whereas 3 models did not explicitly report their perspectives. Further, treating and preventing HIV may involve a variety of costs: (1) direct medical costs (e.g. costs for HIV testing, HIV care, ART, preventative drugs, treatment to comorbidities), considered in 12/12 models; (2) direct non-medical costs (e.g. costs for program operation, education, capital), considered in 3/12 models; and (3) indirect costs (e.g. productivity loss due to HIV infection), considered in no models (including the two stating a societal perspective). Finally, 6/10 models supporting a health economic evaluation used quality-adjusted life years (QALYs) or disability-adjusted life year (DALYs), as their measures of health outcomes. We also provided an assessment of the quality of reporting among these 19 models by determining whether they met recommendations for each of the CHEERS Checklist items[135], and we found most models upheld a high level of quality in reporting (Appendix A, Figure A4).

Uncertainty analysis is another recommended component of simulation modeling that quantifies the uncertainty of model outputs, enabling decision makers to gauge confidence and identify targets for future research/data collection[60]. However, 5/19 reviewed models did not report any form of uncertainty (Appendix A, Figure A3). Among the 14 models assessing uncertainty, 4 executed more than 1 type of analysis, and most models quantified uncertainty deterministically, particularly by one-way sensitivity analysis (7/14), while only 4 conducted probabilistic sensitivity analysis.

Quality of evidence: Only half of the models (6/12) derived costs/resource utilization from best-quality evidence (prospectively collected or from reliable databases), while the rest based their cost data mainly on other economic evaluation or cost studies. Similarly, only 3/6 models used best-quality evidence for health state utility, with 1/3 prospectively collected and assessed, 1/3 from meta-analysis, and 1/3 from existing utility repository.

2.4. Discussion

We have provided a detailed assessment of the structural design and quality of evidence supporting 19 HIV/AIDS simulation models. We found consistency in model types according to epidemic context (i.e., generalized versus concentrated), but identified some key structural differences, particularly in characterizing the level of availability of effective HIV treatment and prevention services, a finding which has important implications for guiding combination implementation strategies. Otherwise, there was generally less consistency in the quality of evidence used to inform models, particularly with respect to risk group classification, parameters capturing health system engagement (e.g. HIV testing, ART engagement), and several intervention effect sizes (e.g. condom efficacy, ART effect on disease progression). The lack of explicit guidelines in data identification and quality assessment likely contributed to these inconsistencies; however, our results also suggest several key data points are not routinely or systematically collected in many jurisdictions.

A key finding of this review was that HIV testing was not modeled explicitly in almost half of the reviewed models. HIV testing initiatives have been shown to be cost-effective[136-138], and explicitly modeling testing provides the opportunity to account for changes in risk behaviours following testing[139-141], and the odds of subsequent ART initiation[142,143]. Although many of the models we assessed were purpose-built to evaluate one or several specific interventions, it is critical to note that individual interventions may be enhanced or diminished when delivered in combination with others. For example, while the benefits of ART are well-documented, the effect of treatment interventions may only be maximized in combination with a sufficient level of HIV testing. There is a growing recognition of the critical importance of combination HIV prevention in achieving epidemic control[88,144]. In the context of informing combination implementation strategies, in general, focusing on individual interventions or selected combinations may obscure the value of other efficacious interventions, and may constrain a model's capacity to identify the highest-valued combination strategies[11].

Another key finding of our review was that the highest-quality local administrative/registry data was often unavailable or otherwise not cited. Instead, some models based their estimates for elements like the HIV testing rate, ART initiation, and retention in care on sample-based observational studies or RCTs. Similarly, while readily

available, high-quality census data was used in most models to inform population-level demographic parameters, only half of the models used best-quality, setting-specific evidence to derive initial values for the size of risk groups or for the distribution of people at different levels of risk for HIV infection. Routinely-collected surveillance and administrative data can provide reliable, population-based healthcare utilization and behavioural data that could enhance a model's validity. The infrastructure to facilitate this level of data collection is however costly to construct and may be infeasible in some settings. Sensitivity analysis is recommended by best practices guidelines to address concerns regarding parameter uncertainty[38,60] and 14/19 of the studies we reviewed featured some form of sensitivity analysis. Further, 14/19 of the studies we assessed set parameters with the greatest uncertainty as 'free' parameters in calibration, which also constitutes recommended practice[38,60]. However it should be clear that better quality evidence is preferable even in setting ranges for calibration and sensitivity analysis. Value of information analysis[145]– built on the level and source of uncertainty in cost-effectiveness analyses – can guide efforts to ensure the limited resources available for data collection are focused on the most influential parameters, thus reducing uncertainty in resource allocation decisions to the greatest possible extent[70]. These features are integral to producing valid representations of local contexts and should be a focal point for analysts moving forward.

While the models we assessed generally upheld a high level of transparency in their descriptions of model structure, we found more substantial variation in the reporting of data sources and their selection, particularly as the evidence dictating the initialization of the infected population (at each state) was often underreported. Likewise, in contrast to a number of best practice guidelines informing model design, there is less consensus on the practical and methodological challenges related to the use of evidence in simulation models, including: (1) the definition and identification of 'relevant' evidence, (2) the assessment of evidence quality, and (3) the synthesis of evidence[104]. Only one[126] of the nineteen reviewed models explicitly presented its process of systematic evidence gathering, whereas in most models, quality assessment and how evidence was synthesized were unclear. Explicitly reporting and assessing the quality of data entered into a model can improve its replicability and identify focal points for sensitivity analysis and further data collection. The quality assessment framework (Table 2.2) we have proposed can contribute to the development of standardized approaches to identifying and

assessing the quality of model inputs in the application of model development or critical review. For example, this framework can be used to structure and formalize the evidence synthesis supporting a modeling study, increasing transparency, rigor and ultimately credibility. It can also help identify parameters with the greatest uncertainty, which should be targets for calibration, sensitivity analysis or further value of information analysis.

In deliberations on model complexity and intensity of data requirements, researchers need to find the right balance between parsimony and complexity, as every additional parameter could introduce new sources of uncertainty and can potentially have a counterintuitive effect on model results[146]. Complex models are not necessarily more accurate or reliable than simpler ones that are developed with high-quality data. Rather, models should only be sufficiently complex to address the policy question and key epidemiological features, with careful consideration of the availability and quality of data. Sensitivity analysis on model structure could be used to identify the degree of parsimony in a model, by ensuring conclusions and the degree of uncertainty are robust to changes in model structure[146]. We did not attempt to make a judgement on what constitutes a sufficient level of complexity for a given context and research question. This qualitative description of the models we have selected provides a guide for model developers to consider when determining the most appropriate and feasible design. We believe this type of review, with explicit focus on structure and data quality can be useful across disease areas, particularly those with fewer historical precedents or where data is more sparse.

This narrative review has several potential limitations. First, the selection of models was not systematic. Given the large amount of existing HIV models and the breadth and depth of this review, we believe a narrative review was most practical and appropriate for our aims. The snowball sampling approach we undertook, which included a majority of HIV models in the HIV Modeling Consortium database[147], was designed to yield a group of highly influential models representing various typologies, geographic and application contexts currently used in practice, though they may not be representative of all HIV models published within the study timeframe. It was not our intention to exhaustively detail the structural design characteristics and their underlying data for all published models in HIV, but rather underline areas of consensus and divergence on key aspects of model development; we have been careful to avoid sweeping conclusions that would require a systematic review. By explicating different structural/analytical designs and sources/quality of data in the selected models, we hope this review can provide guidance

for model developers in selecting an appropriate model structure, identifying data sources and assessing uncertainty, as well as reviewers in critically assessing HIV modeling applications. Second, the internal validity of evidence quality was only assessed by study design rather than a full investigation of the quality of source study. While there is certainly room for greater scrutiny in this domain, we believe even a limited assessment of evidence quality can improve the rigor and credibility in simulation modeling. Finally, several aspects of modeling were not covered in this review, such as the interventions being evaluated and the prognosis of comorbid conditions, as these were beyond the scope of this exercise. Rather, we focused on assessing the structural design and quality of evidence used in the reference case, whose implications are generalizable to all HIV modeling regardless of context or decision problem.

2.5. Conclusion

Simulation modeling has become an indispensable tool in evidence-based decision making[81], particularly in the public health response to HIV/AIDS where significant investment still needs to be made to reach international targets. We believe this narrative review advances the ability of model developers to critically select and assess the appropriate model structure for a given epidemiological context, as well as the corresponding data requirements. Formal assessment of the influence of poorer-quality data on model inferences should be used to guide decisions to collect more data, in the interest of reducing decision uncertainty. Finally, developing guidelines on evidence syntheses supporting decision models, with an emphasis on quality assessment, should be a priority in the field.

Table 2.1. Definitions of the epidemic context and dynamic model types.

Stratification	Types	Definition
Epidemic	Generalized	Settings where HIV is firmly established in the general population, e.g. the sub-Sahara African countries where the HIV prevalence is as high as 20%[148]
	Concentrated	Settings where the HIV epidemic is disproportionally higher within several key subgroups of the population, but is not well established in the general population[148]
Model	Deterministic Compartmental Model (DCM)	Model that divides the study population into various compartments according to individuals' characteristics and disease statuses, representing their average state, and uses differential or difference equations to track the rate of transition of individuals between compartments[38]
	Individual-based microsimulation model (IBMM)	Model that simulates the study population at the individual level, whereby individuals' transitions in disease status or other states are generated using a random process and are drawn from probability distributions[60]
	Agent-based model (ABM)	A special case of IBMM that explicitly incorporates the interactions between autonomous agents and between agents and a simulated environment, capturing dynamic network effects[41]

Table 2.2. Data quality assessment criteria used to evaluate supporting evidence

Evidence category	Pertinent parameters in model	Model component‡	Internal validity			External validity
			Best quality evidence	Moderate quality evidence	Lowest quality evidence‡‡	Generalizable data‡‡‡
Clinical effect size	HIV testing effect on behavior	3.4	Systematic synthesis of RCTs, single RCTs*, or systematic synthesis of cohort studies**	Observational studies: cohort, case control	Non-analytical studies***, expert opinion	No
	ART effect on HIV progression	3.3				No
	ART effect on mortality	3.3				No
	Preventative intervention effect size^	3.4				Yes
Natural history of disease	Disease progression	3.3	Longitudinal cohort studies and case series, nationally collected or compiled statistics or routinely collected admin data, disease registries, or epidemiological database	Data from RCTs	Expert opinion	Yes
	Infectivity (baseline and cofactors)	3.4				Yes
	Opportunistic infections	3.3				Yes
	HIV-related mortality	3.3				Yes
ART-related adverse events and complications	ART failure	3.2	Systematic synthesis of RCTs, single RCTs*, or systematic synthesis of cohort studies**	Observational studies: cohort, case control	Non-analytical studies***, expert opinion	No
	ART toxicity	3.2				No
	ART resistance	3.2				No
Health system engagement	PrEP	3.1	Case series or analysis of reliable admin database	Old case series, estimates from RCTs, or other observational studies	Other modeling studies, expert opinion	No
	HIV testing rate/coverage	3.2				No
	ART initiation/scale-up	3.2				No
	ART retention/drop-out	3.2				No
Population characteristics	Initial population & demographics^^	3.1	Central statistics, health care system statistics#, life tables	Sample-based studies##	Expert opinion	No
	Population change	3.2				No
	Background mortality	3.2				No
	Initial epidemic†	3.1				No
	Medical male circumcision	3.1				No
	Sexually transmitted infections	3.1				No
Behavioral	Risk group / risk level stratification	3.1	Population-based surveys, health care system statistics#	Sample-based studies##	Expert opinion	No
	Risk behaviour intensity††	3.4				No
	Partnership mixing	3.4				No
Cost	Direct medical/non-medical cost	3.5	Prospective data collection, reliable database	Other health economic evaluation or cost studies	Personal communications, expert opinion	No
	Indirect cost (e.g. productivity loss)					No
Health state utility (HSU)	Utility for each health state	3.5	HSU repository, direct utility assessment, meta-analysis	Indirect evidence from the literature (CEA/CUA)	Expert opinion	Yes

Legend: ‡ in conformity with the section number; ‡‡ also including data whose source is unclear (not explicitly presented in the paper), or derived not directly from evidence-based information sources, such as other modeling study, assumption, and calibration with priors based on assumptions; ‡‡‡ generalizable data are those applicable across settings (i.e. outside the context of the source study), in which case context-specific evidence is not required. ^ e.g. the efficacy of antiretroviral therapy (ART), medical male circumcision (MMC), pre-exposure prophylaxis (PrEP) and condom use on reducing transmission risk; ^^ e.g. population size, age, gender, race; † i.e. the initial prevalence and population size for each compartment among people living with HIV in the baseline year; †† e.g. number of partners, coital frequency, sexual activity, condom use, sex type; * if multiple randomized controlled trials (RCTs) are not available for meta-analysis; ** if RCTs are infeasible; *** e.g. case reports and case series; # e.g. national or regional surveillance; ## e.g. RCTs, cohort studies, non-population-based surveys.

Table 2.3. Design characteristics of the selected modeling studies

Context;	Classification			Cycle length;	Comparator strategies		Outcomes^
Study population	**Context**	**Model**	**Analysis**	**Time horizon**	**Intervention**	**Reference case**	
Bershteyn et al. 2013 – ***EMOD***[110] Objective: compare a broad set of structural and parametric modeling assumptions in order to identify a set of possible explanations for the HIV epidemic							
South Africa; GP (initial 75,000)	G	ABM	Epi	1 day; 1960-2050	Epidemic under different structural or parametric assumptions		Incidence
Smith et al. 2015 – ***Smith***[111] Objective: assess the health effect and cost-effectiveness of a community-based package of home HIV counselling and testing							
KZN, South Africa; 10,000 adults (>18 y)	G	ABM	CEA	1 month; 10 years	Home-based screening	Status quo: facility-based screening (observed)	Incidence, prevalence, morbidity, ICER (DALY)
Hontelez et al. 2011 – ***STDSIM***[112] Objective: evaluate public health impact, cost-effectiveness, and budget impact of repeated vaccination strategies in combination with ART							
KZN, South Africa; GP	G	ABM	CEA	1 month; 20 years	Vaccine	No vaccine	Incidence, prevalence, ICER (DALY)
Bendavid et al. 2010 – ***Bendavid***[113] Objective: assess the epidemiologic and health effects of 4 strategies to increase access to ART							
South Africa; 10,000 people (>15 y)	G	IBMM	Epi	1 month; 10 years	Universal testing and ART, linkage and adherence to care	Status quo (observed)	Incidence, life expectancy
Walensky et al. 2013 – ***CEPAC***[114] Objective: project the cost-effectiveness of early ART, as compared with delayed ART, among serodiscordant couples							
South Africa and India; Serodiscordant couples	G	IBMM DCM*	CEA	1 month; Lifetime	Early ART	Delayed ART (CD4<250)	Incidence, survival rate, ICER (LY)
Phillips et al. 2014 – ***Synthesis***[115] Objective: compare the effectiveness and cost-effectiveness of different potential public health responses to substantial levels of transmitted drug resistance							
South Africa; 100,000 people (>15 y)	G	IBMM	CEA	3 months; 15 years	Regimen, monitoring	SOC (regimen and monitoring based on current guideline)	Prevalence, PLHIV mortality, % resistance, % VL suppression, NB (QALY)
Anderson et al. 2014 – ***Anderson***[10] Objective: examine how a fixed amount of resources for HIV prevention can be used to reduce HIV infections using two forms of resource allocation: uniform and focused approach							
Kenya; GP (>15 y)	G	DCM	CO	1 year; 15 years	Optimal localized health production function: MMC, behaviour change, early ART, PrEP	Optimal national uniform health production function under fixed budget	Incidence

Context; Study population	Classification: Context	Model	Analysis	Cycle length; Time horizon	Comparator strategies: Intervention	Reference case	Outcomes^
Bärnighausen et al. 2012 – ***BBH***[116] Objective: compare the health effects and costs of different combinations of three interventions: TasP, ART and medical male circumcision							
South Africa; GP (>15 y)	G	DCM	CEA	1 year; 10 years	TasP, ART, MMC	Status quo (observed coverage)	Incidence, prevalence, PLHIV mortality, ICER (incidence)
Eaton et al. 2014 – ***Eaton***[117] Objective: quantify how the proportion of transmission that comes from persons who have been infected recently affects the impact of treatment scale-up on HIV incidence							
South Africa; GP (>15 y)	G	DCM	Epi	1 year; 1990-2020	Current and projected ART scale-up	Counterfactual no ART	Incidence
Granich et al. 2009 – ***Granich***[118] Objective: examine a strategy of universal voluntary HIV testing and immediate treatment with ART and examine the conditions under which the epidemic could be eliminated							
South Africa; GP (>15 y)	G	DCM	CCA	1 month; 42 Years	Universal testing with immediate ART	SOC (eligibility under current guideline)	Incidence, prevalence, PLHIV mortality
Nichols et al. 2013 – ***Macha***[119] Objective: determine the impact of different PrEP strategies on averting HIV infections, prevalence, drug resistance and cost-effectiveness							
Macha, Zambia; Rural population (>12 y), fixed as 90,000	G	DCM	CEA	1 month; 10 years	PrEP	Status quo (observed)	Incidence, prevalence, % resistance, ICER (QALY)
Cori et al. 2014 – ***PopART***[120] Objective: predict the impact of the intervention package that will be delivered during the trial							
Zambia and South Africa; GP (>15 y)	G	DCM	Epi	N/C; 3 years	Home-based screening, ART, MMC	SOC (under current guideline)	Incidence
Johnson et al. 2012 - ***STI-HIV***[121] Objective: assess how much of the change in HIV incidence can be attributed to the impact of previously introduced prevention and treatment programs							
South Africa; GP	G	DCM	Epi	1 month; -8 years	ART, condom use promotion (existed)	Counterfactual no intervention	Incidence
Birger et al. 2014 – ***Birger***[122] Objective: assess the impact of interventions along the continuum of care, leading to virologic suppression							
Newark, NJ, USA; GP (>15 y)	C	DCM	Epi	1 year; 10 years	Screening, linkage to care and ART	Status quo (observed)	Incidence, PLHIV mortality
Stover et al. 2011 - ***CD4-HIV***[123] Objective: estimate the potential impact and cost of the revised guidelines							
All LMIC and 7 countries; HIV+ only	C	DCM	CCA	1/10 year; 6 years	Early ART	SOC (current eligibility: CD4<200)	Incidence, PLHIV mortality, LY vs. cost

Context;	Classification			Cycle length;	Comparator strategies		Outcomes^
Study population	**Context**	**Model**	**Analysis**	**Time horizon**	**Intervention**	**Reference case**	
*Mishra et al. 2014 – **Mishra**[124]* Objective: examine the impact of the existing ART program beyond that achieved by existing condom-based interventions & the incremental benefit of multiple ART expanding strategies							
3 cities in South India; GP (>15 y)	C	DCM	Epi	N/C; -10 years, +10 years	Condom use promotion, behaviour change	Past: counterfactual no intervention; Future: status quo (observed)	Incidence, prevalence
*Long et al. 2010 – **Portfolio**[125]* Objective: evaluate the effects on the U.S. HIV epidemic of expanded ART, HIV screening, or interventions to reduce risk behaviour							
USA;GP (15-64 y)	C	DCM	CEA	1 year; 20 years	Screening and ART expansion	Status quo (observed scale-up)	Incidence, ICER (QALY)
*Zhang et al. 2013 – **Prevtool**[126]* Objective: estimate the cost-effectiveness and returns on prior investments of HIV prevention programs and identify the optimal allocation of resources across combinations of programs							
Vietnam; GP (15-49 y)	C	DCM	CEA CO	1 year; -10 years, +10 years	NEP, condom use promotion, MMT, voluntary testing, STI care under current/ optimal allocation of funds	CEA: counterfactual no intervention; CO: current allocation of funds (observed)	Incidence, PLHIV mortality, ICER (DALY)
*Lasry et al. 2011 - **US-CDC**[127]* Objective: optimize the apportionment of prevention resources among interventions and populations so that HIV incidence is minimized, given a budget constraint							
USA; GP (13-64 y)	C	DCM	CO	1 month; 5 years	Optimal allocation of funds to: screening, behaviour change	Current allocation of funds (observed)	Incidence

Legend: ABM: agent-based model; ART: antiretroviral therapy; C: concentrated epidemic; CCA: cost-consequence analysis; CEA: cost-effectiveness analysis; CO: constrained optimization; DALY: disability-adjusted life year; DCM: deterministic compartmental model; Epi: epidemiologic model (no cost estimated); G: generalized epidemic; GP: general population; IBMM: individual-based microsimulation model; ICER: incremental cost-effectiveness ratio; LMIC: low- and middle-income countries; MMC: medical male circumcision; NEP: needle exchange program; PrEP: Pre-exposure prophylaxis; QALY: quality-adjusted life year; STI: sexually transmitted infection; SOC: standard of care; TasP: treatment as prevention; VL: viral load; * CEPAC model were composed of two modules: the International Module (CEPAC-I), IBMM, to simulate the disease progression and outcome of disease and the Transmission Module (CEPAC-T), DCM, to examine the disease transmission and associated clinical impacts.

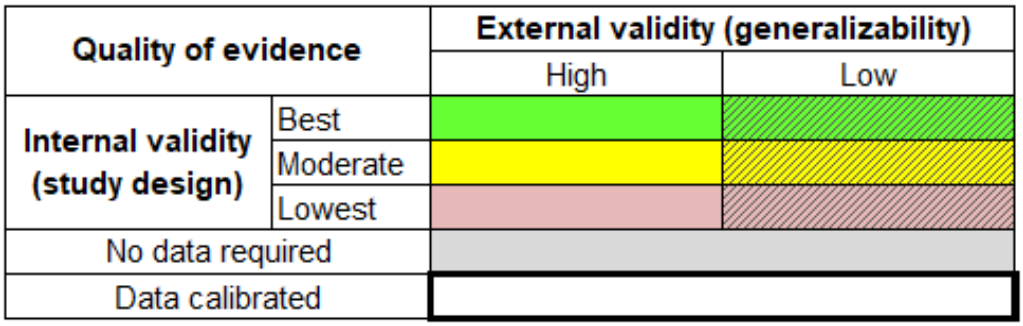


Figure 2.1. Colour codes of the quality of evidence

Legend: In each of the following model component figures (Fig. 2.2-2.7), colored cells indicate the inclusion of a structural characteristic in each respective model (as opposed to a blank cell indicating that the model did not incorporate the structural characteristics), grey cells indicate that no data was required for an included structural characteristic, and cells with bold outlines indicate that the data required for an included structural characteristic were calibrated

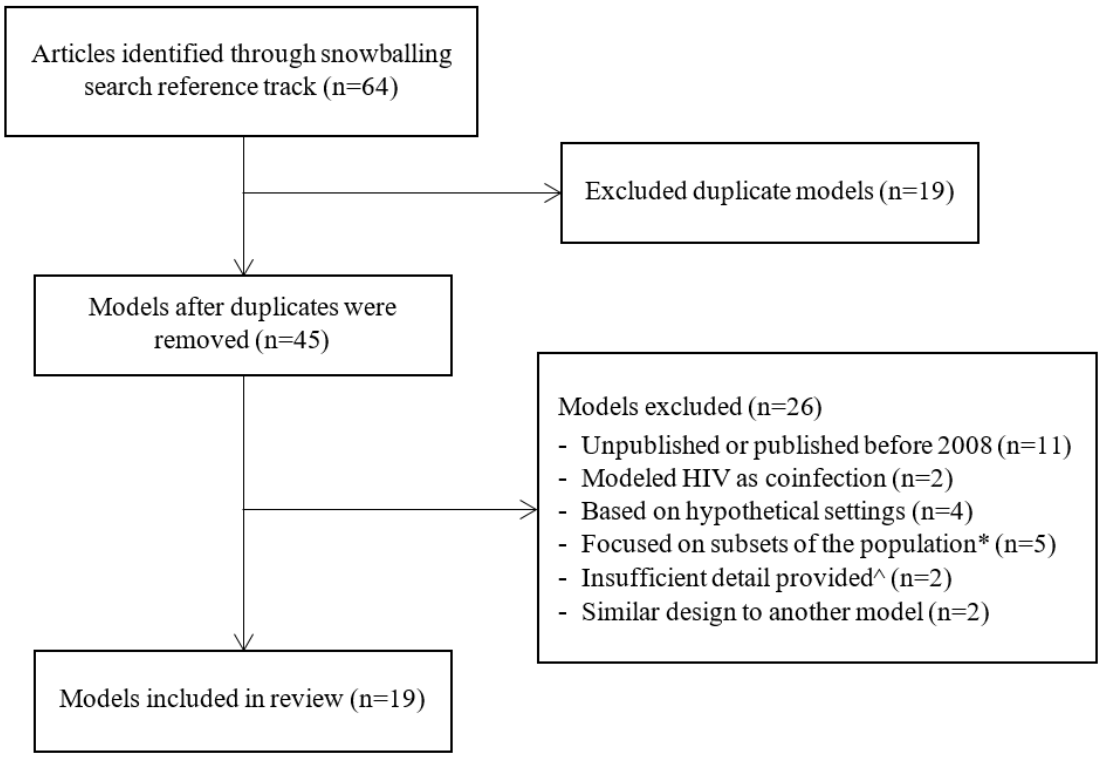


Figure 2.2. Flow diagram of the process for model identification

Legend: Seed articles:[56,57,102]. * e.g. models focusing exclusively on men who have sex with men (MSM), people who inject drugs (PWID), etc.; ^ models failed to provide sufficient detail (in the manuscript or supporting appendix) to capture the majority of the information required for this review were excluded

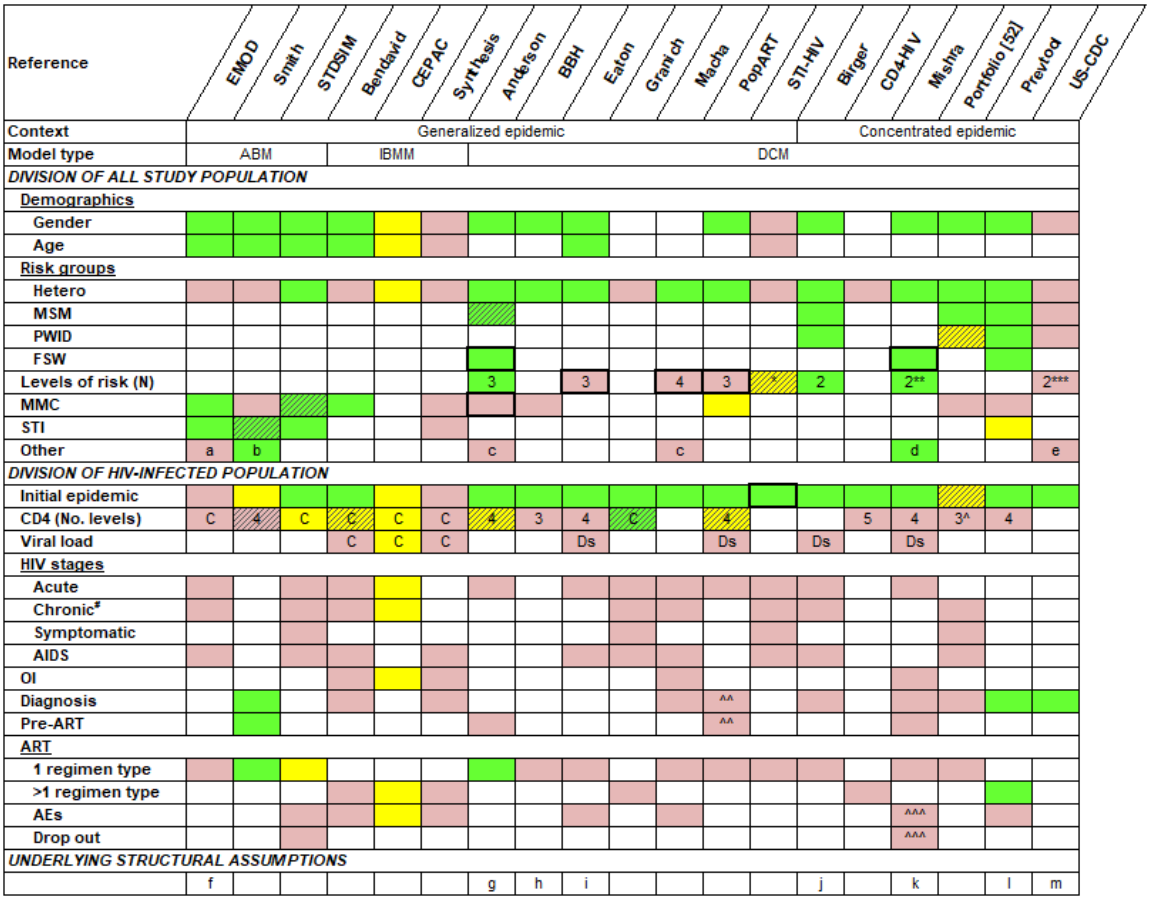


Figure 2.3. Population construction

Legend: The color schemes presented reflected the evidence used to inform the initial population size of the according compartment or the initial distributions.

Uppercase letter: AEs: adverse events, including ART failure, resistance and toxicity; ART: combination antiretroviral therapy; C: continuous measure of CD4 count or viral load; Ds: dichotomous measure of viral load (suppressed or unsuppressed); FSW: female sex workers; Hetero: heterosexuals; MMC: medical male circumcision; MSM: men who have sex with men; OI: opportunistic infections; PWID: people who inject drugs; STI: other sexually transmitted infections;

Symbol: # chronic or asymptomatic; * multiple definitions used; ** among female sex workers only; *** among heterosexuals only; ^ equivalent to the three HIV stages; ^^ identical compartment; ^^^ identical compartment;

Lowercase letter: a. Fertility; b. Household roles; c. PrEP; d. Sexual activity class; e. Race; f. All the attributes were drawn independently from their empirical distributions; g. Entry rate adjusted to ensure constant proportions within each sexual risk group; h. Entry rate adjusted to equivalence in the number of males and females. i. (1) Age 15-49 sexually active; (2) Age ≥50 sexually inactive; (3) Allowing transitions between risk levels; j. Allowing transitions between non-PWID and PWID; k. (1) Retired FSW or clients were the same as low-risk individuals; (2) Fixed prevalence of HCV-2; (3) A proportion of people were sexually inactive; l. Female PWID were not modeled directly; m. Homogeneity between the susceptible and the undiagnosed.

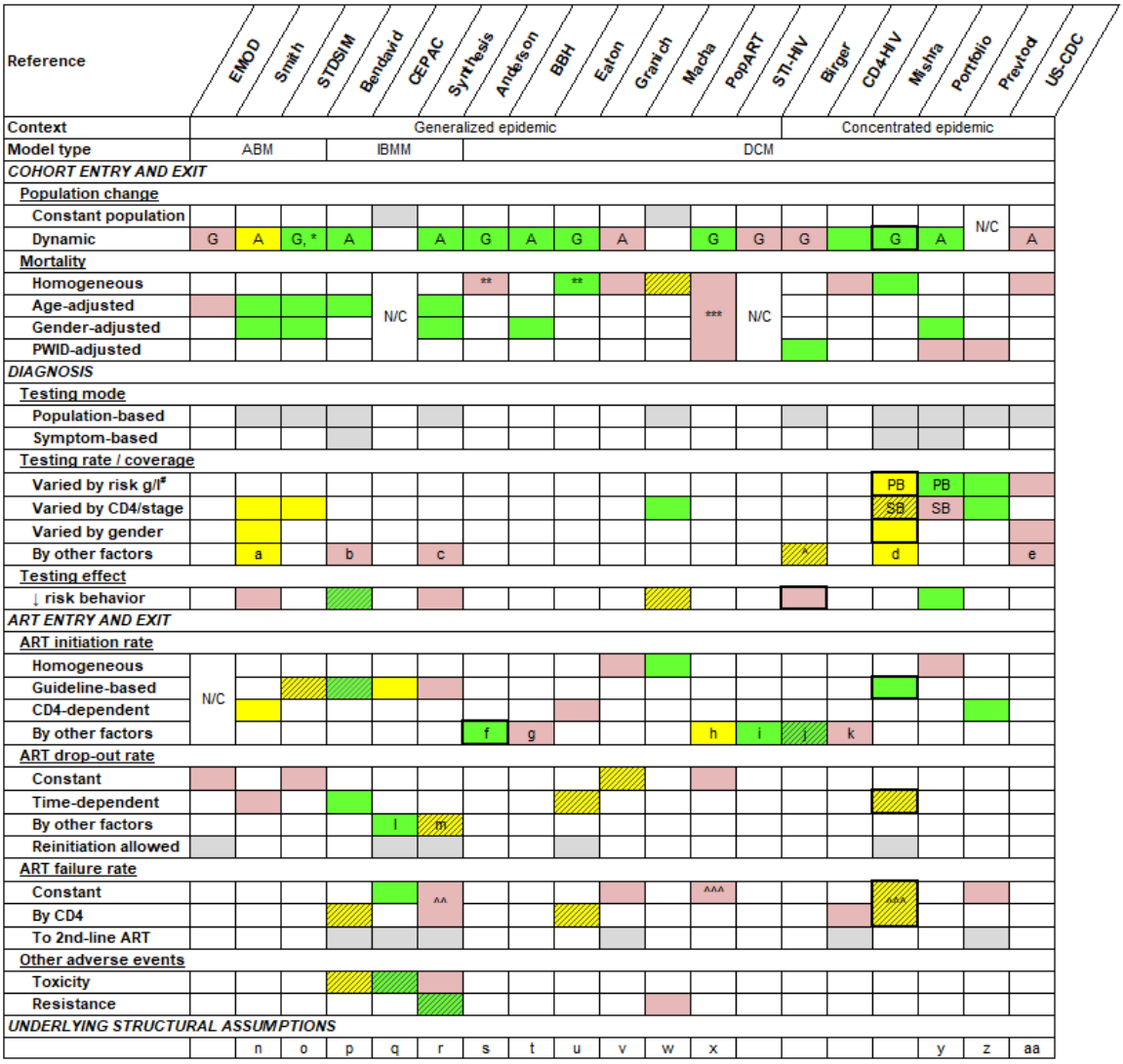


Figure 2.4. Model entry, exit and HIV care engagement

Legend:

Uppercase letter: A: population change was characterized by the estimated rate of aging-in and -out into or out of the defined study population age range; G: population change was characterized to match observed population growth or fertility rate; N/C: not clear; PB: population-based; SB: symptom-based;

Symbol: # risk g/l: risk groups or risk levels; * age-, sex-specific migration rate (in & out); ** among 50+ only; *** calibrated; ^ the reciprocal of the duration between infection and testing; ^^ meeting failure definition (VL, CD4, OI); ^^^ jointly considered with ART drop-out;

Lowercase letter: a. Infection state, age; b. Infection state (PB), opportunistic infection state (SB); c. Opportunistic infection state, age, time-increasing; d. Time-increasing; e. Race; f. Linear time-increasing; g. Once certain number of years since infection has passed; h. As a Hill function increase, with greater rate for CD4>200; i. Estimated number of ART initiations over the annual number of new AIDS cases; j. As the reciprocal of the duration between eligibility and treatment; k. By the assumed coverage; l. Regimen; m. (1) Adherence profile, (2) Drug supply; n. (1) Repeat testing occur ≥1 years for HIV- individuals; (2) Longer wait time and lower initiation rate for higher CD4 strata; o. (1) Linear increase in testing rate with stage number; (2) ART Dropout was permanent; p. (1) Retesting no sooner than every 3 years; (2) Treatment stops 3 month after loss to follow-up; (3) ART monitoring occurs every 3-6 months; (4) Toxicity: rate varied by time since

ART, can trigger 2nd-line ART; q. (1) Same efficacy for 1st and 2nd line ART; (2) Toxicity: rate varied by regimen, can cause mortality increase; r. (1) Testing rates drawn from lognormal distribution; (2) Toxicity: rate varied by regimen, can trigger 2nd-line ART; (3) Resistance: can be developed (by adherence and # of active drugs) or acquired (by % of resistance presence in the concurrent PLHIV), can reduce number of active drugs; s. (1) Assuming an ART coverage ceiling as 90%; (2) Equal scale-up rate across all locations; t. ART provided to CD4≥350 was considered as TasP and<350 was considered as treatment; u. Re-initiation rate varied by CD4, and then back to the normal track as on ART; v. (1) ART discontinued PLHIV same as untreated; (2) 2nd-line ART same as 1st-line except in cost; w. Resistance: homogeneous rate; x. (1) ART failed cases same as untreated; (2) No ART initiation for CD4>350; y. Testing sensitivity and specificity also considered; z. (1) Same failure rate for 1st and 2nd-line ART; (2) PLHIV who failed 2nd-line ART were the same as the untreated; aa. Resource allocation as the sole impetus of testing, and the testing coverage was proxied by the resources allocated.

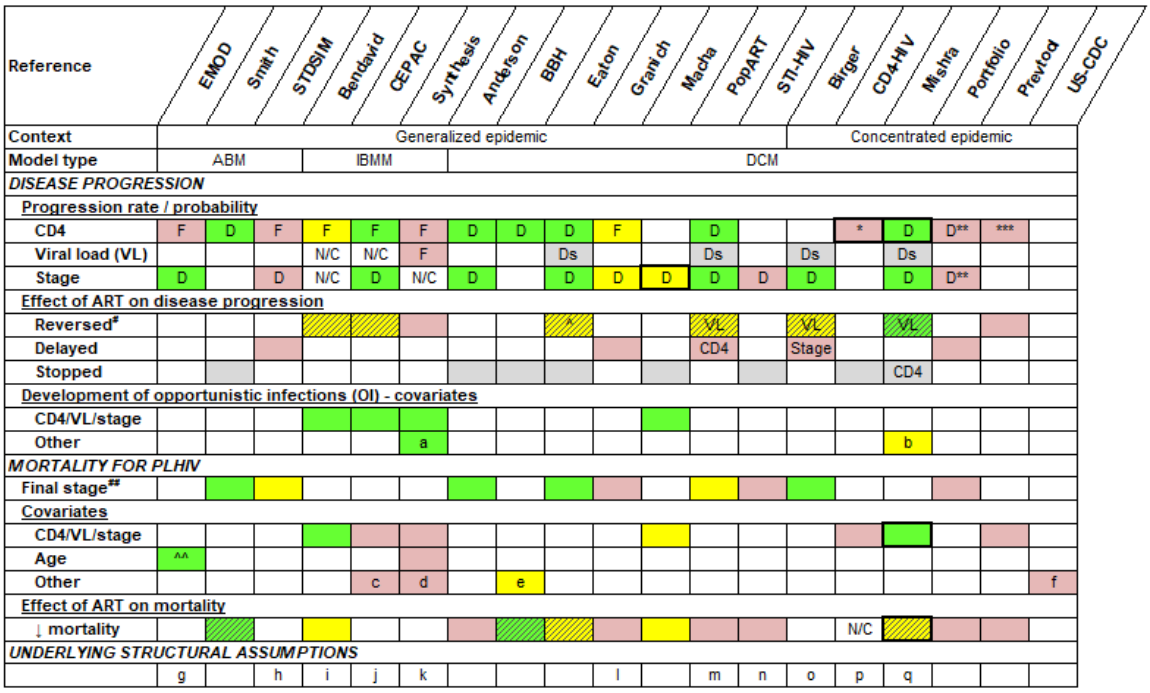


Figure 2.5. HIV disease progression

Legend:

Uppercase letter: D: characterized by the duration between two stages or strata (i.e. as the reciprocal); Ds: characterized by dichotomous measure, suppressed or unsuppressed; F: characterized by functions (linear, non-linear), see underlying assumptions; N/C: not clear;

Symbol: # including CD4 recovery, VL decrease and VL suppression; ## HIV-related mortality considered for final stage (e.g. AIDS, CD4<200) only; * calibrated; ** equivalent; *** different progression rate by CD4 strata; ^ may return to a higher CD4 stratum after dropout; ^^ Weibull distribution;

Lowercase letter: a. Age; b. Homogeneous; c. OI, toxicity; d. OI; e. Gender, time since infection; f. Diagnosis; g. (1) CD4 declines according to a quadratic function with prognosis; (2) Total survival time for PLHIV was stochastically sampled from an age-dependent Weibull distribution (with fixed duration for acute and AIDS stages); (3) Assuming all new infected cases started with the same initial CD4 counts as 594 cells/mm^3; h. Linear decrease of CD4 in different stages; i. CD4 modeled continuously based on VL, and ART; j. (1) CD4 decrease determined by VL; (2) Progression and clinical events were observed periodically at clinical visits or when OIs occur; k. (1) VL changes sampled from normal distribution. CD4 changes by declining rate, adjusted by VL and age; (2) Initial VL randomly sampled from log normal distribution. Initial CD4: 756 cells/mm^3; (3) ART effects on progression varied by number of active drugs and adherence level; l. (1) Linear decrease of CD4; (2) Survival after infection followed a Weibull distribution (with fixed duration for acute and AIDS stages); (3) CD4 decreased by 25% immediately after infection; m. (1) PLHIV may enter any CD4 strata after acute stage; (2) CD4 during ART represented the stage to which when treatment being interrupted; n. The duration for each stage was exponentially distributed; o. (1) Post-ART AIDS (treated but unsuppressed) stage is a dead-end: no regimen changes allowed; (2) Treated and suppressed stage is a dead-end: no failure allowed; p. % of VL suppression as the multiplication of conditional % of linked to care, % retained to care, % linked to treatment and % achieving suppression; q. HSV-2 co-infection assumed to have stable prevalence and increase HIV infectivity.

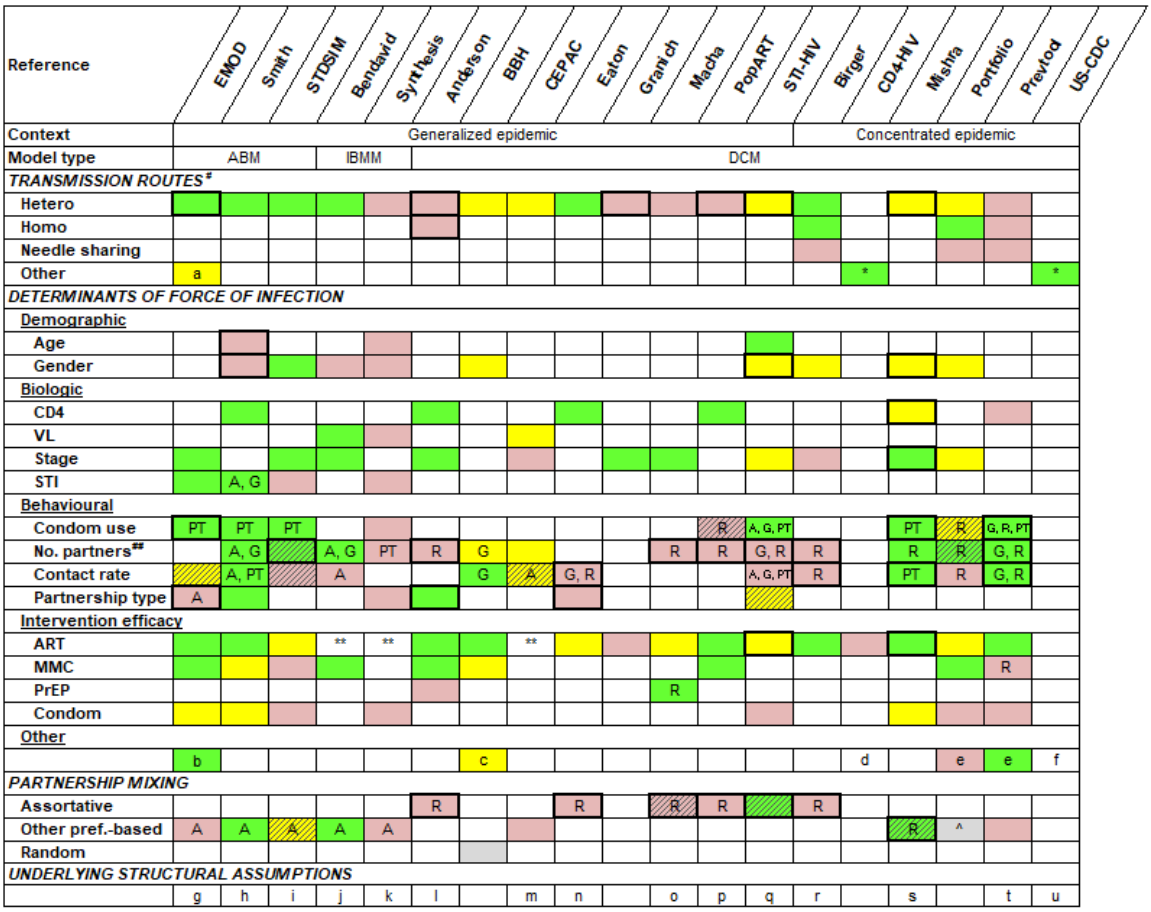


Figure 2.6. The force of HIV infection

Legend:

Uppercase letter: A: age-dependent; G: gender-dependent; pref.: preference; PT: partnership type-dependent; R: risk group or risk level-dependent;

Symbol: # colors indicate the assessment of evidence used to inform the baseline infectivity of different transmission routes; ## number of partners (sexual or injection-sharing), also referred to as the rate of partner change in some models; * all transmission routes were jointly modeled in one force of infection; ** the effect of ART on reducing transmission was modeled indirectly through viral load; ^ proportional mixing;

Lowercase letter: a. Mother to child (MTC); b. Coital type: only the evidence evaluation for its effect on was infectivity shown; the behavioral parameter was based on best quality evidence with lowest external validity; c. Years since infection; d. Based on a Spectrum projections (exogenous to the model), influenced by the distribution of CD4 strata due to their distinct infectivity; e. Probability of needle sharing; f. Reversely estimated by the observed incidence; g. (1) Partnership types: transitory, informal, and marital, with different duration (Weibull distribution); (2) Assuming exponential distribution of the interval between coital acts; (3) Allowing coital dilution for multiple partnerships; h. (1) Partnership mostly within the community; (2) Maximum 2 partners (1 long-term) at a time; (3) Allowing external short-term partnership; (4) Males tended to be older than females in pairs; i. (1) Partnership type: marital, casual, commercial; (2) The rate of sex partner change is determined by a supply and demand mechanism (from previous studies) depending on age, sex and marital status; j. (1) Partnership type: spousal and non-spousal; (2) The risk of having HIV-positive partner was age- and gender-specific; k. Partnership type: long-term, short-term; l. (1) No interactions between locations; (2) No transmission considered for population aged 50+; m. Partnership type: primary and secondary; n. (1) Sexual contact rate reduction followed a logistic function ensuring symmetry

around the midpoint of behavior change period; (2) # of sexual contacts geometrically adjusted to balance the male and female contacts; o. No sexual activity in final AIDS stage; p. (1) Reduced sexual activity in the wound healing period after MMC; (2) 5% of the partnerships formed with outside partners; q. (1) Partnership type: marital, casual, commercial; (2) Disease advanced PLHIV had reduced sexual behaviors; r. Frequency of needle sharing decayed over time according to observed trends; s. Partnership type: occasional commercial, regular commercial, and main; t. Partnership type: commercial, casual, and regular; u. Fixed force of infection.

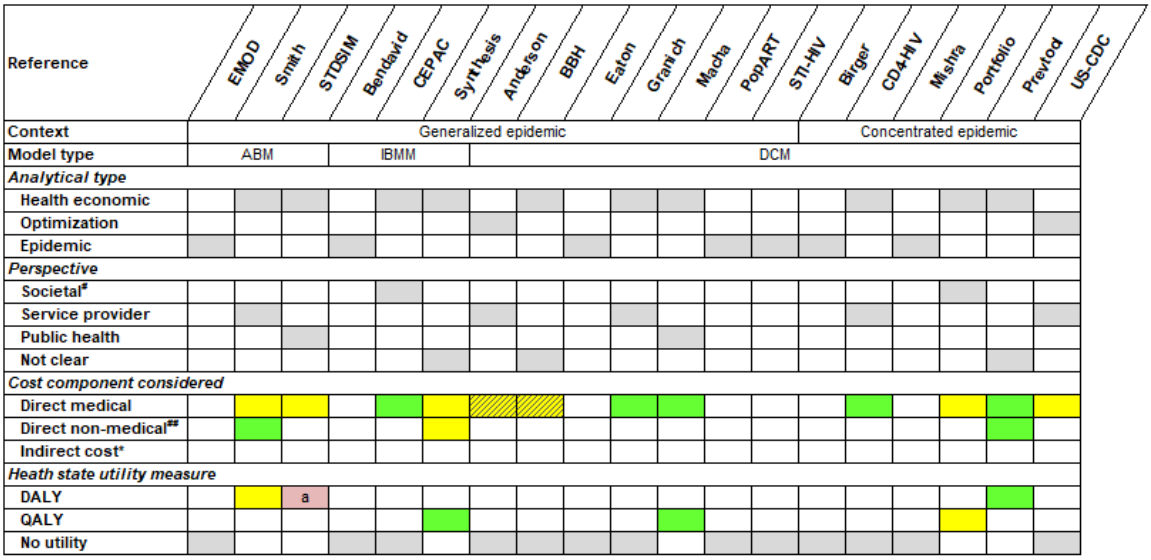


Figure 2.7. Health economic evaluation

Legend:

Symbol: # also including modified societal; ## e.g. capital cost, program operational cost, research cost; * e.g. productivity loss.

Lowercase letter: a. Approximated by life-years gained.

Chapter 3.

Development and calibration of a dynamic HIV transmission model for 6 US cities

Background: Heterogeneity in HIV microepidemics across US cities necessitates locally-oriented, combination implementation strategies to prioritize resources. We calibrated and validated a dynamic, compartmental HIV transmission model to establish a status quo treatment scenario, holding constant current levels of care for six US cities. **Methods**: Built off a comprehensive evidence synthesis, we adapted and extended a previously-published model to replicate the transmission, progression and clinical care for each microepidemic. We identified a common set of 17 calibration targets between 2012 and 2015 and used the Morris method to select the most influential free parameters for calibration. We then applied the Nelder-Mead algorithm to iteratively calibrate the model to generate 2,000 best-fitting parameter sets. Finally, model projections were internally validated with a series of robustness checks, externally validated against published estimates of HIV incidence, while the face validity of 25-year projections were assessed by a Scientific Advisory Committee (SAC). **Results**: We documented our process for model development, calibration and validation to maximize its transparency and reproducibility. The projected outcomes demonstrated a good fit to calibration targets, with a mean goodness-of-fit ranging from 0.0174 (New York City (NYC)) to 0.0861 (Atlanta). A majority of incidence predictions were within the uncertainty range for 5/6 cities (ranging from 21% (Miami) to 100% (NYC)), demonstrating good external validity. The face validity of the long-term projections were confirmed by our SAC, showing that incidence would decrease or remain stable in Atlanta, Los Angeles, NYC and Seattle while increasing in Baltimore and Miami. **Discussion**: This exercise provides a basis for assessing the incremental value of further investments in HIV combination implementation strategies tailored to urban HIV microepidemics.

3.1. Introduction

In the United States (US) and most other countries featuring concentrated HIV epidemics, the majority of people living with HIV/AIDS (PLHIV) reside in large urban centers and geographic “hotspot” areas[18-20], each with distinct underlying epidemiological

and socio-structural features[5]. There are also dramatic disparities among minorities, with black and Hispanic men who have sex with men (MSM) accounting for over half of reported new infections[149]. Our previous study on six US cities, Atlanta, Baltimore, Los Angeles (LA), Miami, New York City (NYC) and Seattle, home to nearly a quarter of US PLHIV, found fundamental differences in demographic composition, epidemic characteristics and rates of new HIV diagnoses[5]. Heterogeneity in microepidemics across cities necessitates locally-oriented combination implementation strategies to prioritize resources according to the greatest public health benefit. This approach, however, requires detailed, context-specific information on a range of factors characterizing each HIV microepidemic and the level of available health services.

Mathematical models are simplifications of reality, designed to capture the essence of a problem with a minimally acceptable level of complexity and synthesis of evidence from multiple sources, to extrapolate outcomes that are unavailable, unobservable or unethical to collect. They can provide a unified framework to quantify the public health and economic impact of multiple health interventions, accounting for the synergistic effects between different interventions. Furthermore, setting-specific models can be adapted to capture heterogeneity across settings and are increasingly used to provide objective, localized evidence to prioritize resources according to the greatest public health benefit.

Model complexities and uncertainty surrounding key model inputs can diminish the confidence of decision makers and raise concerns about the credibility of the model-generated results. Assessing the validity and representativeness of a model generally entails explicitly assessing the quality of input data used for its parameters[150], calibrating uncertain inputs to observed epidemiological endpoints (calibration targets)[60], and validating the accuracy of model projections against empirical data on outcomes of interest[80]. Comprehensive and transparent reporting of these development processes can not only add confidence to the process, but also establish a basis to determine data collection targets to reduce uncertainty in the decisions a model recommends.

Building on an evidence synthesis we've described separately[151], our objective was to calibrate and validate a dynamic, compartmental model of HIV transmission for six US cities. The 25-year projections of the model are designed to serve as a 'status quo'

comparator in assessing the incremental value of a range of possible combination implementation strategies to address the unique HIV microepidemics of each city.

3.2. Methods

In this section, we first provide a brief description of the construction of the model, followed by a detailed documentation of our calibration and validation process. Model calibration is the process by which uncertain model input values or ranges can be estimated so that model projections match pre-specified calibration targets[63,147].[61,152] While there is currently no consensus on what constitutes best practice for calibrating a model[61], recently-published guidelines offer detailed guidance for model validation, which include the evaluation of a model's accuracy by comparing its outputs to external empirical data[80].

3.2.1. Model description

3.2.1.1. Model construction

We adapted and extended a previously-published HIV dynamic transmission model that was used to estimate the health benefits and costs of HIV prevention and treatment interventions in the United States[125,153,154], British Columbia, Canada[155-157], and Guangxi province, China[66]. We modified the compartmental model both to accommodate the distinctive features in HIV microepidemics across US cities[5], and to allow for assessment of a range of HIV treatment and prevention interventions to be evaluated jointly in future applications. For each demonstration city, the adult population aged 15-64 was partitioned into compartments on the basis of: biological sex; race/ethnicity (Black/African American [Black], Hispanic/Latino [Hispanic], and non-Hispanic White/others [White]); and HIV risk behavior type (MSM, people who inject drugs [PWID], MSM-PWID, and heterosexual [HET]). To account for within-group heterogeneity, MSM, MSM-PWID and HET were further partitioned into subgroups based on HIV sexual risk behavior intensity (high- vs. low-risk for each of the 3 risk groups), as defined by the proportion of MSM reporting condom-less sex with casual partners[158] (conforming to the CDC recommended indications for PrEP use[159]) for MSM and MSM-PWID, and by the proportion of individuals who had 5 or more sexual partners in the past 12 months[160] for HET. PWID and MSM-PWID were also classified based on engagement in opioid agonist treatment (OAT).

Individuals within each of these 42 groups (MSM: 6, MSM-PWID: 12; PWID: 12; HET: 12) progressed through health states outlined in Figure 3.1. Susceptible (HIV-uninfected) individuals could be screened for HIV prior to HIV infection, and high-risk MSM (including MSM-PWID) could access pre-exposure prophylaxis (PrEP). Following HIV infection, individuals progressed through acute infection (duration=1.7 months, range: 1-6.8)[161] and three CD4 cell count strata (CD4≥500, 200-499, and <200 cells/μL), and were classified according to diagnosis and treatment status as those infected but undiagnosed, diagnosed but ART-naïve, on ART and off ART. Health state transitions occurred at monthly intervals, with mortality a possible transition from each of the health states.

3.2.1.2. HIV transmission

HIV transmission occurred through three modes: heterosexual contact, homosexual contact, and needle/syringe sharing**.** We incorporated a mixture of assortative and proportional mixing by race/ethnicity and sexual risk behavior intensity[162] through Newman's assortativity coefficient, where a value of 0 indicates random mixing, and a value of 1 indicates complete assortative mixing[163] (see Appendix B Section 1.2 for details). The rate of transmission through homo- and heterosexual sex was a function of the probability of partnership, the number of sexual partnerships, the probability of condom use, and the probability of transmission per sexual partnership at each CD4 stratum. Similarly, transmission via needle/syringe sharing was a function of injection frequency, the probability of needle/syringe sharing, and transmission per shared needle/syringe at each CD4 stratum. These transmission rates were time-dependent, subject to changes in the distribution of PLHIV at different stages of disease progression, risk behaviours and scale-up of interventions. We assumed ART reduced the risk of sexual transmission by 91% (range: 79%-96%)[7,164], and the risk of transmission via needle/syringe sharing by 50% (range: 10%-90%)[157], while PrEP reduced transmissibility of HIV per unprotected sexual partnership and per needle/syringe sharing both by 60% (range: 56.3%-61.9%)[165]. We note that access to PrEP was only modeled among high-risk MSM and MSM-PWID population in this study. Furthermore, we also allowed for changes to people's risk behaviours, including following HIV diagnosis (reduction in the number of sexual partners)[166], OAT receipt (reduction in the frequency of injection drug use),[167] and access to syringe services programs (SSP) (reduction in the probability of needle/syringe sharing)[157].

3.2.1.3. Model parameters

All model input parameters were derived by a comprehensive evidence synthesis published separately[151]. We synthesized evidence from 59 peer-reviewed publications, 24 public health and surveillance reports, and executed primary analyses using 11 data sets to inform the 1,667 parameters needed to populate our model. Parameters ranked as best- to moderate-quality evidence comprised 47% of the 169 common (non-city-specific) parameters. In contrast, 61% to 63% all of all city-specific input parameters were populated with at least moderate quality evidence. The parameter grouping, common versus city-specific, is based on whether a common prior value and uncertainty range/distribution can reasonably be used across cities. For parameters with lower quality of evidence, we allowed greater variability, including wider uncertainty ranges or imposing more dispersed distributions (uniform or pert distribution).

3.2.2. Model calibration

A review of calibration methods by Stout et al. identified five key components, including identifying the calibration target variables, goodness-of-fit (GoF) metric, search algorithm, acceptance criteria and stopping rule[168]. An overview of the specifications for the calibration process adopted in this paper is presented in Table 3.1 and described in more detail below. The calibration routine was applied to each of the six cities separately by repeatedly adjusting a set of 'free' parameters until model projections matched empirical calibration targets. For each city, the model calibration period was set to 2012-2015 in order to capture at least two data points on both the calibration and validation variables.

3.2.2.1. Calibration targets

We selected calibration targets that provided the most concrete indicators of the course of each city-level microepidemic. Three sets of target data were chosen as our calibration targets for each city during the model calibration period 2012-2015: (1) the number of diagnosed PLHIV at each year end, stratified by sex, race/ethnicity, and risk group; (2) the annual number of new HIV diagnoses, separately for the overall estimate, among the Black population, and among MSM (including MSM-PWID), respectively; and (3) the annual number of all-cause deaths among diagnosed PLHIV, separately for the overall estimate, among Black individuals, and among MSM (including MSM-PWID).

These 17 calibration targets were available from city-specific annual surveillance reports from each city.

3.2.2.2. Selection of free parameters

We identified the most influential set of free parameters by applying the Morris method[64,169,170], an empirical parameter selection approach that systematically analyzes the impacts of variations of each input on model outputs. This method was chosen due to its efficiency, flexibility (e.g. no requirement for monotonicity), and capability to examine a parameter's influence at multiple time points[64,169,170]. All uncertain parameters determining model dynamics (thus excluding parameters used to determine initial population sizes) were assumed to be candidates for free parameters and were explored in this parameter selection process for each city. In the interest of maximizing transparency, we present point estimates, prior ranges, and calibrated ranges for these parameters in the Supplementary Appendix B.

3.2.2.3. Goodness-of-fit metric

A GoF metric serves as the objective function in an optimization procedure, measuring the accuracy of the model's predictions against the targets. While there is no consensus on the most appropriate GoF metric[61], we utilized an overall weighted GoF metric (global criterion), that was computed by a weighted sum of the individual calibration target fits, a common practice in addressing multi-objective optimization. The weighting factors allow the modellers to place preferences on the set of targets being evaluated[171].

Given the disparate scale and importance of the 17 targets, we used the weighted mean percentage deviation as the overall goodness-of-fit metric (shown in the following equation), with the calibration objective to minimize this metric by fitting with different sets of input parameters.

$$GoF_{overall} = \sum_{i} w_i * \frac{|proj_i - obs_i|}{obs_i}$$

where w_i is the weight assigned to the ith target, $proj_i$ is the model-projected result for the ith target, and obs_i is observed point estimate for the ith target. Smaller values of the GoF metric indicate a better fit to the observed data.

The weighting factors are usually imposed by assumption on the basis of the relative importance as well as the existence of biases of these targets[61]. We generated the weights using a best-worst method (BWM)[167,168] to elicit the perceived relative importance of each target from our Scientific Advisory Committee (SAC), for which we developed a brief questionnaire asking them to rank and compare each target in respect of their importance for the model to fit against (see further details and weight vectors in the Supplementary Appendix B).

3.2.2.4. Search algorithm

The search algorithm determines the best fitting sets of parameter values, drawn from their plausible ranges, which optimize the GoF metric such that the model can reproduce the observed historical trends. We adopted a mixed calibration approach with two distinct steps. Latin hypercube sampling was first applied to draw 10,000 parameter sets from predefined distributions as the initial simplexes (starting values), from which the Nelder-Mead search algorithm was performed to minimize the overall GoF metric. Latin hypercube is a multidimensional grid sampling method enabling the whole parameter space to be covered efficiently[172]. The Nelder-Mead algorithm is an iterative, directed-search method with high computational efficiency and superior performance over manual and random calibration[173]. We used Latin hypercube sampling to generate 10,000 simplexes for the Nelder-Mead algorithm to sufficiently explore the parameter space to overcome its potential drawback of settling on local, rather than global optima, as well as to facilitate uncertainty analysis, as recommended by the ISPOR-SMDM guidelines[60].

3.2.2.5. Acceptance criteria

Choosing an acceptance criteria entails defining acceptable sets of input parameter values by defining either the worst acceptable GoF level or the acceptable ranges for the targets or the GoF metric[61]. With each simplex seeded, the Nelder-Mead algorithm seeks to produce one optimal set of input parameter values that locally minimize the overall GoF metric, while we only deemed the calibrated parameter sets that best minimize GoF (i.e. below 20th percentile) as acceptable. The cutoff of 20th percentile was determined by the actual GoF distributions to warrant the inclusion the densest proportion to the left of the mode providing the best and most similar GoF.

3.2.2.6. Stopping rule

The stopping rule determines whether the calibration process is complete, usually defined by deriving a sufficient number of acceptable input sets[61]. In this exercise, we seeded the Nelder-Mead optimization algorithm with 10,000 simplexes (that varied only by starting seed), by repeating the same process, to generate 10,000 calibrated parameter sets, from which we selected the 2,000 best-fitting sets with the minimal GoF metric as the acceptable samples for subsequent analysis.

3.2.3. Model validation

Model validation refers to the process of evaluating a model's accuracy in making relevant projections[80]. It entails a comprehensive evaluation of how well the model performs, from the problem construct to the credibility of model results, against a variety of internal and external inputs, including expert opinions, clinical knowledge, and empirical evidence. In accordance with ISPOR-SMDM guidelines[80], based on the 2,000 calibrated parameter sets, we formally assessed the internal, external and face validity of our model, as follows (Table 3.2).

3.2.3.1 Internal validity

Internal validation investigates and verifies the accuracy and consistency of all mathematical equations and program coding. To secure a high level of internal validity, we performed a series of checks:

(1) Each mathematical equation and program coding script was cross-checked by at least one other analyst other than the developer.

(2) Given its complexity, we performed double programming for the force of infection module where two programmers independently coded the functions until the results were identical.

(3) An extensive model walk-through was performed internally wherein detailed model structure, underlying assumptions, and corresponding codes were presented by the developers and checked by other team members.

(4) We ran extreme value analyses on several scenarios and assessed model predictions against our anticipated outcomes (Supplementary Appendix).

3.2.3.2 External validity

External validation entails comparison of city-specific model projections to external estimates of key clinical and epidemiological data not used in the model[83,84,174]. We

selected HIV incidence over 2012-2015 as the external validation target, both for the total estimates and among the MSM population (including MSM-PWID). Independent, city-level annual incidence estimates between 2012-2015 were only reported in NYC and partially in LA (2012-2013), while estimates for other cities were otherwise triangulated from annual state-level incidence estimated by the CDC[174] (triangulation process detailed in the evidence synthesis[151]). We selected these endpoints based on their availability from a common, authoritative source, the availability of confidence intervals for each estimate, and their importance in decision-making.

3.2.4. Establishing the status quo scenario in each city

The status quo scenario for each city was defined by holding treatment and prevention service levels (including the proportion of PLHIV being tested, receiving treatment and accessing OAT and PrEP) at the most recent year for which data was available. In addition, we held constant the proportion of people in high- and low-risk strata. To account for heterogeneity in the rate of aging, we used surveillance data to derive city-level, PLHIV-specific maturation rates (i.e. PLHIV who are 64 turning 65). Finally, we modelled a dynamic cohort allowing model entry and exit (more details in Supplementary Appendix B) to match external adult population growth projections throughout the study time horizon for each city, accounting for changes in ethnic compositions.

3.2.4.1 Assessing the face validity of longitudinal status quo projections

Face validation refers to the subjective review of the model projections by individuals with clinical and epidemiologic expertise in the disease area. Following each of the above steps, we prepared a report for each city detailing 25-year (2016-2040) status quo projections on population growth, stratified by race/ethnicity; longitudinal projections of the number of people in each of the primary HIV stages of the model; rates of incidence and new diagnoses, overall and stratified by race/ethnicity and by risk group; and rates of incidence and new diagnoses among MSM, overall and stratified by race/ethnicity. At least one clinical/epidemiological expert in our SAC from each city was invited to provide qualitative responses on the projections for their city and the modeling team followed-up individually with respondents to resolve any discrepancies.

3.3. Results

3.3.1. Model calibration

We identified 381 independent parameters as candidate free parameters in the calibration process, 37 of which were common across cities, 54 capturing sexual risk behaviours, 56 characterizing health service delivery, and 234 dictating movement between ART states (including from/to death and off ART states). Following application of the Morris method, we included 52 unique (176 in total) free parameters in the model calibration across all cities (Table 3.3). The set of free parameters selected varied across cities, driven in part by variations in race. In cities like Atlanta and NYC where the HIV epidemic is mainly concentrated in the Black population, the behavioural parameters for this population were more likely to be selected, as compared with cities like LA and Miami where parameters determining behaviours for the Hispanic population were more often chosen.

Following calibration, we compared the calibrated values (median and 95% credible intervals [CI]) of free parameters against their prior values and ranges (Supplementary Appendix Figure A2). Post-calibration values differed across cities. For example, the probability of MSM transmission (at CD4 ≥ 500) was calibrated to be higher in LA (0.0674, 95% CI: [0.0250-0.1000]) compared to Atlanta (0.0251, 95% CI: [0.0250, 0.0433]).

The resulting epidemiological estimates from the 2000 best-fitting calibration runs demonstrated a good fit to most targets. Figure 3.2 shows the model projections for the number of new HIV diagnoses (total and among MSM) against their corresponding targets (two targets deemed most important by our SAC) for each city. The overall mean GoF, based on the 2,000 best-fitting parameter sets, differed across cities, ranging from 0.0174 in NYC (range: 0.0167-0.0176) to 0.0861 in Atlanta (range: 0.0844-0.0868, Supplementary Appendix B Figure A3). The bimodal distribution for GoF values observed in Atlanta and Miami indicate the presence of local optima at poorer levels of GoF. Model calibration results for all 17 targets are presented in Supplementary Appendix B Figure A4. While calibration yielded close matches to most targets in most cities, we also observed mismatches for some of the mortality targets. In particular, our model consistently overestimated the number of all-cause deaths in comparison to the three

death-related targets in Atlanta, even with mortality-related free parameters being calibrated to the lower ends of their respective ranges, likely due to an underreport of the target mortality estimates.

3.3.2. Model validation

With the 2,000 calibrated parameter sets, most model projections (2012-2015) fell within the confidence interval of the external validity targets. Figure 3.3 shows the model projections for the rate of total HIV incidence against the external estimates (after transforming the absolute number of infections to rates). The proportion of annual incidence projections, total and for MSM, that fit within the confidence interval varied by cities, from 100% in NYC to 21% in Miami.

We assessed the face validity of our model projections via survey distributed to our SAC. We performed further evidence collection and reanalysis to resolve any discrepancies between model projections and experts' expectations. Further details regarding this process are available in the Supplementary Appendix B.

Over a 25-year time horizon with all HIV services maintained at their 2015 levels (except PrEP, for which we incorporated data up to 2017 to acknowledge its rapid scale-up), our model predicted that the overall rate of new infections would drop in Atlanta (from 45 [95% CI: 43-51] to 37 [33-41] cases per 100,000 population), NYC (from 31 [31-32] to 15 [12-17] cases per 100,000 population) and Seattle (from 15 [14-16] to 10 [8-14] cases per 100,000 population, Figure 3.3, Panel A, E and F), while remain relative constant in LA at 33-34 [27-38] cases per 100,000 population (Figure 3.3, Panel C). In contrast, the rate of new infections was projected to rise slightly in Baltimore (from 27 [26-28] to 33 [27-35] cases per 100,000 population, Figure 3.3, Panel B). Projections for Miami suggest a slight increase in the rate of new infections in the first few years, ultimately stabilizing at 102 [81-120] cases per 100,000 respectively (Figure 3.3, Panel D). Projections used in the face validation process, displaying overall and stratified estimates and credible ranges of incidence and new diagnoses, are presented the Supplementary Appendix B. Model projections suggest the risk for HIV infection will remain highest among MSM and MSM-PWID and these two risk groups will continue to contribute the majority of all new incident cases across cities: 69.8% [62.3%-76.3%] in Seattle to 90.9% [87.7%-92.0%] in Baltimore in 2040. Further, while our model estimated that Black individuals will continue to have the

highest rate of HIV incidence across all cities, it also suggests Hispanic MSM will contribute most to the increasing rate of HIV incidence in Miami and LA (Appendix B Figure A6).

3.4. Discussion

We have detailed our process for calibrating and validating a dynamic HIV transmission model to six US cities with disparate HIV microepidemics using a systematic and empirical approach to determining the most influential parameters necessitating calibration. The model provided an excellent fit to the calibration targets across cities, particularly to those determined to be of the greatest importance. On the basis of the 2,000 best-fitting calibrated parameter sets, short-term external validation yielded a majority of incidence projections that were within the uncertainty range for 5 of 6 cities, while the face validity of the long-term status quo epidemiological projections was confirmed with our SAC.

The status quo projections in the selected cities predict the HIV epidemic will stabilize in most urban centers at current service levels, though greater efforts will be required if the US is to achieve its goal of ending the HIV epidemic by 2025[175]. While we predicted that incidence would decrease or remain stable in Atlanta, LA, NYC and Seattle, we also projected a slight increase in the incidence rate in Baltimore and Miami, driven primarily by projected increases in incidence among Black MSM (Baltimore) and Hispanic MSM (Miami).

Disparities in overall incidence correspond to the current features of the distinct city-level microepidemics, and the current level of services available for HIV treatment and prevention. Most notably, substantial resources have been devoted to the control of HIV in NYC and Seattle, which have aggressively combatted incidence in the MSM and PWID populations, and have led the nation in the expansion of PrEP, particularly for MSM[5].

From a methodological standpoint, we found that some parameters were consistently calibrated to the lower/higher end of prior ranges, implying either: (1) the model over-/underestimated these parameters; (2) the underlying evidence for the input parameters were biased or inconsistent; or (3) the model simply captured the dynamics in question too coarsely. For example, the number of homosexual partners were consistently

calibrated towards the lower bound of the empirical estimates for White high-risk MSM across all cities, while to the upper bound for Black high-risk MSM. This difficulty in closely reproducing the racial disparities in HIV incidence among MSM has also been noted in a recent modeling study by Goodreau et al[54]. Further, sexual risk behaviour parameters (such as the number of sexual partners and the probability of condom use) and per-partnership transmission probabilities were more likely to be selected for calibration. Collecting additional information on these parameters may help reduce the potential opportunity cost from a suboptimal decision. Value of information analysis[70,71] can estimate a monetary value for additional research to reduce uncertainty in these critical domains, and will serve as an important subsequent step in furthering this argument.

Despite the importance of validating the accuracy of model projections against empirical data on outcomes of interest[176], external validation has yet to become a standard component of the model development process.[177] Best-practice guidelines have noted that it may not be possible to establish an absolute criteria to assess the validity of a model, and that one of the key impediments to standardizing the validation process is the availability of target data not previously used to inform the model. In addition, assessing how close a model's predictions fit the external targets remains mostly subjective[177], particularly when there is a need to incorporating uncertainty of the validation targets (as opposed to trying to fit a target to a point estimate). Specifically, determining HIV incidence in city-level microepidemics poses challenges; these estimates are typically generated at the state-level, and even estimates generated at a higher level of aggregation are subject to limitations[178]. In each of our cities aside from Miami, a majority of the incidence predictions used for external validation were within the externally-estimated uncertainty range. In a growing epidemic like Miami, and particularly given its relatively low HIV service levels, the discrepancy we found between model projections and short-term incidence validation targets may reflect the long delay between HIV infection and diagnosis. Nonetheless, experts from our SAC confirmed the validity of our model projections for the long-term trend of the epidemic in Miami.

We aimed for comprehensive and transparent reporting of our calibration and validation process to enhance the credibility and reliability of our results, hoping that this effort can help inform the standardization of methods for model calibration and validation and promote better integration of locally-oriented modelling in decision-making. Despite existing guidelines on model calibration and validation, substantial subjectivity remains in

the process, particularly in the selection of parameters for calibration[61,64] and determination of the summary measure of model fit when multiple targets are used[10,11,36]. While we adopted the Morris method[169] to establish an objective criteria for free parameter selection, the technique also substantially improved the efficiency of the calibration. Establishing the weight metric for summary GoF is another common challenge, and we used the best-worst method[179,180] to synthesize information on the preferences of our SAC on each target and solve the weight metric from these preferences. Finally, we also leveraged the expertise of our SAC to assess the face validity of our 25-year status quo scenario projections. The approach proved useful not only in refining the model and its estimates, but also in communicating both the functioning and limitations of our model to a multidisciplinary audience. It is possible this approach can be further refined and extended to include a broader range of public health practitioners and policymakers.

Our analysis was not without limitations. First, we imposed a relatively simple proportional mixing assumption among needle/syringe-sharing contacts, rather than a more complex structure that may better approximate PWID networks[181]. Also, we modelled HIV infectivity indirectly through stages of disease progression based on CD4 cell counts rather than viral load, a limitation we have previously outlined[155]. However, these approximations were consistent with the precision of available evidence and was sufficient in replicating the city-level HIV epidemics with a high degree of precision. Second, drug resistance is not explicitly modeled, but it has been accounted for in disease progression estimates, though resistance levels are stably low and likely to decrease with broader access to new medication regimens[182]. Third, the model is not age-structured. Given the existing complexity of the model, adding age strata would increase the number of health states substantially, with limited ability to populate these health states with data specific to their description. Instead, we restricted the study population to individuals aged 15-64 to reduce the impact of age on some risk factors. Fourth, we only explicitly modeled PrEP among high-risk MSM. This is in line with current guidelines prioritizing PrEP among individuals at high risk of infection and previous evidence that PrEP may not be cost-effective for other populations[183-185]. Our future work with this model will explore the cost-effectiveness of PrEP for other risk groups. Fifth, one difficulty associated with the choice of a calibration search algorithm such as the Nelder-Mead algorithm is its possibility to converge on local optima. To remedy this potential problem, we randomly drew 10,000 sets of starting values for the algorithm, ensuring the parameter space was adequately

covered by the search strategy and substantially improving the likelihood of capturing the global optima. We aim to append the 2,000 best-fitting calibrated parameter sets with samples for all other uncalibrated parameters (aside from parameters defining initial values in each compartment), drawn from their prior distributions to support probabilistic sensitivity analysis of our assessments of combination implementation strategies for each city[64]. Lastly, cross-validating this model to assess its structural uncertainty[80], remains a topic for future research, as comparable city-level models are developed.

We provided a comprehensive and transparent description for the calibration and validation of a dynamic HIV transmission model to six US cities with diverse HIV microepidemics. The resulting model projections will serve as status quo scenarios in each city to identify optimal combination implementation strategies for the HIV treatment and prevention services we have considered in this model, including HIV testing, treatment, SSP, OAT and PrEP. We believe this standardized framework can be applied to diverse settings and disease areas, further underlining the potential value of this approach.

Table 3.1. Specifications for calibration process

Key elements[61]	Calibration specifications
Target	Total number of diagnosed PLHIV (2012-2015) • MSM: race/ethnicity • PWID: total • MSM/PWID: total • Heterosexual: gender x race/ethnicity Annual number of new HIV diagnoses (2012-2015) • Total • Black/African American • MSM Annual number of all-cause deaths among PLHIV (2012-2015) • Total • Black/African American • MSM
Free parameter	The set of free parameters for calibration is selected by Morris method: randomized one-factor-at-a-time sensitivity analysis to identify parameters leading to the most significant uncertainty in target outcomes
Goodness-of-fit metric (GoF)	Weighted mean percentage deviation: target weights determined by collecting and analyzing SAC's preferences using best-worst method
Search algorithm	The Latin hypercube sampling is applied to draw multiple sets of parameter values from their predefined distributions as the simplexes, from which the Nelder-Mead search algorithm was performed to optimize the overall GoF metric
Acceptance criteria	The set of parameter values that minimize the GoF metric with each simplex seeded
Stopping rule	The same calibration routine is repeated 10,000 times with each simplex seeded to derive 2,000 best-fitting parameter subsets

Table 3.2. Specifications for validation process

Key elements[80]	Validation specifications
Internal	Extensive checks and evaluations • Cross-check on all codes and equations • Double-coding force of infection module • Extreme scenario analysis • Weekly meeting and updates
External	Validation target – new HIV incidence (range) • Total • MSM and MSM/PWID
Face	Continuous consultation with SAC • Evidence synthesis • Model development Projection outcomes • Population dynamics, by race/ethnicity • Rate of new infections, overall, by race/ethnicity and by risk group • Rate of new diagnoses, overall, by race/ethnicity and by risk group • Rate of new infections among MSM, overall and by race/ethnicity • Rate of new diagnoses among MSM, overall and by race/ethnicity

Table 3.3. Model parameters selected as free-parameters by Morris method

Common Parameter	*ATL*	*BAL*	*LA*	*MIA*	*NYC*	*SEA*
1.3 Population Dynamics - Mortality Rate						
PLHIV (CD4 200-499)	■	■	■	■	■	■
PLHIV (CD4 <200)	■	■	■	■	■	■
PLHIV - PWID multiplier (CD4 200-499)	■	■	■	■	■	■
PLHIV - PWID multiplier (CD4 <200)	■	■	■	■	■	■
2.1 Sexual Risk Behaviors - Number of Sexual Partner Multipliers						
PWID relative to HET	■		■			■
Decrease in sexual partners post-diagnosis	■	■	■	■	■	■
2.2 Injection Risk Behaviors						
Injection frequency		■	■		■	■
Decreased probability of injection sharing post-diagnosis		■	■		■	■
SSP effect on reducing injection sharing						■
2.4 Probability of Transmission (per partnership)						
Sex - Female to Male (CD4 ≥500)	■		■	■	■	■
Sex - Female to Male (CD4 200-499)	■					
Sex - Female to Male (CD4 <200)	■			■		
Sex - Male to Female (CD4 ≥500)	■	■	■	■	■	■
Sex - Male to Female (CD4 200-499)	■					
Sex - Male to Female (CD4 <200)	■					
Sex - Male to Male (CD4 ≥500)	■	■	■	■	■	■
Sex - Male to Male (CD4 200-499)	■	■	■	■	■	■
Sex - Male to Male (CD4 <200)	■	■	■	■	■	■
Shared injection (CD4 ≥500)	■	■		■		■
Shared injection (CD4 200-499)		■				
Shared injection (CD4 <200)		■				
Transmission probability multiplier (Acute HIV)	■	■	■	■	■	■
ART effect on reducing transmission - Sexual		■	■	■	■	■
ART effect on reducing transmission - Shared Injection		■				
Condom effect on reducing transmission - Heterosexual Sex	■		■			■
Condom effect on reducing transmission - Homosexual Sex	■	■	■	■	■	■
3.1 HIV Testing - Annual Change in HIV Testing Rate	■	■	■	■	■	■
3.5 HIV Disease Progression Transition Rate from Acute to Chronic HIV	■	■	■	■	■	■
City-Specific Parameter	***ATL***	***BAL***	***LA***	***MIA***	***NYC***	***SEA***
2.1 Sexual Risk Behaviors - Number of Sexual Partners						

Heterosexual partners, White, Low-risk MSM	■					
Heterosexual partners, White, High-risk MSM				■		■
Heterosexual partners, Black, High-risk MSM	■					
Heterosexual partners, Hispanic, High-risk MSM				■		
Heterosexual partners, Male, White, High-risk HET	■					
Heterosexual partners, Male, Black, High-risk HET	■		■			
Heterosexual partners, Female, White, High-risk HET	■				■	
Heterosexual partners, Female, Black, High-risk HET	■					
Heterosexual partners, Female, Hispanic, High-risk HET			■			■
Homosexual partners, White, Low-risk MSM		■				■
Homosexual partners, Black, Low-risk MSM		■	■		■	
Homosexual partners, White, High-risk MSM	■	■	■	■	■	■
Homosexual partners, Black, High-risk MSM	■	■	■	■	■	■
Homosexual partners, Hispanic, High-risk MSM	■	■	■	■	■	■
2.1 Sexual Risk Behaviors - Condom Use Probability						
Heterosexual, Male, White, High-risk HET	■					
Homosexual, Male, White, Low-risk MSM						■
Homosexual, Male, Black, Low-risk MSM		■	■	■	■	
Homosexual, Male, Hispanic, Low-risk MSM			■	■	■	
Homosexual, Male, White, High-risk MSM		■	■	■	■	■
Homosexual, Male, Black, High-risk MSM		■		■	■	■
Homosexual, Male, Hispanic, High-risk MSM		■		■	■	■
2.1 Assortativeness of Heterosexual Partnership Paring, High-risk Black	■					
3.2 ART Initiation						
Proportion linked to care post-diagnosis (CD4 ≥500), Male, Black, PWID					■	
Proportion linked to care post-diagnosis (CD4 ≥500), Female, Black, PWID		■				

ATL: Atlanta; BAL: Baltimore; LA: Los Angeles; MIA: Miami; NYC: New York City; SEA: Seattle; Shaded cells represent parameters selected for calibration.

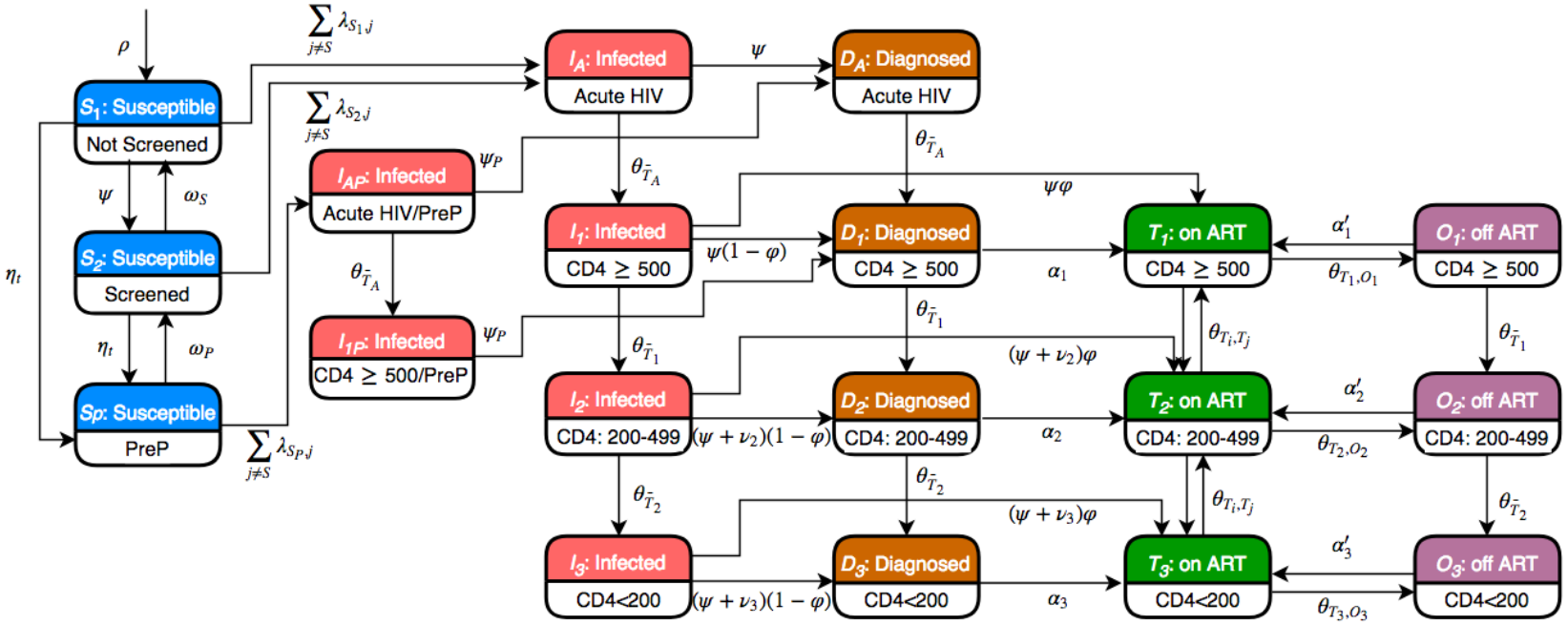


Figure 3.1. Model schematic diagram

The schematic shows the 19 compartments that constitute each of the 42 population groups in the model. A key for the symbols denoting transitions within the model is available in the Supplementary Appendix.

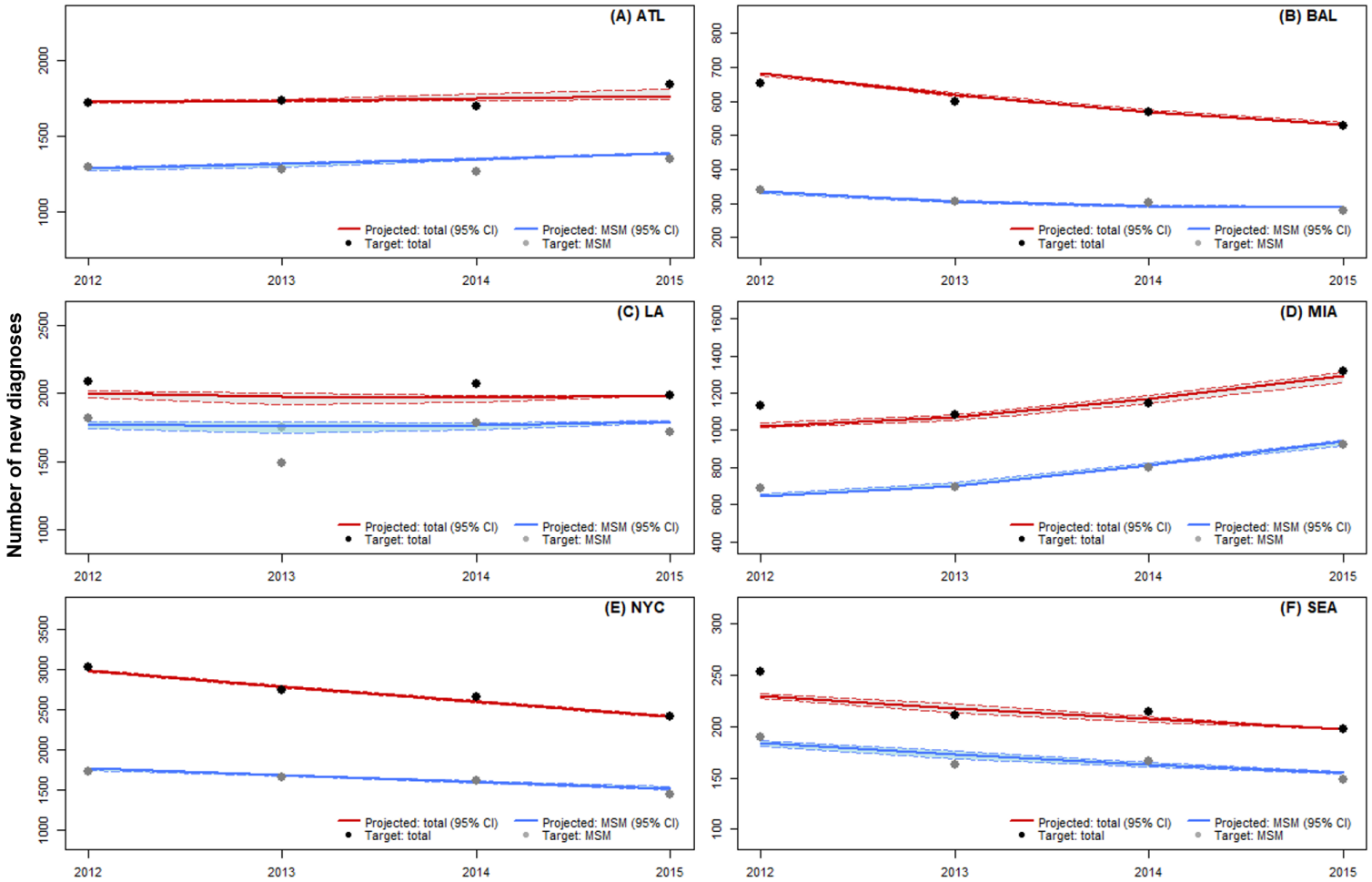


Figure 3.2. Model fit of new diagnoses for calibration

(A) ATL: Atlanta; (B) BAL: Baltimore; (C) LA: Los Angeles; (D) MIA: Miami; (E) NYC: New York City; (F) SEA: Seattle; 95% CI: 95% credible interval. MSM: men who have sex with men (excluding MSM-PWID)

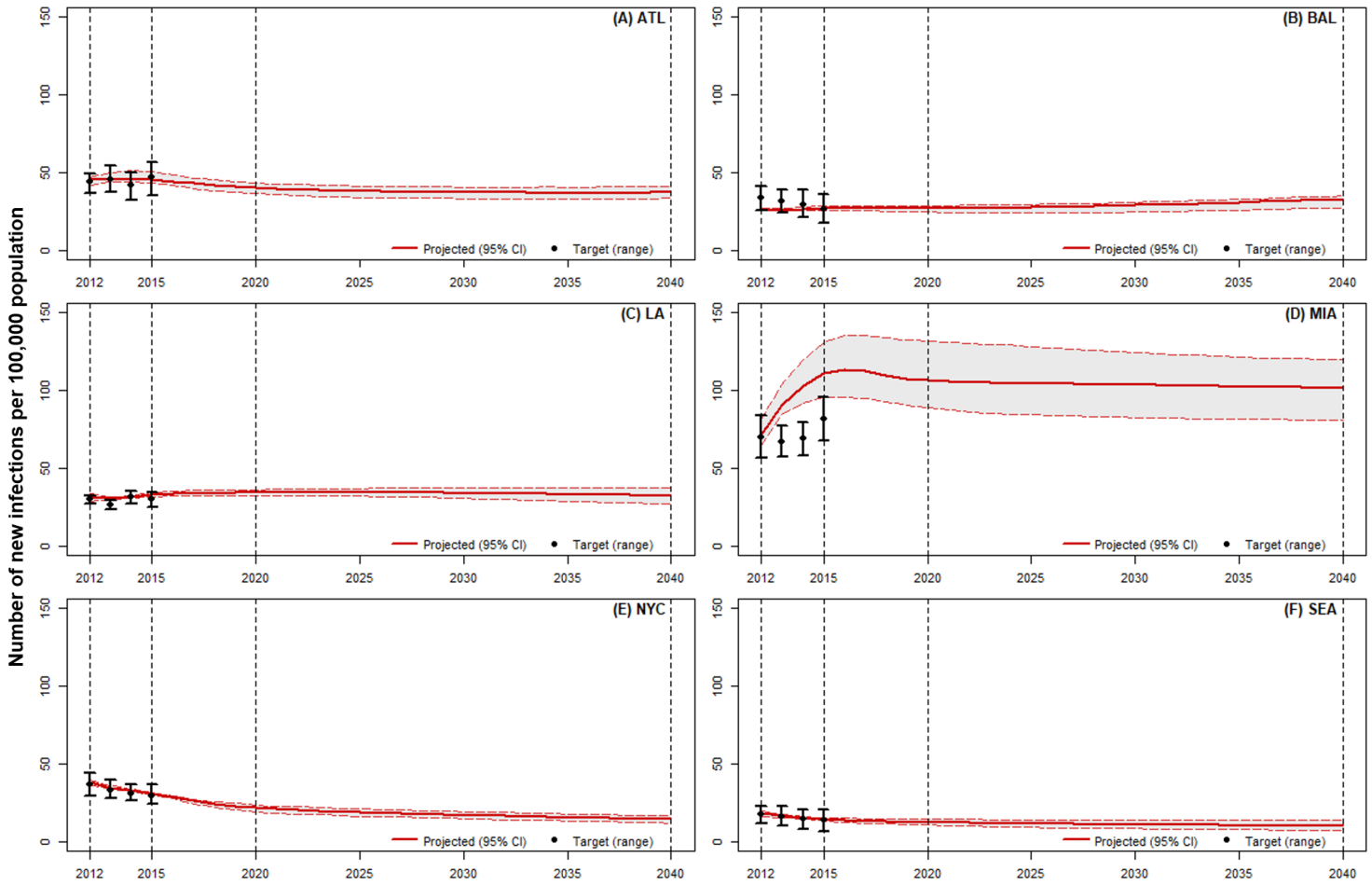


Figure 3.3. Model external validity and status quo projections for the rate of new incidence
Year 2012-2015: calibration period; Year 2016-2040: projection period; Year 2021-2040: evaluation period. (A) ATL: Atlanta; (B) BAL: Baltimore; (C) LA: Los Angeles; (D) MIA: Miami; (E) NYC: New York City; (F) SEA: Seattle.

Chapter 4.

Prioritizing additional data collection to reduce decision uncertainty in the HIV/AIDS response in 6 US cities: a value of information analysis

Background: The ambitious goals of the US "Ending the HIV Epidemic" will require a targeted, context-specific public health response. Model-based economic evaluation provides useful guidance for decision-making but is subject to uncertainty. **Objectives**: To quantify the value of collecting additional data to reduce decision uncertainty in selecting combination implementation strategies to reduce the public health burden of HIV/AIDS in 6 US cities. **Methods**: We used a dynamic compartmental HIV transmission model developed for 6 US cities to evaluate the cost-effectiveness of a range of combination implementation strategies. Using a metamodeling approach with nonparametric and deep learning methods, we calculated the expected value of perfect information (EVPI), representing the maximum value of further data collection to eliminate decision uncertainty, and the expected value of partial perfect information (EVPPI) for key groups of parameters that would be collected together in practice. **Results**: The population EVPI ranged from $59,683 (Miami) to $54,108,679 (Los Angeles). The rank ordering of EVPPI results on key groups of parameters were largely consistent across cities and highest for parameters pertaining to HIV risk behaviors, probability of HIV transmission, health service engagement, HIV-related mortality, health utility weights and health care costs. Los Angeles was an exception, where parameters on retention in pre-exposure prophylaxis ranked highest in contributing to decision uncertainty. **Conclusions**: Funding additional data collection on HIV/AIDS may be warranted in Baltimore, Los Angeles and New York City. Value of information analysis should be embedded into decision making processes on funding future research and public health intervention.

4.1. Introduction

Despite over $20B of annual federal funding directed towards the domestic HIV/AIDS response, 38,000 new cases were diagnosed in 2017 in the USA[186,187]. The recently announced "*Ending the HIV Epidemic: A Plan for America*" initiative has set ambitious goals to reduce new HIV infections by 75% within 5 years and by 90% within 10 years[188]. Achieving these goals necessitates "an infusion of resources to employ strategic practices in the right places targeted to the right people to maximize impact and end the HIV epidemic in America"[188]. While a range of tools to end the HIV epidemic are available, resources – both financial and human – are scarce and compete with other priorities outside HIV[13].

As the global public health response moves towards localized combination implementation strategies to combat HIV/AIDS[11-13,99], economic models are increasingly used to inform health decision-making in the care and prevention of HIV/AIDS. They provide a unified framework to quantify the health and economic value of different strategies while accounting for their synergistic effects[34,35,89]. Adequately characterizing city-level HIV microepidemics in a simulation modeling framework is data-intensive, particularly given the substantial disparities in access to services and health outcomes observed across HIV risk and race/ethnic groups in the US[189]. The inherent uncertainty in estimating many of the required parameters, which span population composition and dynamics, health service engagement, disease progression, HIV transmission, cost and utility weights[151,189], may obscure value-based recommendations and lead to potentially suboptimal decisions.

The US has invested in a range of multi-site surveillance studies that provide vital information for simulation modeling, including HIV risk behaviors from the National HIV Behavioral Surveillance (NHBS); ART surveillance data from Medical Monitoring Project from the US Centers for Disease Control and Prevention (CDC) and clinical data from the HIV Research Network[151]. Nonetheless, our previous study found a paucity of representative, high-quality local administrative data, particularly on rates of HIV testing and ART engagement[151]. This is in many cases due to structural barriers where data are either not systematically collected or organized in isolated silos, creating barriers to access and linkage with other data sources[190]. The infrastructure to facilitate data collection is costly to construct, and not all model parameters will impact recommendations equally. Efforts to collect additional data should focus on those with the most potential to reduce uncertainty in funding allocation decisions[191].

Value of information (VoI) analysis quantifies the opportunity cost of acting on suboptimal recommendations due to model uncertainty. It also helps guide efforts to ensure the limited resources available for data collection are focused on the most influential parameters for a given decision[70]. Expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI) estimate the value of eliminating uncertainty from all parameters jointly and from a subset of parameters respectively, providing guidance for setting research priorities. The conventional approach to EVPPI is based on a nested Monte Carlo procedure that is computationally costly, particularly for a complex model with many competing interventions[75,192,193]. Metamodeling, a tool that simplifies the relationship between the inputs and outputs of a simulation model[74], has been increasingly used as an alternative method to expedite value of information analysis[192,194]. A previous EVPPI analysis using a metamodeling approach shortened the computation time from weeks to minutes while consistently yielding similar estimates[75].

On the basis of a comprehensive evidence synthesis[151]; a systematic model calibration and validation[195]; and an extensive economic evaluation of 16 evidence-based interventions individually[67] and in combination[69] for 6 US cities with diverse HIV microepidemics, we identified combination strategies to address the HIV/AIDS epidemic in each city along with uncertainty underlying the selection of the optimal (highest-valued) strategy. A decomposition of the sources of this uncertainty, coupled with a judgement on the value of eliminating it in each setting, can guide future research efforts focused explicitly on reducing decision uncertainty. Our objective is to quantify the value of collecting additional data to eliminate decision uncertainty regarding the cost-effectiveness of HIV combination implementation strategies in six US cities. We also aimed to identify future research priorities through EVPPI analysis on key groups of uncertain parameters using a metamodeling approach with advanced regression techniques.

4.2. Methods

4.2.1. Model Description

We adapted a previously published dynamic compartmental HIV transmission model[156,157,195,196] to simulate the HIV microepidemics in six US cities: Atlanta, GA; Baltimore, MD; Los Angeles (LA), CA; Miami, FL; New York City, NY; and Seattle, WA. Each city features distinct epidemiological characteristics and public health responses to HIV[99]. In the model, the adult population aged 15-64 in each city was partitioned by biological sex, HIV risk group, race/ethnicity,

sexual risk behavior level (high- vs. low-risk), and access to opioid agonist treatment among people who inject drugs (42 population groups). Individuals within each group progress through 19 health states illustrated in Appendix C Figure A1. We considered dynamic HIV transmission through heterosexual contact, homosexual contact or needle sharing. The model captured heterogeneity in the risk of HIV transmission, maturation, mortality, and accessing health and prevention services. Full details about the model are available in prior articles[67,69,195].

The model's input parameters were grouped in seven categories: (1) Initial population estimates and population dynamics [N=1,074]; (2) parameters used to calculate the probability of HIV transmission [N=201]; (3) screening, diagnosis, treatment and HIV disease progression [N=312]; (4) HIV prevention programs [N=23]; (5) the costs of medical care [N=30]; (6) health utility weights [N=26]; and (7) intervention parameters (e.g. effect, scale of delivery and cost) [N=184]. The derivations, point estimates, uncertainty distributions and quality of evidence were reported for all model parameters in a manuscript detailing the evidence synthesis for this project[67,151]. For parameters with lower quality of evidence, we allowed greater variability, including wider uncertainty ranges or imposing more dispersed distributions (e.g. uniform or pert distribution)[60]. Although parameters were assumed to be independent, for potentially correlated parameters with an empirically established rank ordering (e.g. quality-adjusted life year (QALY) weights, costs for different health states), we used a recently-proposed method[68] to establish joint uncertainty distributions from parameters' marginal distributions and their ordinal preferences.

4.2.2. Cost-effectiveness analysis

We evaluated the cost-effectiveness of 16 evidence-based HIV interventions and their combinations within three domains: **HIV prevention**, including Syringe Service Program, medication for opioid use disorder (MOUD), either buprenorphine or methadone, targeted PrEP for high-risk men who have sex with men (MSM); **HIV testing**, including opt-out testing in the hospital emergency room and in primary care, electronic medical record (EMR) testing offer reminder, nurse-initiated rapid testing, MOUD initiated rapid testing; and **Treatment engagement**, including case management (ARTAS) for ART initiation, care coordination for ART retention, targeted care coordination (CD4<200), EMR ART engagement reminder, RAPID ART initiation, enhanced personal contact for ART re-initiation, ART re-linkage program. We considered combinations of the 16 interventions for each city, excluding any that would not practically be implemented jointly, for a total of 23,040 unique combinations. After identifying those that produced the greatest health benefits while remaining cost-effective[69], we conducted

probabilistic sensitivity analysis by comparing the selected strategies against those producing the most proximal value to quantify uncertainty in the recommended strategy. For practical reasons, these analyses were based on initially-calibrated parameter sets and did not incorporate uncertainty from initial population estimates.

Consistent with our previous studies, we maintained the same evaluation time horizon of 20 years (2020-2040) to capture the long-term individual benefits of ART and 2nd-order transmission effects. All costs were reported in 2018 US dollars, and we chose a base cost-effectiveness threshold of $100,000/QALY while varying this threshold in three discrete levels ($50,000/QALY, $100,000/QALY, and $150,000/QALY) for EVPI analysis. Decisions were made by choosing the strategy i with the highest net monetary benefit (NMB), as estimated by:

$$NMB_i = QALY_i \times Threshold - Cost_i$$

4.2.3. Probabilistic Sensitivity Analysis

The probabilistic sensitivity analysis (PSA) dataset for input parameters was constructed by randomly sampling all uncertain parameters (including initial population estimates) simultaneously from their prior distributions or fitted joint distributions. The PSA dataset also contains the estimated total costs and QALYs associated with each combination implementation strategy resulting from each set of the PSA inputs (representing one PSA simulation). As a vast majority of the over 23,000 competing strategies we estimated had a zero or near-zero probability of being the health-maximizing strategy for a given threshold, we performed PSA only on the subset of combination implementation strategies with a non-zero probability of selection.

4.2.4. Value of Information Analysis

VoI analysis provides a systematic approach to quantify the value of research in reducing decision uncertainty. EVPI represents the maximum a decision maker should be willing to pay to eliminate uncertainty from all model parameters. For a given cost-effectiveness threshold, we first evaluated and ranked the NMB of all combination strategies keeping all input parameters in their point estimates as the base case (deterministic) and identified the 25 combination strategies with the highest NMB for each city. We then generated 2,000 sets of PSA model inputs, conducted PSA on these 25 highest-valued strategies and estimated their corresponding NMB. We chose 25 to make the problem tractable given computation limitations and the final number was

determined through an iterative process: at each threshold level, we gradually expanded the inclusion of top-ranked strategies from 5 to 25 in an increment of 5 while assessing their probabilities of being the highest-valued in the 2,000 PSA simulations. We proceeded the process until we found that strategies with deterministic NMB ranked below 20 had nearly zero probability to be selected as optimal. We then calculated the opportunity loss for a given simulation as the difference of NMB between the optimal strategy (i.e. with highest NMB) in a given simulation and the overall optimal strategy - the combination strategy with the highest expected NMB across all simulations. Finally, EVPI was estimated by averaging the opportunity loss across all simulations. Given that our model is developed at the population level, the computed EVPI directly represents a population estimate, thus requiring no extrapolation. We also expressed this uncertainty as a cost per million residents to clarify relative differences across cities.

EVPPI provides an estimate of the value of eliminating uncertainty for specific parameters or groups of parameters. The value of collecting additional information for particular parameters depends on both their influence on the cost-effectiveness of competing strategies and the extent of its uncertainty[197]. Using a metamodeling approach[192,194], we modeled the opportunity loss of each strategy (same as in EVPI) as a function of the parameters of interest at the base threshold of $100,000/QALY. We adopted two advanced metamodeling methods with a generalized additive model (GAM) and a deep learning artificial neural network (ANN) model to approximate the inner expectation of the conventional nested Monte Carlo approach[75,192,193]. In simulation models like ours where the relationship between opportunity loss and parameters is non-linear, these methods provide highly flexible functions requiring no parametric assumptions and are found to outperform linear modeling approaches[198,199]. The GAM is efficient and more straightforward to implement with high precision, but is constrained by the size of regression parameters because the required PSA sample size increases exponentially[192]. We therefore used GAM for each individual parameter and the ANN model, which can approximate complex, non-linear relationships in data with high dimensionality, to estimate the full EVPPIs for parameters in groups. Given the large number of input parameters, we required a larger number of PSA runs to avoid overfitting and achieve more precise EVPPI estimates. The outputs from GAM for each individual parameter were used to inform the selection of key groups of parameters for ANN metamodel analysis. Following a procedure displayed in **Figure 4.1**, we expanded the PSA samples to 20,000 and performed EVPPI analysis with the two aforementioned methods. We then compared the resulting EVPPI estimates to inform targets for prioritizing future data collection. We constructed the ANN for each metamodel with 4 hidden layers and 10 hidden nodes per layer

to prevent overfitting[200]. To address the randomness in generating initial weights for the ANN algorithm, we repeated each estimation ten times and averaged the results for the final EVPPI values. We described the process for result validation and tuning for the ANN model in detail in Appendix C.

4.3. Results

4.3.1. Uncertainty in cost-effectiveness

Results from our PSA demonstrate that the optimal combination implementation strategies, i.e. the strategies with the highest NMB, varied across cities and at different thresholds (**Figure 4.2**). The number of individual interventions comprising the highest-valued strategies increased with threshold levels and were mostly concordant at the highest thresholds. We found that the level of uncertainty generally decreased with higher cost-effectiveness thresholds in all cities. At the base threshold of $100,000/QALY, the probability of the most probable strategies to be highest-valued ranged from 30% (LA) to 56% (Atlanta). This uncertainty may result in opportunity costs due to acting on the suboptimal decision and is strongly associated with the magnitude of EVPI and EVPPI.

4.3.2. Expected value of perfect information

Figure 4.3 shows the EVPI for each city at different cost-effectiveness thresholds. EVPI values became smaller with increasing threshold levels when the decision uncertainty was reduced, except for LA. The large increase in EVPI for LA from $50,000/QALY to $100,000/QALY reflected uncertainty surrounding the inclusion of PrEP in the combination implementation strategy (an effective yet very costly strategy) at the higher threshold. At a threshold level of $50,000/QALY, the city-level EVPI ranged from $802,370 (Miami) to $ 17,251,221 (New York City). When the threshold was $100,000/QALY, the city-level EVPI was found to be small in Miami ($59,683), Atlanta ($92,684), and Seattle ($340,439) and relatively greater in Baltimore ($1,348,364), New York City ($7,649,541), and LA ($54,108,679). Per individual EVPI, after standardizing with city population size, was highest in LA ($8,009,105 per million residents) and lowest in Atlanta ($20,880 per million residents).

4.3.3. Expected value of partial perfect information

We presented in Appendix C Figure A2 the distribution of EVPPI values we estimated at a threshold of $100,000/QALY from metamodeling analysis with a GAM on each individual parameter for each city. Many parameters were found to have an EVPPI of $0, implying acquiring additional information on them is unlikely to impact the allocation decision. We found a high degree of consistency across cities on the parameters that were most influential on decision uncertainty and we grouped them accordingly: (1) mortality rate estimates for people living with HIV (PLHIV), stratified by injection drug use status and ART receipt (N=58); (2) the probability of immediate ART engagement (within 1 month of diagnosis) (N=15); (3) the rate of ART initiation (N=15); (4) the rate of ART dropout (N=54); (5) the number of sexual partners, both heterosexual and homosexual (N=25); (6) HIV transmission probabilities per heterosexual partnership (N=6); (7) HIV transmission probabilities per homosexual partnership (N=3); (8) HIV transmission probabilities per shared injection contact (N=3); (9) the HIV testing rate across strata (N=30); (10) QALY weights (N=11); and (11) health care costs for individuals receiving ART (N=18) (Appendix C Table A1). Some additional groups of influential parameters specific to individual cities included injection frequency among people who inject drugs and the effectiveness of SSP in reducing the probability of shared injection (Atlanta, Baltimore and Miami) and the PrEP retention rate (LA). **Figure 4.4** compares the EVPPI for these key groups of parameters, showing that the value of information associated with reducing parameter uncertainty was highest for the number of sexual partners (ranged from $36,695 in Miami to $19,619,277 in LA), the probability of immediate ART engagement (ranged from $32,380 in Miami to $8,660,878 in LA), and HIV testing parameters (ranged from $34,094 in Miami to $9,665,386 in LA) except in LA where the EVPPI for PrEP retention rate ($22,861,668) exceeded all other parameters.

4.4. Discussion

We performed a VoI analysis to determine the potential value of additional data collection in reducing decision uncertainty on the cost-effectiveness of localized HIV combination implementation strategies in six US cities. The high EVPIs we estimated for Baltimore, New York City and LA suggest there is substantial value in further data collection to reduce decision uncertainty in these cities. Through an extensive EVPPI analysis, we identified the primary contributors to the uncertainty in these decisions and recommended further data collection on HIV

risk behaviors, probability of HIV transmission per sexual partnership or shared injection contact, health service engagement, HIV-related mortality, health utility weights and health care costs.

The low EVPI values we estimated for Atlanta, Miami and Seattle at a $100,000/QALY threshold were a result of their relatively smaller populations and lower levels of decision uncertainty. Although this may suggest that funding further data collection may not be justified, these findings should be interpreted with caution as they reflect the current status of a given microepidemic (and our knowledge of it) and thus may change over time. For example, the current high incidence of HIV in Miami makes most interventions highly cost-effective despite substantial uncertainty in expected costs and benefits of implementation. However, if incidence declines in the future, the probability of a suboptimal implementation decision – and accordingly, the EVPI, will increase. EVPI calculations should thus be updated alongside prospective modeling efforts.

EVPPI analysis provides insight into the value of reducing uncertainty for model parameters that are most influential to decision uncertainty. We identified several key groups of parameters that were consistently detected as potential targets across cities for future research, including HIV risk behaviors; probability of HIV transmission; health service engagement; HIV-related mortality; health utility weights; and health care costs (for PLHIV on ART). Many model parameters within these groups were also found to be highly influential on epidemiological targets in a global sensitivity analysis in our previous model calibration work[195]. The value of other parameters was low or negligible. This does not mean that their uncertainty is unimportant, but that gathering more accurate information about these parameters would be unlikely to help us reduce decision uncertainty and narrow the ultimate decision. In particular, improving estimates on the rate of PrEP retention was valued at over $20 million in LA but was negligible in other cities. Though effective in preventing HIV transmission, PrEP is a costly intervention whose value is highly dependent on recipients' persistence[201]. However, in all cities except LA, this intervention had either 100% or 0% probability of entering as a component in the optimal strategy and thus had negligible impact on decision uncertainty, resulting in a stark contrast in valuation of EVPPI.

Collectively, parameters pertaining to the number of sexual partners contributed to a high degree of decision uncertainty across all cities. The importance of these behavioural parameters has also been noted in many prior modeling studies[202,203]. Our current model parameter values were informed by evidence from NHBS[158] and the National Survey of Family Growth (NSFG)[160]. Although these population-based surveillance databases provide the best available evidence on this topic, these surveys featured several threats to internal and external validity that could

potentially be improved upon with greater investments. For example, NSFG only provided regional rather than city-level data while in NHBS, where city-specific data were available, sample sizes for some population groups were small, resulting in wide uncertainty ranges. Equally importantly, the framing of the survey questions did not always correspond to how the model parameters in this particular application were encoded, which may have inevitably introduced additional uncertainty from data triangulation. Enhancing behavioural evidence on the basis of current surveillance system should focus on subpopulations with high risk behaviours[204]. An ongoing project may provide an example for a multi-site community-engaged study that engages a high-coverage sample of MSM recruited using respondent-driven sampling[205]. Notably, in this application researchers also applied standardized adjustment methods to generate population-representative estimates[206].

Health service engagement was another parameter category found to be influential. Good-quality evidence for population-level HIV testing rates in the US is sparse. We derived these testing parameters from NHBS[207,208], the Behavioral Risk Factor Surveillance System[209], and other sources in the peer-reviewed literature. Further, in the absence of city-specific data, ART engagement parameters were derived from corresponding regional HIVRN data[210] and corresponding primary analysis[211]. These data, available from sample-based studies in selected sites, may have been unrepresentative of the general population. Establishing a centralized public health database to systematically collect and combine surveillance and health administrative data across different jurisdictions and agencies could substantially reduce the bias and uncertainty of population-level evidence. Although CDC is making efforts to enhance the collection, analysis, visualization, and dissemination of its surveillance data, challenges exist in coordinating information sharing, developing a broader surveillance workforce, and building health information systems to integrate data collected from various parties[212-214].

Although several modern methods have been developed to replace the conventional nested Monte Carlo procedure in VoI estimation[194], few applications using dynamic transmission models have been published[75]. Further, this study presents one of the few examples of applying advanced metamodeling approaches, including a deep learning method, in estimating the EVPPI for large groups of parameters and many competing strategies. We demonstrated a pragmatic approach in applying VoI analysis while maintaining a high level of rigor. We also found limited guidance on several critical steps of VoI analysis. One question we encountered was whether to include calibrated parameters with their posterior calibrated values or their prior uncertainty ranges in the PSA. We chose the latter option as we felt that the calibration process may arbitrarily

shrink decision uncertainty attributable to these parameters. We note that this was a departure from our prior analysis[69], and explains the differences in the PSA results presented herein.

This analysis has several limitations. First, the procedure we undertook to only perform PSA on a subset of the highest-valued combination strategies identified in the deterministic base case might inevitably omit several strategies that had very small probabilities of being chosen as optimal. We felt these omissions had a negligible impact on the VoI while significantly improving computational efficiency in this application. Second, we did not consider potential developments in HIV interventions. Emerging evidence, which may comprise longer-acting ART and PrEP formulations or substantial cost reductions from the introduction of generic formulations could alter the VoI estimates. Third, we did not attempt to calculate the expected value of sample information, which can extend the findings of EVPPI analysis to generate a value of reducing the uncertainty for a specific study design and sample size. This remains a topic for further inquiry. Finally, the structural uncertainty attributable to our model was outside the scope of this VoI analysis, which focuses explicitly on parameter uncertainty. As decisions about model structure may also influence decision uncertainty, cross-model comparisons can provide a robust validation of the recommendations of a given model and highlight additional priorities on the nature of data that should be incorporated to reduce decision uncertainty.

4.5. Conclusion

We found uncertainty on the combination implementation strategies that would be most cost-effective for HIV prevention. This uncertainty is associated with high opportunity cost where benefits are highly likely to outweigh the cost of future research to improve parameter precision in three out of six cities we considered in this project. To refine decision making for HIV, priority should be given to data collection on the identified key groups of parameters. Value of information analysis, combined with other information, such as the feasibility, relevance and the cost of future research, should be embedded into decision making processes on funding and identifying targets for data acquisition efforts.

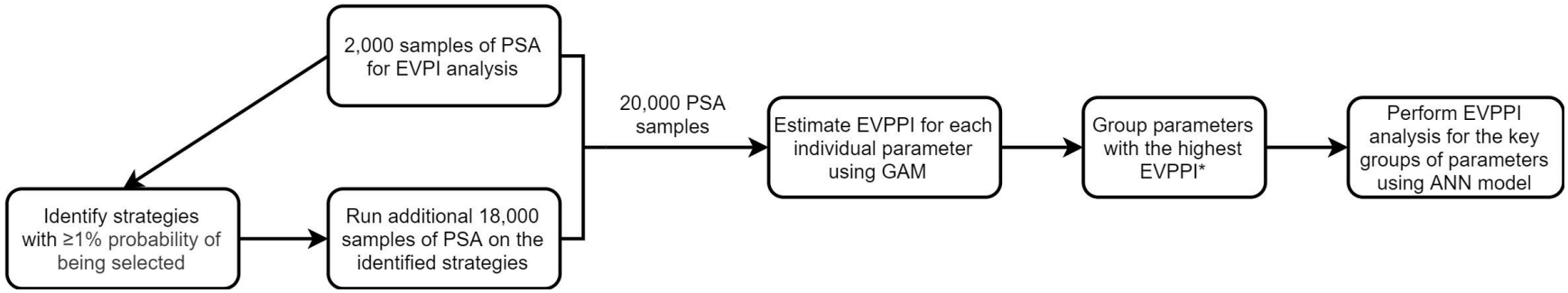


Figure 4.1. Flowchart depicting the process of the expected value of partial perfect information analysis

PSA: probabilistic sensitivity analysis; EVPI: expected value of perfect information; EVPPI: expected value of partial perfect information; GAM: generalized additive model; ANN: artificial neural network. * Key groups of parameters were defined by having at least one parameter whose EVPPI > (0.05 x EVPI) and groupings were based on parameters' content and whether the information would likely be collected jointly in practice.

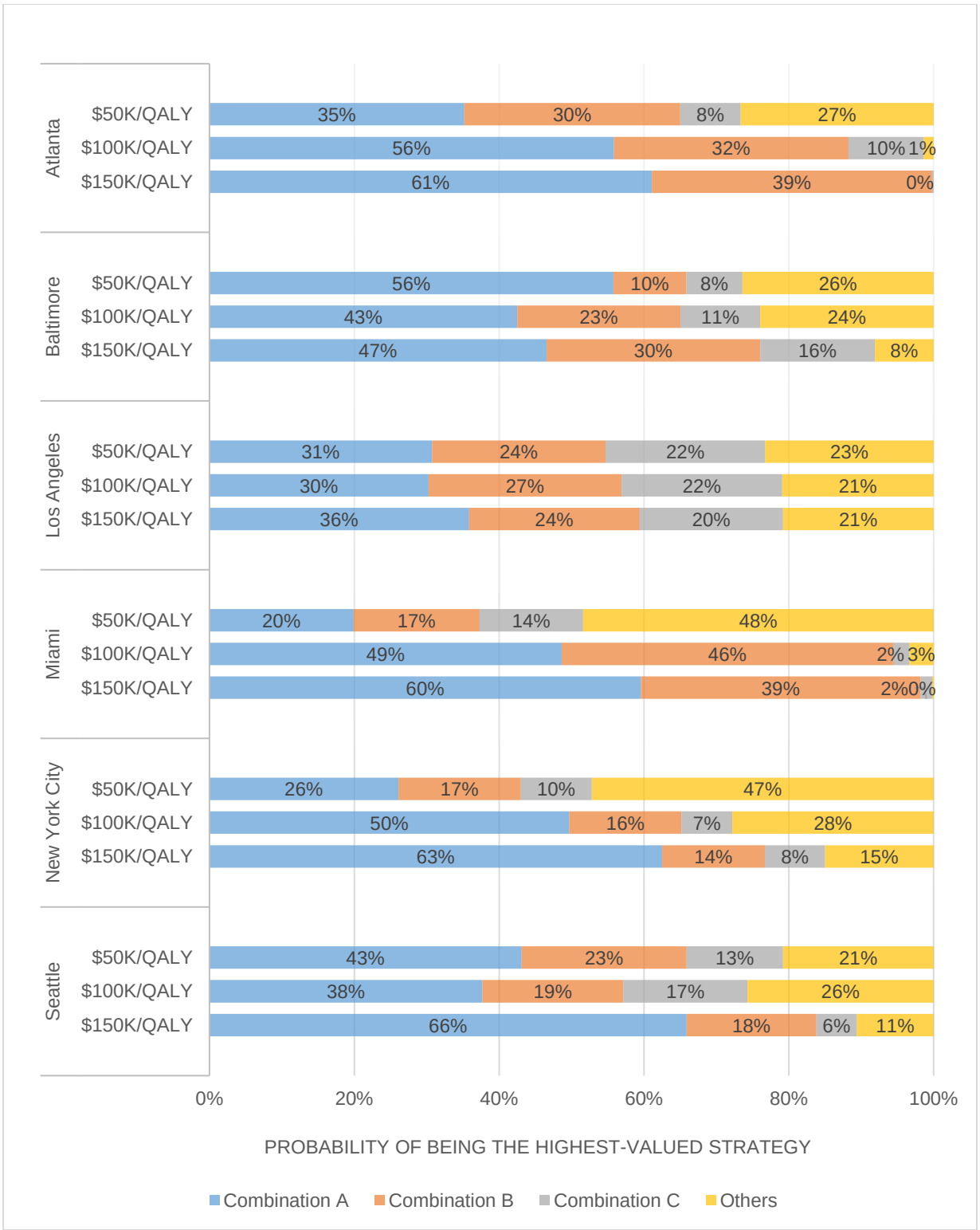
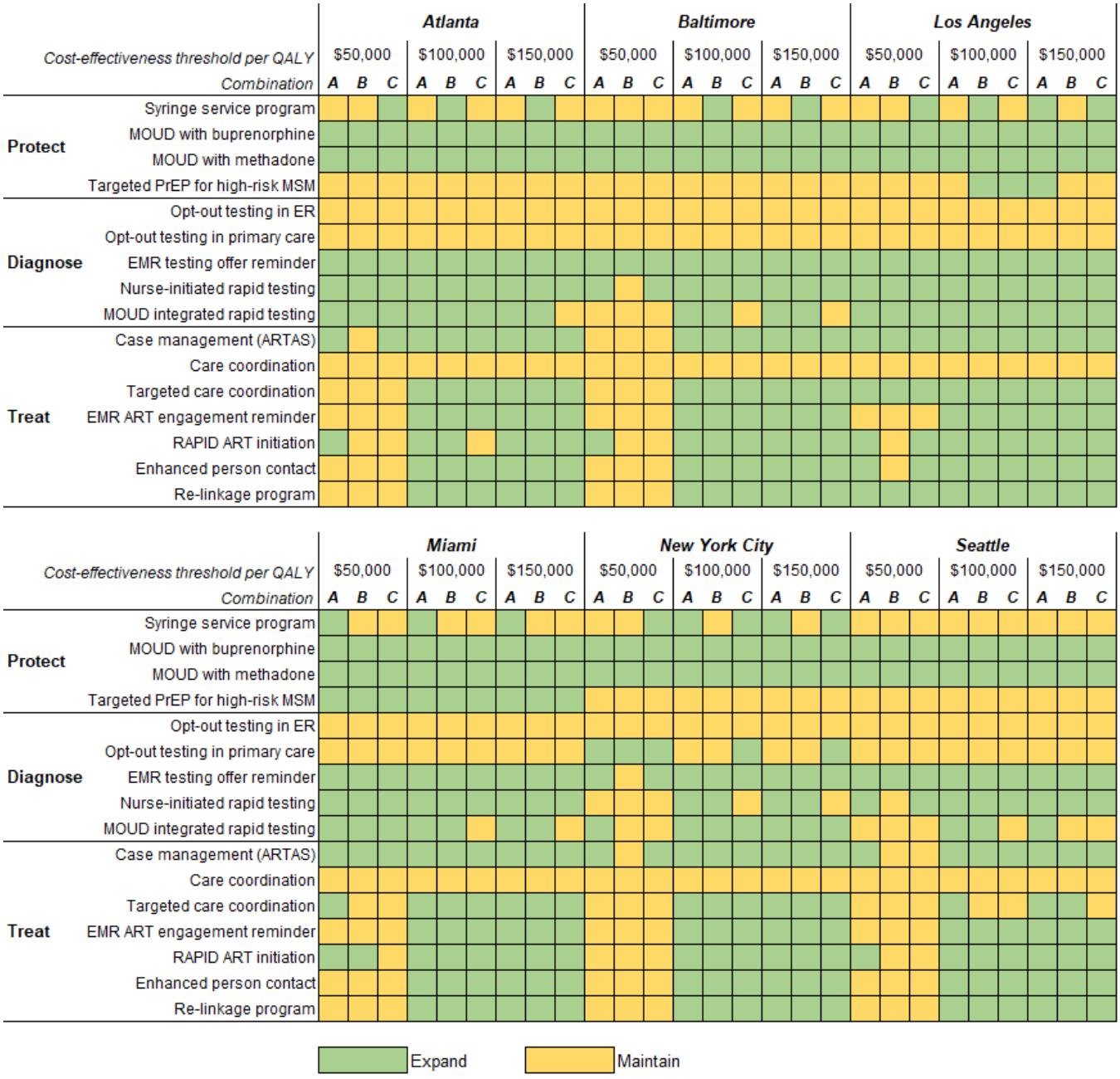


Figure 4.2. The selected optimal combination implmentation strategies
(A) The probabilities of competing combination strategies representing the highest value at different cost-effectiveness thresholds. QALY: quality-adjusted life year.



(B) The composition of the optimal combination implementation strategies at different cost-effectiveness thresholds. MOUD: Medication for opioid use disorder; PrEP: Pre-exposure prophylaxis; MSM: Men who have sex with men; ER: Hospital emergency room; EMR: Electronic medical records; ART: antiretroviral therapy.

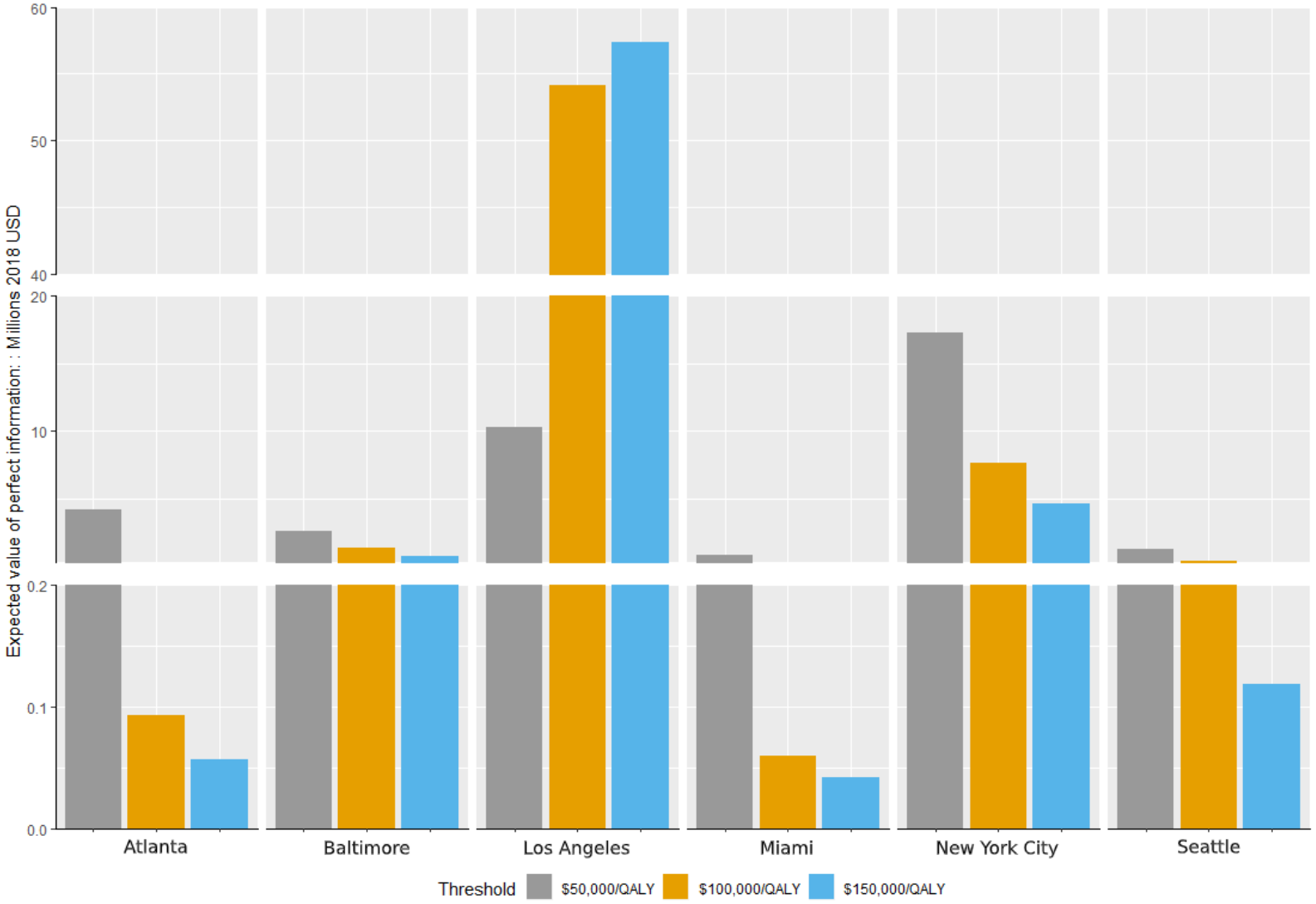


Figure 4.3. The city-level expected value of perfect information under different cost-effectiveness thresholds

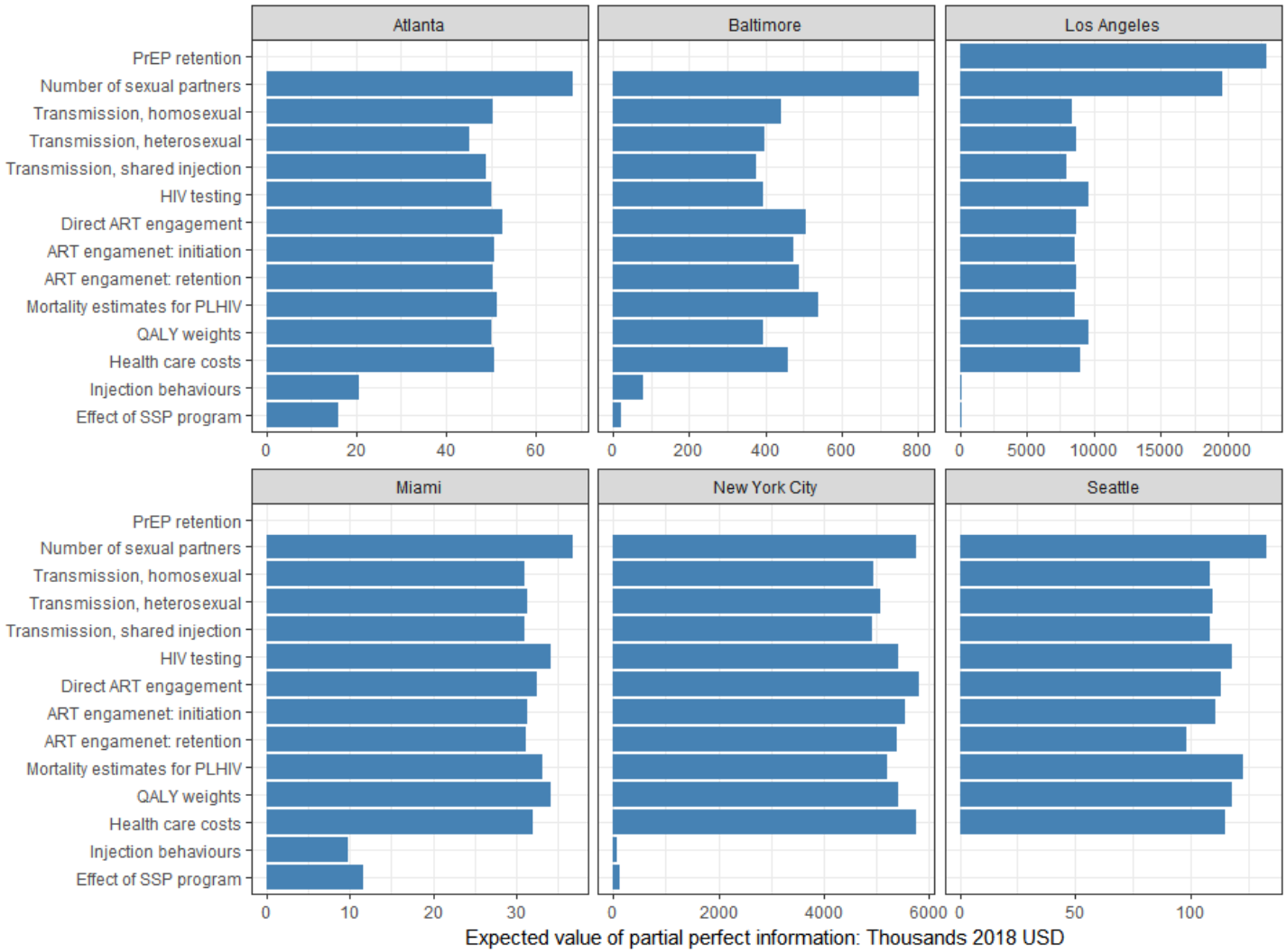


Figure 4.4. The city-level expected value of partial perfect information for identified parameter groups

Chapter 5.

Conclusion

This final chapter provides an overview of the research findings and contributions to the literature of this thesis, its limitations, as well as methodological and clinical implications for model developers, users and policy makers. The chapter concludes by identifying areas of future research which could improve, extend, or deepen the research presented in this thesis.

5.1. Overview of thesis findings

The overarching aim of this thesis was to provide methodological advances in decision-analytic modeling in HIV/AIDS, with a focus on model design, the quality of supporting evidence, calibration, validation and analysis of uncertainty. Study findings provide a tool to assess various HIV interventions and identify targets for future data collection efforts. In this thesis, a comparative review of HIV decision analytical models used in health decision-making was performed, with a focus on structural designs and data quality. Following that, a dynamic compartmental HIV transmission model was developed, systematically calibrated and validated to replicate the diverse microepidemics across six US cities. This framework can be used to evaluate a variety of HIV interventions and their combinations. One application of this model was then demonstrated by an extensive value of information analysis to quantify decision uncertainty attributable to all uncertain parameters and specific groups of input parameters, results that are most informative for setting priority for future research and data collection efforts.

5.1.1. Chapter 2 – Modeling review

Various decision analytical models of HIV were built for different purposes, while little discussion was found on what constitutes a good model design, and high-quality evidence for different components of an HIV model. There is also a paucity of standardized guidelines for data identification and quality assessment, with key population-based surveillance and health service data not always available in many settings. In Chapter 2,

we performed an in-depth methodological review of a selection of 19 HIV models used to facilitate healthcare decision making, focusing on the structural design and quality of evidence supporting the four fundamental structural components and two analytical components of a model. Our goal was to provide explicit discussion on the choice of model structure and data quality as well as implications of these choices for model developers and to inform targets for data collection. To facilitate evidence quality assessment, we developed a two-dimensional quality assessment framework for HIV simulation modeling considering both the internal and external validity of input data. This framework can contribute to the development of more standardized approaches to identifying and assessing the quality of model inputs during model development and critical review. This framework has been applied in our current HIV economic modeling project to guide evidence synthesis, quantify input data quality distribution and identify key domains for uncertainty analysis. The applicability of this framework can also expand beyond HIV modeling and is useful for other disease areas too. Our review found consistency in model structure but wide disparities in the quality of supporting evidence. Some key findings include that HIV testing, an essential HIV control service and strategy, was not explicitly modeled in many of the reviewed models, which may constrain a model's capacity to construct effective combination implementation strategies. We also found issues with the transparency of data reporting regarding the source and selection (e.g. data used to define initial population), as well as the unavailability of heath services data (e.g. HIV testing, treatment engagement). We believed that models should only be sufficiently complex to address the policy question and key epidemiological features. However, when designing a model, careful consideration should also be given to the availability and quality of data. From the perspective of evidence quality, we recommended to integrate reporting and assessing input data quality in modeling to improve its replicability, which was often absent in current CEA modeling studies. Based on that, model developers should also perform formal assessment of the influence of poorer-quality data on model inferences.

Current guidelines on evidence synthesis are primarily limited to RCT data and standard meta-analysis techniques to inform the main clinical effects[105,215]. However, decision models are typically built using parameters from a wide range of evidence sources where there is less consensus on the hierarchy of evidence and synthesis methods[105,106]. The development of generalized guidelines is feasible and should focus on the quality of the data identified for use within the model, the methods used to incorporate

the data into the model and the transparency of reporting[216]. The creation of a standardized checklist emulating CHEERS may improve the reporting of evidence selection, quality ranking, valuation and synthesis/triangulation to allow detailed evaluation and replication of the model. The proposed quality assessment framework can be used as a template to design more tailored criteria according to the disease or decision question and corresponding input data requirements.

5.1.2. Chapter 3 – Model calibration and validation

Based on the implications from Chapter 2 and a comprehensive evidence synthesis, we adapted and extended a previously-published model to replicate the transmission, progression and clinical care for the six HIV microepidemics in the US. The developed model featured the heterogeneity in the risk of HIV infection and access to various health services across different population groups (gender, ethnicity, and risk behaviour). Nevertheless, models are based on scientific abstraction of reality, simplifying assumptions and input data with different levels of uncertainty that entails an assessment of the congruence between model results and observational data or expert opinion. Despite existing guidelines on model calibration and validation, substantial subjectivity remains along many steps in the process. In Chapter 3, in addition to a transparent and comprehensive description of our developed model, we detailed our process for calibration and validation following methodological guidelines and explicitly provided justifications for each methodological decision (e.g. choice of free parameters, GoF measure), with the goal to improve the objectivity and replicability of the framework. We made substantial efforts to ensure the rigor, comprehensiveness and transparency throughout this study that was beyond current standards on many fronts. In particular, in calibration, we found sparse guidance on the selection of parameters for calibration and determination of the summary GoF when multiple targets are to be fit[62,63,171]. Two innovative approaches were employed to address these challenges: Morris method, an efficient and flexible global sensitivity analysis method used to identify the most influential parameters necessitating calibration; the best-worst method, an easy-to-implement tool to assign target weighting based on experts' preferences elicited from a brief and intuitive questionnaire. Despite its usefulness, robustness and lower requirement for comparison data, challenges existed in performing pairwise comparisons of BWM to quantify a qualitative measure of relative importance between many targets where no best practice is available. We carefully

designed the survey to be well-structured and intuitive and invited multiple experts with substantial insight over local epidemics to complete the survey. We then averaged the results to generate more reliable and credible target weight vector to guide our calibration work. Another practice worth highlighting was the involvement of a Scientific Advisory Committee in providing valuable insights throughout the exercise. Our calibrated model provided an excellent fit to the calibration targets across cities. Long-term status quo epidemiological projections were confirmed by our advisory committee and were designed to serve as a 'status quo' comparator in assessing the incremental value of combination implementation strategies to address the unique HIV microepidemic in each city.

5.1.3. Chapter 4 – Value of information

Value of information analysis has been increasingly recommended for analyzing model uncertainty to guide decisions on funding future research and data collection efforts[217]. Despite these useful features of VoI analysis, its uptake in health economic evaluation remains low. VoI analysis has been hindered by two main factors. First, the concept and interpretation of the expected value of information is not straightforward nor well-understood and thus is rarely used to inform real-world decision-making[218]. The second barrier comes from the computational challenges in performing VoI analysis, particularly in the estimation of EVPPI and EVSI for complex models[219,220]. Many new approaches have emerged to reduce this computational burden and more recent studies have used a metamodeling approach to provide good approximation for the value of information[198]. Given the substantial uncertainty underlying model inputs and decision regarding the most cost-effective combination strategies in our previous studies, in Chapter 4 we performed a VoI analysis calculating both the EVPI and EVPPI to ascertain the value and priority for future data collection for each city. The metamodeling approach with generalized additive modeling and deep neural network modeling we employed in this study has considerably improved the efficiency of our analysis on evaluating more than 20,000 different combinations within a complex modeling framework while relaxing the assumptions of net monetary benefit normality and model linearity[198], otherwise required by a linear metamodel. Our VoI analysis demonstrated that, in three out of the targeted six cities, decision uncertainty and associated opportunity cost is high where benefits of future data collection to improve parameter precision are highly likely to outweigh the cost. Priority should be given to data collection on parameters pertaining to

HIV risk behaviours, probability of HIV transmission, health service engagement, HIV-related mortality, QALY weights and health care costs. Questions remain about to what extent these VoI results are transferable across settings. For parameters that were based on common evidence and generalizable across epidemiological contexts, e.g. transmission probabilities, it may be reasonable that the localized EVPPI values should be summed to represent the true value of collecting further data on these parameters. With the advances in more efficient and accurate methods, we made the case that VoI should be embedded into decision making processes on funding future research and identifying key areas where data acquisition efforts can be worthwhile.

5.2. Limitations

The component studies comprising this thesis had several limitations, the implications of which we have considered carefully. First, the review of HIV simulation models in Chapter 2 was not systematic. Unlike previous systematic reviews of HIV modeling or economic evaluations, our review did not focus on any specific interventions, subpopulations or regions, while given the breadth and depth of this review, conducting a full systematic review was practically infeasible. We maintain that a narrative review is most practical, and appropriate for our aims. Through reviewing a selection of highly influential models, representing various typologies, geographic and application contexts currently used in practice, our goal was to underline areas of consensus and divergence on key aspects of model development. Second, the quality assessment framework we developed in the review and used in our own economic modeling can be improved. Currently the internal validity of the evidence was only assessed by the study design, rather than a full investigation of the quality of source study. Given the potentially large number of input parameters in a given model, this limited assessment is most practical and can greatly improve the rigor of modeling practice. Nonetheless, when identifying or assessing key model inputs, such as intervention effect size, we deem it necessary to apply greater scrutiny to the source study (e.g. sample size, existence of bias) according to evidence guidelines.

In chapter 3, we have noted some structural limitations of the dynamic compartmental model. We also identified a challenge in the use of models to guide prospective decision making, which was not only limited to our model: the projections and

cost-effectiveness results of a model only represent our assessment of the intervention scenarios based on historical trends and knowledge, while the HIV epidemic is dynamic and constantly changing, which may pose challenges and uncertainty for the long-term valuation of a given intervention. For example, while HIV transmission among drug users had been well controlled in Seattle in the past decade, the recent spike in HIV diagnoses among drug users in 2018[221] was difficult to capture in our model that was calibrated to 2012-2015 data. We therefore intend to keep updating the model when new data become available to make our analysis as timely and practical as possible, however the lags in surveillance data collection is an obstacle for any attempts at forward-looking modeling analyses.

Despite a comprehensive evidence synthesis, some model parameters were informed by less-than-ideal evidence, as high-quality data were not always available. This issue was particularly prominent in the US, compared to our previous modeling studies in British Columbia[155-157]. Some surveillance and epidemiological data were either unavailable (HIV testing numbers), or collected within non-representative samples (e.g. behavioral data). This parameter uncertainty may translate into greater uncertainty in the ultimate decision. To address this, we employed a systematic approach in model calibration and validation to ensure the consistency between model projections and observed targets. We also conducted an extensive probabilistic sensitivity analysis in our current health economic evaluation (although not presented in this thesis), where we combined the 2,000 best-fitting calibrated parameter sets (for the selected free parameters) with 2,000 random samples for all other uncalibrated parameters, drawn from their prior distributions, to comprehensively explicate result variability from both calibration and PSA. In Chapter 4, we also performed a value of information analysis to disentangle decision uncertainty and provide implications for further research to improve estimates for key groups of parameters.

Notwithstanding the extensive uncertainty analysis we performed, model structural uncertainty, which also often received very little attention in the economic modeling literature[222,223], was not formally examined in our studies. Quantifying the uncertainty underlying a model's structural assumptions remains a challenging task that may involve a redesign or redevelopment of the model[39,224]. Although in adapting our model to the US context, we strived to incorporate the most appropriate design (with all the lessons learned from Chapter 2) to capture the core, driving factors in each microepidemic, cross-model

comparisons can help improve the robustness and credibility of model inferences. Therefore, in our future investigation, we proposed to compare our model with an agent-based model, the most popular alternative design for a cross-model validation (more details given in Section 5.4).

Meanwhile, we only considered biomedical interventions that have a direct impact on HIV-related outcomes, although some behavioural interventions have shown to be effective in preventing HIV[225]. Although this may remain a topic for future investigation, little evidence is available to support the characterization of these behavioural interventions at the population level, and questions remain whether they are capable of widespread effectiveness under real world conditions.

Finally, in Chapter 4, we identified several key groups of model parameters on which further data collection can be worthwhile. However, these results did not probe, for each parameter group, whether data collection was feasible nor how to collect the data (e.g. design a new epidemiological study, establish new or improve existing data collection infrastructure). Future studies on the feasibility and valuation of acquiring information from a specific study design and sample size (i.e. the expected value of sample information) can provide more direct evidence to guide data collection efforts to reduce decision uncertainty in HIV/AIDS responses. Nonetheless, for most model parameters, the data acquisition will not be as straightforward as obtaining relative risk from randomized controlled trials, while different forms of evidence can be generated with various types of data and collection mechanisms.

5.3. Study implications

This comprehensive study of health economic modeling in HIV/AIDS will be among the few to systematically probe the design of models and provide unique insights regarding their dependence on high-quality data to make sound inferences. Findings of this study will make substantial methodological and public health contributions, providing meaningful implications for health decision-makers and scientists alike.

From a methodological perspective, the narrative review of a selection of decision-analytical HIV models in Chapter 2 can provide critical guidance on model design and data collection. The evidence quality assessment framework we have proposed can contribute

to the development of standardized approaches to identifying and assessing the quality of model inputs in HIV and other disease areas. Further, the methods and procedures we outlined in building the HIV modeling framework in Chapter 3 may contribute to standardizing the process of model calibration and validation, and guiding methodological choices at each critical step. The value of information analysis presented in Chapter 4 demonstrated a pragmatic example of using a novel metamodeling approach with flexible regression methods, including an advanced deep learning method, in estimating the expected value of partial perfect information for groups of parameters with high dimensionality within a dynamic transmission model. To our knowledge, this was the first application of ANN metamodeling methods in value of information analysis, which provides a powerful tool in establishing complex, non-linear relationships between opportunity loss and input parameters with high dimensionality.

From a public health practice perspective, we provided a transparent and comprehensive documentation of our modeling work to improve public health implementation. Through detailing all model assumptions and equations, the process of calibration and validation, and examining the decision uncertainty, we hope to unpack the 'black box' of the dynamic HIV model to enhance its accountability and replicability as well as people's confidence in model inferences. The evidence-based localized economic modeling (Chapter 3) we developed will serve as a means to evaluate various HIV prevention and treatment programs and identify the combination intervention strategies that maximize public health benefits. Findings of the VoI analysis (Chapter 4) will provide informative implications for whether further data collection is worthwhile. In cities where it was found to be worthwhile, this analysis may help prioritize future data collection efforts to where they can achieve the greatest expected value in reducing decision uncertainty in the context of US HIV epidemic.

Most importantly, once established this whole framework can be applied to diverse settings across North America and internationally, as well as to other disease areas, further underlining the potential value of this approach.

5.4. Future work

In addition to updating and recalibrating our model when new evidence becomes available, we have identified several areas where further research could be built upon the work of this thesis:

Given combination implementation strategies are gaining more interest in the public health response to HIV/AIDS, we propose a systematic review of HIV models used to evaluate combination implementation strategies. In the review, several aspects of modeling will be extracted and compared, including the inclusion of HIV interventions, how strategies are combined, the construction of the cost-effectiveness efficiency frontier, the evidence used to inform intervention effects and costs, the methods used for decision making, and the reporting of uncertainty analyses.

Using the calibrated model, our current research[69] assesses the cost-effectiveness of different combination implementation strategies, aiming to identify the highest-valued combinations for each demonstration city. In the meanwhile, it is worth looking more closely at specific interventions within different populations, e.g. PrEP, to identify optimal PrEP delivery strategies. PrEP strategies targeting men who have sex with men at different levels of risk behaviour, people who inject drugs and high-risk heterosexuals will be assessed individually and in combination. Health production functions, demonstrating optimal implementation for a range of investment levels will be estimated to define population subgroups for which PrEP should be prioritized within each urban centre.

We also intend to examine the joint and independent impacts of PrEP and other evidence-based interventions at a range of implementation levels on reaching benchmarks for epidemiological control, elimination and eradication of HIV/AIDS. Findings of this modeling study will have implications globally and provide recommendations for future HIV implementation efforts to achieve the greatest health benefits while remaining cost-effective.

Based on a consistent set of model inputs, we propose to develop an agent-based model and compare results with our dynamic compartmental model. Population-level sexual contact networks will be constructed for the agent-based model, while assortative mixing will be applied in the compartmental model. These disparate models will be calibrated and validated according to best practice guidelines, and a cross-model

validation will be performed to assess the impact of model design and the influence of the underlying data on each model's respective fit to observed epidemiological data.

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Appendix A.

Supplementary Material for Chapter 2

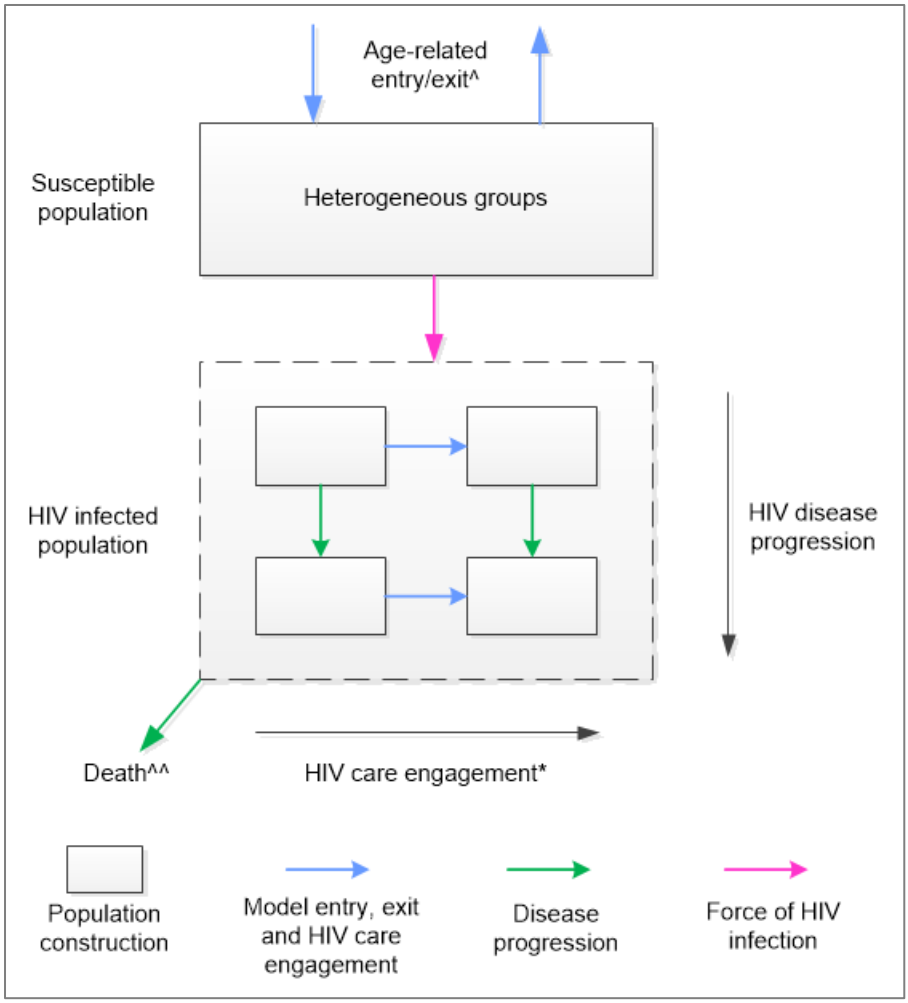


Figure A1. Stylized schematic of the core structural design components of a dynamic HIV transmission model

Legend: structural designs differ among different HIV models and we used a conceptual compartmental model as an example to demonstrate what the four core structural components refer to. ^also including HIV-free background death; ^^HIV-related death; *including HIV testing, HIV care, antiretroviral treatment, etc.

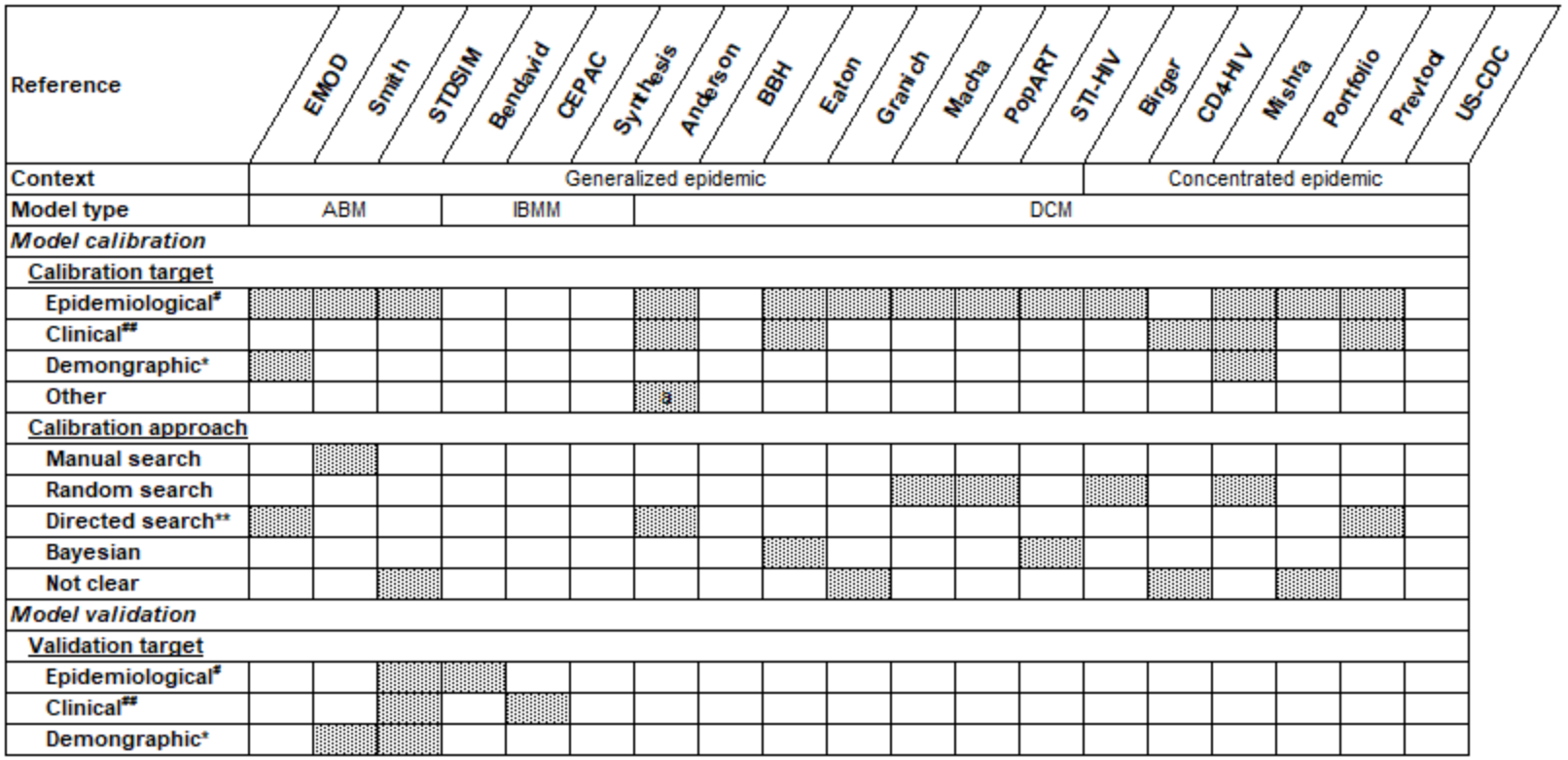


Figure A2. Model calibration and validation

Legend: Reference indexes in the headers are consistent with the manuscript; no colour coding due to no data required.

Symbol: # e.g. HIV incidence, prevalence, new diagnoses; ## e.g. PLHIV retained in HIV care or antiretroviral treatment, testing positivity rate, distribution of CD4 cell counts; * e.g. population composition of age, gender and risk group; ** e.g. Nelder-Mead algorithm, golden section search, stochastic linear gradient-descent optimization.

Lowercase letter: a. Scale-up of male medical circumcision.

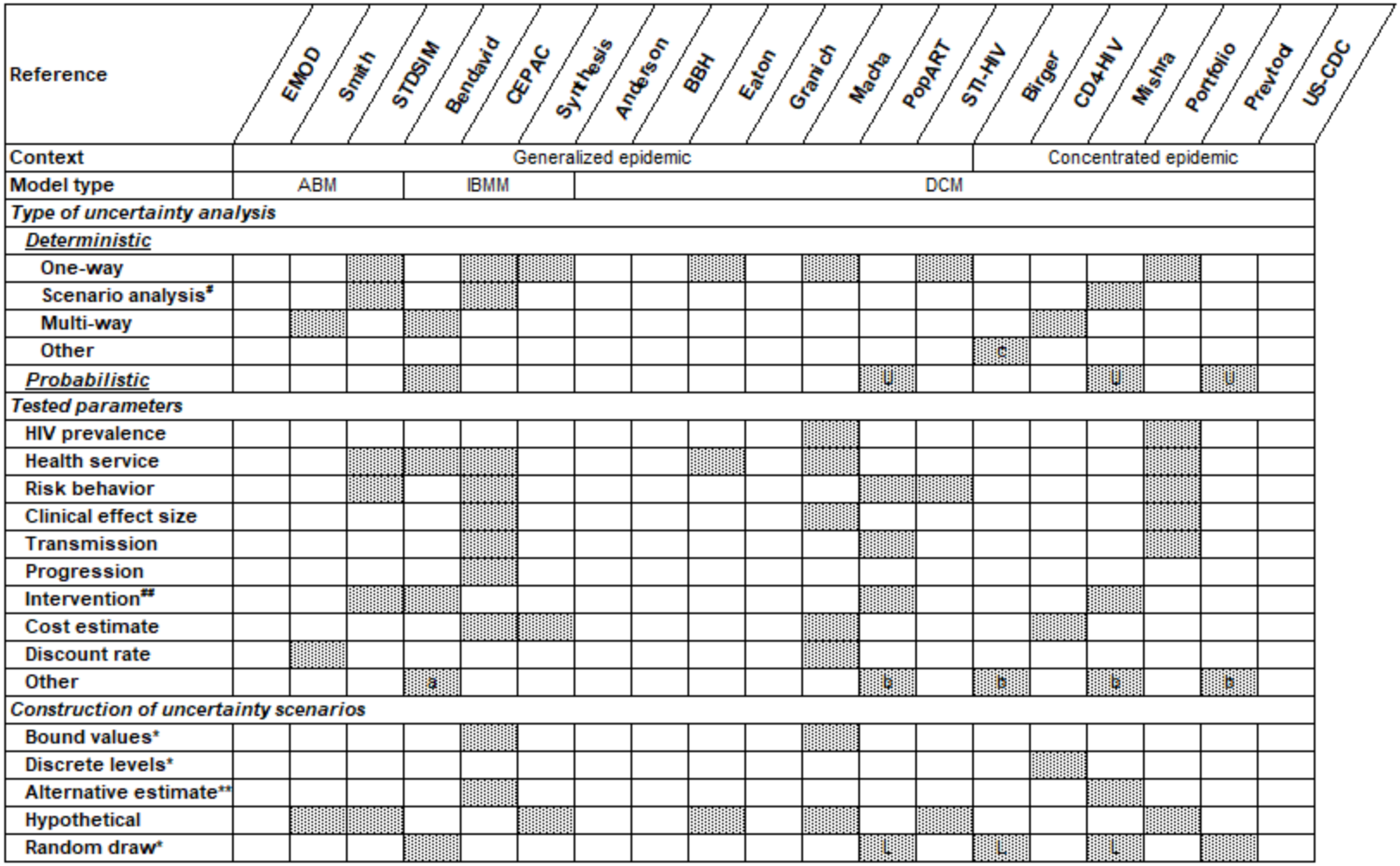


Figure A3. Uncertainty analysis

Legend: Reference indexes in the headers are consistent with the manuscript; some studies might have performed multiple uncertainty analyses; no colour coding due to no data required.

Uppercase letter: L: Latin hypercube sampling; U. A special case assuming uniform distribution for uncertain parameters (no distribution fitted), thus samples drawn from prior ranges rather than distributions.

Symbol: # e.g. optimistic/pessimistic or other hypothetical scenarios; ## Intervention implementation: including intervention reach, duration, frequency, scale-up, eligibility, etc.; * values taken from prior range/distribution; ** including optimistic/pessimistic scenarios derived from alternative evidence.

Lowercase letter: a. A formal probabilistic sensitivity analysis varying all uncertain parameters; b. Calibrated parameters, performed alongside model calibration; c. One-factor-at-a-time.

CHEERS Checklist	Item No	Smith	STDSIM	CEPAC	Synthesis	BBH	Granich	Macha	CD4-HIV	Portfolio	Prevtod	Anderson	US-CDC	EMOD	Bendavid	Eaton	PopART	STI-HIV	Birger	Mishra
Analytical type		Health economic									Optimization		Epidemic							
Title and abstract																				
Title	*1*	1	0	1	1	1	0	1	1	1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA
Abstract	*2*	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
Introduction																				
Background & objectives	*3*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Methods																				
Target population & subgroup	*4*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Setting and location	*5*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Study perspective	*6*	1	1	1	0	0	1	1	1	1	0	1	1	NA	NA	NA	NA	NA	NA	NA
Comparators	*7*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Time horizon	*8*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Discount rate	*9*	1	1	1	1	1	0	1	1	1	1	0	0	NA	NA	NA	NA	NA	NA	NA
Choice of health outcomes	*10*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Measures of effectiveness	*11*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Preference based outcomes	*12*	1	1	NA	1	NA	NA	1	NA	1	1	NA	NA	NA	NA	NA	NA	NA	NA	NA
Estimating resources & costs	*13*	1	1	1	1	1	1	1	1	1	1	1	1	NA	NA	NA	NA	NA	NA	NA
Currency, price date, and conversion	*14*	1	1	1	1	0	0	1	0	1	0	0	1	NA	NA	NA	NA	NA	NA	NA
Choice of model	*15*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Assumptions	*16*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Analytical methods	*17*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Results																				
Study parameters	*18*	1	0	1	1	1	0	1	1	1	1	1	1	NA	1	1	1	1	1	1
Incremental costs & outcomes	*19*	1	1	1	1	1	1	1	1	1	1	1	1	NA	NA	NA	NA	NA	NA	NA
Characterizing uncertainty	*20*	1	1	1	1	0	0	1	0	1	1	1	0	1	1	1	1	1	1	1
Characterizing heterogeneity	*21*	0	1	0	0	0	0	0	1	1	1	1	0	1	0	1	0	1	0	1
Discussion																				
Study findings, limitations, generalizability & knowledge	*22*	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
Other																				
Source of funding	*23*	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
Conflicts of interest	*24*	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
Total % of Yes		96%	92%	96%	92%	83%	74%	96%	91%	100%	75%	91%	86%	94%	94%	100%	94%	100%	94%	100%

Figure A4. Assessment of model reporting against CHEERS checklist
Legend: ‘‘1”: meets the assessment criteria; ‘‘0”: does not fully conform to the assessment criteria.

Table A1. Evidence quality ranking criteria

Evidence category	Pertinent parameters in model	Model component*	Quality ranking criteria
Clinical effect size	HIV testing effect on behavior	3.4 The force of HIV infection	Broad agreement suggested the randomized control trials (RCTs) and their systematic syntheses to be the gold-standard data sources for clinical effect size estimates[106,109,226]. Data obtained from observational studies have downsides in limited control for confounding and certain types of bias[106,226]. In circumstances where RCTs are infeasible (e.g. condom efficacy on sexually transmitted HIV), systematic synthesis of cohort studies is deemed best-quality. Some intervention effects (e.g. HIV testing on behaviors) are dependent on local clinical practice and supporting care, in which case the external validity assessment is also required[226]
	ART effect on HIV progression	3.3 HIV disease progression	
	ART effect on mortality		
	Preventative intervention effect size	3.4 The force of HIV infection	
Natural history of disease	Disease progression	3.3 HIV disease progression	Natural history of disease (in normal clinical practice) might not be well-captured in a setting of clinical trial, and thus preference is given to observational study (e.g. longitudinal cohort study), disease registry, or epidemiological database, also avoiding potential selection bias[106,109]. Disease natural history can vary by geographical and political areas because of many factors (e.g. level of healthcare, genetic predisposition) and thus setting-specific evidence is preferred[109]
	Infectivity (baseline and cofactors)	3.4 The force of HIV infection	
	Opportunistic infections	3.3 HIV disease progression	
	HIV-related mortality		
ART-related adverse events and complications	ART failure	3.2 Model entry, exit and HIV care engagement	Same criteria with clinical effect size[105,108]
	ART toxicity		
	ART resistance		
Health system engagement	PrEP	3.1 Population construction	Health system engagement differ by geographic setting are directly and reliably derivable from local administrative database that involve a minimal level of uncertainty [227]. On the contrary, sample-based RCTs and observational studies might incur uncertain program uptake estimates and selection bias
	HIV testing rate/coverage	3.2 Model entry, exit and HIV care engagement	
	ART initiation/scale-up		
	ART retention/drop-out		
Population characteristics	Initial population & demographics	3.1 Population construction	Population characteristics differ by location and require evidence representing a broader population, and therefore population-based studies or databases for the same locale are preferable to sample-based studies[106], e.g. population demographics can be estimated from local census data, mortality from life tables, and the prevalence of HIV or STI from national or regional surveillance data
	Population change	3.2 Model entry, exit and HIV care engagement	
	Background mortality		
	Initial epidemic	3.1 Population construction	
	Medical male circumcision		
	Sexually transmitted infections		
Behavioral	Risk group / risk level stratification	3.1 Population construction	Same criteria with population characteristics data[106], i.e. behavioral information is better derived from population-based surveys or surveillance reports on a truly representative population
	Risk behaviour intensity	3.4 The force of HIV infection	
	Partnership mixing		
Cost	Direct/indirect cost: medical / non-medical	3.5 Health economic component	Cost/resource use data differ by geographic setting, population and time, and thus are best informed by prospective data collection or a retrospective analysis of existing data sets/administrative databases on the same location as an alternative solution. Bias and subjectivity would be carried if other types of evidence are used[105,228].
Health state utility	DALY/QALY estimate	3.5 Health economic component	The evidence hierarchy places direct evidence collected for the specific study above indirect evidence from the literature since it is hard to ascertain how estimates from originating utilities sources have been derived and incorporated[108]. Publicly available repositories of health state utility values for a variety of health conditions are also a very useful data source[105,228].

Legend: this table presents the criteria used for defining the evidence quality ranking (Table 2.2), i.e. the hierarchy of evidence for internal validity, whether evidence can be generalizable; * corresponding model component and section number in the manuscript.

Appendix B.

Supplementary Material for Chapter 3

1. Model description

The adult population aged 15-64 in the model was partitioned into compartments on the basis of: sex; race/ethnicity (Black/African American (B), Hispanic/Latino (H), and White and other (W)); and HIV risk behavior type (men who have sex with men (MSM), people who inject drugs (PWID), MSM-PWID, and heterosexual (HET)). MSM, MSM-PWID and HET were further partitioned into subgroups based on HIV sexual risk behavior intensity (high- vs. low-risk). High-risk MSM and MSM-PWID were categorized based on whether they were receiving pre-exposure prophylaxis (PrEP) and PWID and MSM-PWID were categorized based on whether they were receiving opioid agonist treatment (OAT). Individuals in the model are thus partitioned within each of these 42 groups (MSM: 6 groups, MSM-PWID: 12 groups; PWID: 12 groups; HET: 12 groups).

1.1 Differential equations

We constructed the following system of nonlinear ordinary differential equations (ODEs), capturing movement between 19 base model states for each of the 42 population groups considered in our model. The complete model is thus comprised of 798 equations (42 population groups ×19 states). We denote S_i, I_i, D_i, T_i and O_i to represent model states capturing individuals susceptible to HIV infection (S_1, unscreened for HIV; S_2, screened for HIV; S_p, receiving PrEP), HIV infected, diagnosed, on antiretroviral treatment (on ART) and ART discontinued (off ART) respectively, in the acute stage (i.e. I_A, D_A) and each CD4-based stage of HIV progression i = [1: CD4≥500μL; 2: 200≤CD4<499; 3: CD4<200] for I_i, D_i, T_i and O_i. We also note additional states for I_i in which PrEP is ascribed (i.e. I_{AP}, I_{1P}). We let X_j denote X_{jt}, representing number of people in compartment *j* at time *t*.

ODEs for MSM and Heterosexual HIV risk groups:

1. $\frac{dX_{S_1}}{dt} = \rho \sum_{\forall i} X_i + \omega_S X_{S_2} - \eta_t X_{S_1} - \psi X_{S_1} - \left(\sum_{j \neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} - \mu_S X_{S_1} - \rho_m \sum_{i \neq S} X_i$
2. $\frac{dX_{S_2}}{dt} = \psi X_{S_1} + \omega_p X_{S_P} - \omega_S X_{S_2} - \eta_t X_{S_2} - \left(\sum_{j \neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \mu_S X_{S_2}$
3. $\frac{dX_{S_P}}{dt} = \eta_t (X_{S_1} + X_{S_2}) - \omega_p X_{S_P} - \left(\sum_{j \neq S} \lambda_{S_P,j(t)}\right) X_{S_P} - \mu_S X_{S_P}$
4. $\frac{dX_{I_A}}{dt} = \left(\sum_{j \neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} + \left(\sum_{j \neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \psi X_{I_A} - \theta_{\overline{T}_A} X_{I_A} - \mu_{\overline{T}_A} X_{I_A} + \rho_m X_{I_A}$
5. $\frac{dX_{I_1}}{dt} = \theta_{\overline{T}_{AI}} X_{I_A} - \psi X_{I_1} - \theta_{\overline{T}_1} X_{I_1} - \mu_{\overline{T}_1} X_{I_1} + \rho_m X_{I_1}$
6. $\frac{dX_{I_2}}{dt} = \theta_{\overline{T}_1} X_{I_1} - (\psi + \upsilon_2) X_{I_2} - \theta_{\overline{T}_2} X_{I_2} - \mu_{\overline{T}_2} X_{I_2} + \rho_m X_{I_2}$
7. $\frac{dX_{I_3}}{dt} = \theta_{\overline{T}_2} X_{I_2} - (\psi + \upsilon_3) X_{I_3} - \mu_{\overline{T}_3} X_{I_3} + \rho_m X_{I_3}$
8. $\frac{dX_{I_{AP}}}{dt} = \left(\sum_{j \neq S} \lambda_{S_P,j(t)}\right) X_{S_P} - \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{I_{AP}} - \mu_{\overline{T}_A} X_{I_{AP}} + \rho_m X_{I_{AP}}$
9. $\frac{dX_{I_{1P}}}{dt} = \theta_{\overline{T}_{AI}} X_{I_{AP}} - \psi_P X_{I_{1P}} - \mu_{\overline{T}_1} X_{I_{1P}} + \rho_m X_{I_P}$
10. $\frac{dX_{D_A}}{dt} = \psi X_{I_A} + \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{D_A} - \mu_{\overline{T}_A} X_{D_A} + \rho_m X_{D_A}$
11. $\frac{dX_{D_1}}{dt} = \theta_{\overline{T}_{AD}} X_{D_A} + \psi(1 - \varphi_1) X_{I_1} + \psi_P X_{I_{1P}} - \theta_{\overline{T}_1} X_{D_1} - \alpha_1 X_{D_1} - \mu_{\overline{T}_1} X_{D_1} + \rho_m X_{D_1}$
12. $\frac{dX_{D_2}}{dt} = \theta_{\overline{T}_1} X_{D_1} + (\psi + \upsilon_2)(1 - \varphi_2) X_{I_2} - \theta_{\overline{T}_2} X_{D_2} - \alpha_2 X_{D_2} - \mu_{\overline{T}_2} X_{D_2} + \rho_m X_{D_2}$
13. $\frac{dX_{D_3}}{dt} = \theta_{\overline{T}_2} X_{D_2} + (\psi + \upsilon_3)(1 - \varphi_3) X_{I_3} - \alpha_3 X_{D_3} - \mu_{\overline{T}_3} X_{D_3} + \rho_m X_{D_3}$
14. $\frac{dX_{T_1}}{dt} = \sum_{j \neq 1} \theta_{T_j,T_1(t)} X_{T_j} + \alpha_1 X_{D_1} + \alpha'_1 X_{O_1} + \psi \varphi_1 X_{I_1} - \sum_{j \neq 1} \theta_{T_1,T_j(t)} X_{T_1} - \theta_{T_1,O_1(t)} X_{T_1} - \mu_{T_1} X_{T_1} + \rho_m X_{T_1}$

15. $\frac{dX_{T_2}}{dt} = \sum_{j\neq 2} \theta_{T_j,T_2(t)} X_{T_j} + \alpha_2 X_{D_2} + \alpha'_2 X_{O_2} + (\psi + \upsilon_2)\varphi_2 X_{I_2} - \sum_{j\neq 2} \theta_{T_2,T_j(t)} X_{T_2} - \theta_{T_2,O_2(t)} X_{T_2} - \mu_{T_2} X_{T_2} + \rho_m X_{T_2}$
16. $\frac{dX_{T_3}}{dt} = \sum_{j\neq 3} \theta_{T_j,T_3(t)} X_{T_j} + \alpha_3 X_{D_3} + \alpha'_3 X_{O_3} + (\psi + \upsilon_3)\varphi_3 X_{I_3} - \sum_{j\neq 3} \theta_{T_3,T_j(t)} X_{T_3} - \theta_{T_3,O_3(t)} X_{T_3} - \mu_{T_3} X_{T_3} + \rho_m X_{T_3}$
17. $\frac{dX_{O_1}}{dt} = \theta_{T_1,O_1(t)} X_{T_1} - \alpha'_1 X_{O_1} - \theta_{\overline{T}_1} X_{O_1} - \mu_{\overline{T}_1} X_{O_1} + \rho_m X_{O_1}$
18. $\frac{dX_{O_2}}{dt} = \theta_{T_2,O_2(t)} X_{T_2} + \theta_{\overline{T}_1} X_{O_1} - \alpha'_2 X_{O_2} - \theta_{\overline{T}_2} X_{O_2} - \mu_{\overline{T}_2} X_{O_2} + \rho_m X_{O_2}$
19. $\frac{dX_{O_3}}{dt} = \theta_{T_3,O_3(t)} X_{T_3} + \theta_{\overline{T}_2} X_{O_2} - \alpha'_3 X_{O_3} - \mu_{\overline{T}_3} X_{O_3} + \rho_m X_{O_3}$

ODEs for PWID and MSM-PWID receiving OAT:

1. $\frac{dX_{S_1}}{dt} = \rho \sum_{\forall i} X_i + \omega_S X_{S_2} - \psi X_{S_1} - \eta_t X_{S_1} - \left(\sum_{j\neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} - \mu_S X_{S_1} - \rho_m \sum_{i\neq S} X_i + \pi X_{S_1}^{off} - \bar{\pi} X_{S_1}$
2. $\frac{dX_{S_2}}{dt} = \psi X_{S_1} + \omega_p X_{S_P} - \omega_S X_{S_2} - \eta_t X_{S_2} - \left(\sum_{j\neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \mu_S X_{S_2} + \pi X_{S_2}^{off} - \bar{\pi} X_{S_2}$
3. $\frac{dX_{S_P}}{dt} = \eta_t (X_{S_1} + X_{S_1}) - \omega_p X_{S_P} - \left(\sum_{j\neq S} \lambda_{S_P,j(t)}\right) X_{S_P} - \mu_S X_{S_P} + \pi X_{S_p}^{off} - \bar{\pi} X_{S_p}$
4. $\frac{dX_{I_A}}{dt} = \left(\sum_{j\neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} + \left(\sum_{j\neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \psi X_{I_A} - \theta_{\overline{T}_A} X_{I_A} - \mu_{\overline{T}_A} X_{I_A} + \rho_m X_{I_A} + \pi X_{I_A}^{off} - \bar{\pi} X_{I_A}$
5. $\frac{dX_{I_1}}{dt} = \theta_{\overline{T}_{AI}} X_{I_A} - \psi X_{I_1} - \theta_{\overline{T}_1} X_{I_1} - \mu_{\overline{T}_1} X_{I_1} + \rho_m X_{I_1} + \pi X_{I_1}^{off} - \bar{\pi} X_{I_1}$
6. $\frac{dX_{I_2}}{dt} = \theta_{\overline{T}_1} X_{I_1} - (\psi + \upsilon_2) X_{I_2} - \theta_{\overline{T}_2} X_{I_2} - \mu_{\overline{T}_2} X_{I_2} + \rho_m X_{I_2} + \pi X_{I_2}^{off} - \bar{\pi} X_{I_2}$
7. $\frac{dX_{I_3}}{dt} = \theta_{\overline{T}_2} X_{I_2} - (\psi + \upsilon_3) X_{I_3} - \mu_{\overline{T}_3} X_{I_3} + \rho_m X_{I_3} + \pi X_{I_3}^{off} - \bar{\pi} X_{I_3}$
8. $\frac{dX_{I_{AP}}}{dt} = \left(\sum_{j\neq S} \lambda_{S_P,j(t)}\right) X_{S_P} - \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{I_{AP}} - \mu_{\overline{T}_A} X_{I_{AP}} + \rho_m X_{I_{AP}} + \pi X_{I_{AP}}^{off} - \bar{\pi} X_{I_{AP}}$
9. $\frac{dX_{I_{1P}}}{dt} = \theta_{\overline{T}_{AI}} X_{I_{AP}} - \psi_P X_{I_{1P}} - \mu_{\overline{T}_1} X_{I_{1P}} + \rho_m X_{I_P} + \pi X_{I_{1p}}^{off} - \bar{\pi} X_{I_{1p}}$
10. $\frac{dX_{D_A}}{dt} = \psi X_{I_A} + \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{D_A} - \mu_{\overline{T}_A} X_{D_A} + \rho_m X_{D_A} + \pi X_{D_A}^{off} - \bar{\pi} X_{D_A}$
11. $\frac{dX_{D_1}}{dt} = \theta_{\overline{T}_{AD}} X_{D_A} + \psi(1-\varphi_1) X_{I_1} + \psi_P X_{I_{1P}} - \theta_{\overline{T}_1} X_{D_1} - \alpha_1 X_{D_1} - \mu_{\overline{T}_1} X_{D_1} + \rho_m X_{D_1} + \pi X_{D_1}^{off} - \bar{\pi} X_{D_1}$
12. $\frac{dX_{D_2}}{dt} = \theta_{\overline{T}_1} X_{D_1} + (\psi + \upsilon_2)(1-\varphi_2) X_{I_2} - \theta_{\overline{T}_2} X_{D_2} - \alpha_2 X_{D_2} - \mu_{\overline{T}_2} X_{D_2} + \rho_m X_{D_2} + \pi X_{D_2}^{off} - \bar{\pi} X_{D_2}$
13. $\frac{dX_{D_3}}{dt} = \theta_{\overline{T}_2} X_{D_2} + (\psi + \upsilon_3)(1-\varphi_3) X_{I_3} - \alpha_3 X_{D_3} - \mu_{\overline{T}_3} X_{D_3} + \rho_m X_{D_3} + \pi X_{D_3}^{off} - \bar{\pi} X_{D_3}$
14. $\frac{dX_{T_1}}{dt} = \sum_{j\neq 1} \theta_{T_j,T_1(t)} X_{T_j} + \alpha_1 X_{D_1} + \alpha'_1 X_{O_1} + \psi\varphi_1 X_{I_1} - \sum_{j\neq 1} \theta_{T_1,T_j(t)} X_{T_1} - \theta_{T_1,O_1(t)} X_{T_1} - \mu_{T_1} X_{T_1} + \rho_m X_{T_1} + \pi X_{T_1}^{off} - \bar{\pi} X_{T_1}$
15. $\frac{dX_{T_2}}{dt} = \sum_{j\neq 2} \theta_{T_j,T_2(t)} X_{T_j} + \alpha_2 X_{D_2} + \alpha'_2 X_{O_2} + (\psi + \upsilon_2)\varphi_2 X_{I_2} - \sum_{j\neq 2} \theta_{T_2,T_j(t)} X_{T_2} - \theta_{T_2,O_2(t)} X_{T_2} - \mu_{T_2} X_{T_2} + \rho_m X_{T_2} + \pi X_{T_2}^{off} - \bar{\pi} X_{T_2}$
16. $\frac{dX_{T_3}}{dt} = \sum_{j\neq 3} \theta_{T_j,T_3(t)} X_{T_j} + \alpha_3 X_{D_3} + \alpha'_3 X_{O_3} + (\psi + \upsilon_3)\varphi_3 X_{I_3} - \sum_{j\neq 3} \theta_{T_3,T_j(t)} X_{T_3} - \theta_{T_3,O_3(t)} X_{T_3} - \mu_{T_3} X_{T_3} + \rho_m X_{T_3} + \pi X_{T_3}^{off} - \bar{\pi} X_{T_3}$
17. $\frac{dX_{O_1}}{dt} = \theta_{T_1,O_1(t)} X_{T_1} - \alpha'_1 X_{O_1} - \theta_{\overline{T}_1} X_{O_1} - \mu_{\overline{T}_1} X_{O_1} + \rho_m X_{O_1} + \pi X_{O_1}^{off} - \bar{\pi} X_{O_1}$
18. $\frac{dX_{O_2}}{dt} = \theta_{T_2,O_2(t)} X_{T_2} + \theta_{\overline{T}_1} X_{O_1} - \alpha'_2 X_{O_2} - \theta_{\overline{T}_2} X_{O_2} - \mu_{\overline{T}_2} X_{O_2} + \rho_m X_{O_2} + \pi X_{O_2}^{off} - \bar{\pi} X_{O_2}$
19. $\frac{dX_{O_3}}{dt} = \theta_{T_3,O_3(t)} X_{T_3} + \theta_{\overline{T}_2} X_{O_2} - \alpha'_3 X_{O_3} - \mu_{\overline{T}_3} X_{O_3} + \rho_m X_{O_3} + \pi X_{O_3}^{off} - \bar{\pi} X_{O_3}$

ODEs for PWID and MSM-PWID not receiving OAT:

1. $\frac{dX_{S_1}}{dt} = \rho \sum_{\forall i} X_i + \omega_S X_{S_2} - \psi X_{S_1} - \eta_t X_{S_1} - \left(\sum_{j\neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} - \mu_S X_{S_1} - \rho_m \sum_{i\neq S} X_i + \bar{\pi} X_{S_1}^{on} - \pi X_{S_1}$
2. $\frac{dX_{S_2}}{dt} = \psi X_{S_1} + \omega_p X_{S_P} - \omega_S X_{S_2} - \eta_t X_{S_2} - \left(\sum_{j\neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \mu_S X_{S_2} + \bar{\pi} X_{S_2}^{on} - \pi X_{S_2}$
3. $\frac{dX_{S_P}}{dt} = \eta_t (X_{S_1} + X_{S_2}) - \omega_p X_{S_P} - \left(\sum_{j\neq S} \lambda_{S_P,j(t)}\right) X_{S_P} - \mu_S X_{S_P} + \bar{\pi} X_{S_p}^{on} - \pi X_{S_p}$
4. $\frac{dX_{I_A}}{dt} = \left(\sum_{j\neq S,} \lambda_{S_1,j(t)}\right) X_{S_1} + \left(\sum_{j\neq S} \lambda_{S_2,j(t)}\right) X_{S_2} - \psi X_{I_A} - \theta_{\overline{T}_A} X_{I_A} - \mu_{\overline{T}_A} X_{I_A} + \rho_m X_{I_A} + \bar{\pi} X_{I_A}^{on} - \pi X_{I_A}$
5. $\frac{dX_{I_1}}{dt} = \theta_{\overline{T}_{AI}} X_{I_A} - \psi X_{I_1} - \theta_{\overline{T}_1} X_{I_1} - \mu_{\overline{T}_1} X_{I_1} + \rho_m X_{I_1} + \bar{\pi} X_{I_1}^{on} - \pi X_{I_1}$
6. $\frac{dX_{I_2}}{dt} = \theta_{\overline{T}_1} X_{I_1} - (\psi + \upsilon_2) X_{I_2} - \theta_{\overline{T}_2} X_{I_2} - \mu_{\overline{T}_2} X_{I_2} + \rho_m X_{I_2} + \bar{\pi} X_{I_2}^{on} - \pi X_{I_2}$

7. $\frac{dX_{I_3}}{dt} = \theta_{\overline{T}_2} X_{I_2} - (\psi + \upsilon_3) X_{I_3} - \mu_{\overline{T}_3} X_{I_3} + \rho_m X_{I_3} + \bar{\pi} X_{I_3}^{on} - \pi X_{I_3}$
8. $\frac{dX_{I_{AP}}}{dt} = \left(\sum_{j \neq S} \lambda_{S_P, j(t)}\right) X_{S_P} - \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{I_{AP}} - \mu_{\overline{T}_A} X_{I_{AP}} + \rho_m X_{I_{AP}} + \bar{\pi} X_{I_{AP}}^{on} - \pi X_{I_{AP}}$
9. $\frac{dX_{I_{1P}}}{dt} = \theta_{\overline{T}_{AI}} X_{I_{AP}} - \psi_P X_{I_{1P}} - \mu_{\overline{T}_1} X_{I_{1P}} + \rho_m X_{I_P} + \bar{\pi} X_{I_{1p}}^{on} - \pi X_{I_{1p}}$
10. $\frac{dX_{D_A}}{dt} = \psi X_{I_A} + \psi_P X_{I_{AP}} - \theta_{\overline{T}_A} X_{D_A} - \mu_{\overline{T}_A} X_{D_A} + \rho_m X_{D_A} + \bar{\pi} X_{D_A}^{on} - \pi X_{D_A}$
11. $\frac{dX_{D_1}}{dt} = \theta_{\overline{T}_{AD}} X_{D_A} + \psi(1 - \varphi_1) X_{I_1} + \psi_P X_{I_{1P}} - \theta_{\overline{T}_1} X_{D_1} - \alpha_1 X_{D_1} - \mu_{\overline{T}_1} X_{D_1} + \rho_m X_{D_1} + \bar{\pi} X_{D_1}^{on} - \pi X_{D_1}$
12. $\frac{dX_{D_2}}{dt} = \theta_{\overline{T}_1} X_{D_1} + (\psi + \upsilon_2)(1 - \varphi_2) X_{I_2} - \theta_{\overline{T}_2} X_{D_2} - \alpha_2 X_{D_2} - \mu_{\overline{T}_2} X_{D_2} + \rho_m X_{D_2} + \bar{\pi} X_{D_2}^{on} - \pi X_{D_2}$
13. $\frac{dX_{D_3}}{dt} = \theta_{\overline{T}_2} X_{D_2} + (\psi + \upsilon_3)(1 - \varphi_3) X_{I_3} - \alpha_3 X_{D_3} - \mu_{\overline{T}_3} X_{D_3} + \rho_m X_{D_3} + \bar{\pi} X_{D_3}^{on} - \pi X_{D_3}$
14. $\frac{dX_{T_1}}{dt} = \sum_{j \neq 1} \theta_{T_j, T_1(t)} X_{T_j} + \alpha_1 X_{D_1} + \alpha'_1 X_{O_1} + \psi \varphi_1 X_{I_1} - \sum_{j \neq 1} \theta_{T_1, T_j(t)} X_{T_1} - \theta_{T_1, O_1(t)} X_{T_1} - \mu_{T_1} X_{T_1} + \rho_m X_{T_1} + \bar{\pi} X_{T_1}^{on} - \pi X_{T_1}$
15. $\frac{dX_{T_2}}{dt} = \sum_{j \neq 2} \theta_{T_j, T_2(t)} X_{T_j} + \alpha_2 X_{D_2} + \alpha'_2 X_{O_2} + (\psi + \upsilon_2) \varphi_2 X_{I_2} - \sum_{j \neq 2} \theta_{T_2, T_j(t)} X_{T_2} - \theta_{T_2, O_2(t)} X_{T_2} - \mu_{T_2} X_{T_2} + \rho_m X_{T_2} + \bar{\pi} X_{T_2}^{on} - \pi X_{T_2}$
16. $\frac{dX_{T_3}}{dt} = \sum_{j \neq 3} \theta_{T_j, T_3(t)} X_{T_j} + \alpha_3 X_{D_3} + \alpha'_3 X_{O_3} + (\psi + \upsilon_3) \varphi_3 X_{I_3} - \sum_{j \neq 3} \theta_{T_3, T_j(t)} X_{T_3} - \theta_{T_3, O_3(t)} X_{T_3} - \mu_{T_3} X_{T_3} + \rho_m X_{T_3} + \bar{\pi} X_{T_3}^{on} - \pi X_{T_3}$
17. $\frac{dX_{O_1}}{dt} = \theta_{T_1, O_1(t)} X_{T_1} - \alpha'_1 X_{O_1} - \theta_{\overline{T}_1} X_{O_1} - \mu_{\overline{T}_1} X_{O_1} + \rho_m X_{O_1} + \bar{\pi} X_{O_1}^{on} - \pi X_{O_1}$
18. $\frac{dX_{O_2}}{dt} = \theta_{T_2, O_2(t)} X_{T_2} + \theta_{\overline{T}_1} X_{O_1} - \alpha'_2 X_{O_2} - \theta_{\overline{T}_2} X_{O_2} - \mu_{\overline{T}_2} X_{O_2} + \rho_m X_{O_2} + \bar{\pi} X_{O_2}^{on} - \pi X_{O_2}$
19. $\frac{dX_{O_3}}{dt} = \theta_{T_3, O_3(t)} X_{T_3} + \theta_{\overline{T}_2} X_{O_2} - \alpha'_3 X_{O_3} - \mu_{\overline{T}_3} X_{O_3} + \rho_m X_{O_3} + \bar{\pi} X_{O_3}^{on} - \pi X_{O_3}$

A schematic representation of the model is shown in **Figure A1**. Boxes in the diagram represent cohorts of individuals, stratified by HIV status, HIV screening status, PrEP status, as well as HIV progression stages, diagnosis and ART status if infected. Arrows represent possible transitions between compartments. Individuals can move from susceptible (unscreened, screened or on PrEP) to infected health states following HIV infection as determined through the total contact rate, or force of infection ($\lambda_{ij(t)}$), between susceptible individuals in state i, from infected individuals in state j at time t (HIV transmission is described further in Section 1.2 below). Individuals can also move from infected states to diagnosed states through screening (ψ) or case finding (υ_i) (i = 2 for 200≤CD4<499, 3 for CD4<200) (Section 1.4); from diagnosed to on ART according to the probability of ART initiation (α_i) (Section 1.5); from on ART to off-ART according to the observed rate of ART drop-out (θ_{T_i, O_i}) (Section 1.5). Furthermore, a proportion of newly diagnosed individuals transition directly from infected states to on ART (φ_i). Transitions from off-ART back to on ART (α'_i) are also allowed in the model (Section 1.5). Untreated people living with HIV (PLHIV) (including I_i, D_i and O_i) followed the empirically estimated natural history of disease progression ($\theta_{\overline{T}_i}$) (Section 2.1). Once on ART, individuals could transition to any of the other ART states $j \neq i$ ($\sum_{j \neq i} \theta_{T_i, T_j(t)}$), or drop out of ART while staying at the same CD4 level ($\theta_{T_i, O_i(t)}$) (Section 2.1). We explicitly modeled the receipt of PrEP and its effect among high-risk MSM (including MSM-PWID) with the time-varying PrEP entry rate η_t (Section 2.6). Although not shown, individuals may also leave each compartment according to the mortality and/or maturation rate (μ_i) (Section 1.3). In addition, to account for the potential in-/out-migration, particularly among PLHIV, in each targeted city, we also incorporated an in-migration rate (ρ_m) for the infected population, as subtracted from S_1 population (Section 2.5). The terms that link the PWID and MSM-PWID receiving opioid agonist therapy (OAT) (X_i^{on}) and not receiving OAT (X_i^{off}) are the OAT entry (π) and exit ($\bar{\pi}$) rates (Section 2.7). Descriptions, valuations and prior distributions and ranges of the key parameters for calibration are presented in **Table A1**. The full list of parameters, their sources and quality rankings were reported separately[229].

1.2 HIV transmission

The dynamic model captures HIV transmission via three modes: heterosexual contact, homosexual contact, and needle-sharing. **Table A2** shows the possible modes of transmission between any two risk groups. Consistent with prior studies[155-157,230], we allowed men who have sex with men (MSM) to potentially have heterosexual contact with women.

For each risk group we assumed one average value for the number of same-sex and opposite-sex partners, adjusting for known HIV-infection status, which reduces their number of sexual partners due to screening. Annualized figures were adjusted to represent monthly figures using the following formula: $(1 - (1 - p)^{1/12})$.

The transmission between uninfected and infected individuals is represented as a matrix, $\lambda = \lambda_{ij}$, representing the total sufficient contact rate between members of (uninfected) compartment i and members of (infected) compartment j. We calculated the total sufficient contact rate, λ_{ij}, as the sum of the three different modes of sufficient contact rates: needle-sharing ($\gamma_{ij(t)}$), heterosexual contact ($\beta^{o}_{ij(t)}$), and homosexual contact ($\beta^{s}_{ij(t)}$). The total sufficient contact rate was calculated by first converting the monthly transmission probability, according to the formula: $rate = \{-ln(1-p)\}/t$ and then summed over the three modes of transmission: needle-sharing, heterosexual contact, and homosexual contact. The total sufficient contact rate at time t between individuals in compartments i and j, $\lambda_{ij(t)}$, is:

$$\lambda_{ij(t)} = \gamma_{ij(t)} + \beta^{o}_{ij(t)} + \beta^{s}_{ij(t)}$$

Most parameters used to estimate HIV transmission within and between risk groups was presented in **Table A1** while the full set is available in the our previous evidence synthesis supplementary materials[229].

In order to adequately characterize changes in the number of shared drug injections, we used data on syringe distribution from syringe service programs (SSP) for PWID to adjust the monthly number of shared injections[231-233], which is calculated by multiplying the number of injections per month with the proportion of injections that are shared. The resulting time-varying monthly number of shared injections (ds_t) at time t is:

$$ds_t = ds_0 * (1 - C_{SSPt})(1 - \Delta_d^{SSP})$$

Where ds_0 denotes the monthly number of shared injections in 2011 and C_{SSPt} denotes the coverage of SSP at time t, as estimated by the volume of syringes being distributed through SSP (assuming proportional distribution across race/ethnicity among PWID) over the total injection demands among each PWID group at time t.

For PWID groups receiving opioid agonist treatment (OAT), the adjusted number of shared injections, ds_t, is estimated by:

$$ds_t = ds_0 * (1 - C_{SSPt})(1 - \Delta_d^{SSP}) * (1 - \Delta_d^{OAT})$$

Where, $C_{SSPt} = \frac{V_t}{D_t} = \frac{V_t}{P_{PWIDt} * d * 12}$

C_{SSPt} denotes coverage of SSP in year t;

Δ_d^{SSP} denotes percentage reduction in injection sharing due to SSP;

Δ_d^{OAT} denotes percentage reduction in injection sharing due to OAT;

V_t denotes total volume of needles being distributed through SSP in year t;

D_t denotes total injection demands for PWID population in year t;

P_{PWIDt} denotes population of PWID in year t;

d denotes monthly number of injections per PWID who doesn't receive OAT.

1.2.1 Transmission via needle-sharing: The needle-sharing sufficient contact rate between uninfected individuals in compartment i and infected individuals in compartment j at time t is:

$$\gamma_{ijt}^{o} = -d_i s_i \ln\left(1 - \frac{X_{jt} d_j s_j}{\sum_k X_{kt} d_k s_k} \tau_j\right),$$

Where i, j, k correspond to compartments of PWIDs. The term in brackets, $\left[\frac{X_{jt} d_j s_j}{\sum_k X_{kt} d_k s_k}\right]$, corresponds to the probability of selecting a needle-sharing partner in compartment j, based on a proportional mixing assumption (i.e. individuals who share many injection are more likely to select a partner who also shares many injection). τ_j represents the probability of transmission per shared injection, stratified by the CD4 stratum of the infected PWID. We note that the probability of transmission is reduced by 50% (δ_I, range: 10%-90%) when the partner in compartment j is on ART[157,234].

1.2.2 Transmission via heterosexual contact: The sufficient contact rate between uninfected heterosexuals in compartment i and infected individuals in compartment j is:

$$\beta_{ijt}^{o} = -n_i^o (1 - u_i^o \kappa)\, In\left(1 - m_{r,r'}^{o} \frac{X_{jt}}{\sum_{k \in r'} X_{kt}} \sigma_j\right), \qquad i \in r, j \in r'$$

Where i is male and j,k are female, or vice versa. We considered a mixture of assortative and proportional partnership mixing that is controlled by $m_{r,r'}^{o}$[230,235], the mixing matrix between group r and r'. Assortative mixing was considered to account for the preferential mixing where individuals are more likely to form partnerships with others in the same class (e.g. race/ethnicity, high-/low-risk), while the proportional mixing (i.e. individuals with many partners are more likely to select a partner who also has many partners) was used to distribute the partnerships (after sorted by assortative mixing) within the same class. Groups r and r' represent opposite sexes and are defined according to race/ethnicity (Black/African American, Hispanic/Latino, and White/other) and sexual intensity level (high, low), resulting in a 6 x 6 mixing matrix $m_{r,r'}^{o}$ (**Table A3**) that is estimated by:

$$m_{r,r'}^{o} = \varepsilon_r^o \delta_{r,r'} + (1 - \varepsilon_r^o) \frac{\sum_{k \in r'} (1 - \varepsilon_{r'}^o) X_{kt} n_k^o (1 - u_k^o \kappa)}{\sum_{\forall k} \left(1 - \varepsilon_{r_k}^o\right) X_{kt} n_k^o (1 - u_k^o \kappa)}$$

A proportion of sexual contacts are to be formed within the same group r, according to an assortative coefficient ε_r^o, and the remaining $(1 - \varepsilon_r^o)$ proportion of partnerships is formed randomly across all groups. If ε_r^o is equal to 1, mixing is

fully assortative, and if ε_r^o is equal to 0, mixing is random. $\delta_{r,r'}$ is the Kronecker delta, which is equal to one if r and r' are equivalent and equal to zero otherwise. No preference is given to choosing a partner in other groups other than the relative proportion of total sexual partnerships with members of each compartment.

In determining the mixing matrix, we categorized high-risk heterosexuals, MSM, MSM-PWID and PWID as the high-risk group in heterosexual mixing, and the rest as the low-risk group. Once the mixing matrix was determined, we further calculated the mixing probability between group r and each subgroup in r' (e.g. black high-risk heterosexuals, black PWID, black MSM, and black MSM-PWID if r' represents the high-risk black group) assuming proportional mixing, that individuals with many partners are more likely to select a partner who also has many partners. More specifically, the mixing probability between group r and subgroup l (of group r') is estimated by:

$$m_{r,l}^o = \varepsilon_r^o \frac{X_{lt} n_l^o (1 - u_l^o \kappa)}{\sum_{k \in r'} X_{kt} n_k^o (1 - u_k^o \kappa)} \delta_{r,r'} + (1 - \varepsilon_r^o) \frac{(1 - \varepsilon_{r'}^o) X_{lt} n_l^o (1 - u_l^o \kappa)}{\sum_{\forall k} (1 - \varepsilon_{r_k'}^o) X_{kt} n_k^o (1 - u_k^o \kappa)}, \qquad l \in r'$$

such that $\sum_{l \in r'} m_{r,l}^o = m_{r,r'}^o$.

To avoid over-mixing between the high- and low-risk population (which may cause an overestimation of heterosexual transmission), we restricted the mixing probability between high- and low-risk individuals to 1% of partnerships formed. More specifically, for each row of $m_{r,r'}^o$ (for group r), we standardized the previously estimated mixing probabilities within or between the high- and low-risk groups to a total of 99% and 1% respectively, e.g. for low-risk white/other HET, the mixing probabilities with other low-risk HET will be augmented proportionally to a sum of 99% (ratio between probabilities with each subgroup remain the same), while the mixing probabilities with high-risk HET will be reduced proportionally to a sum of 1%.

The mixing matrix is then adjusted so that the number of partnerships formed between men and women balance for each pair of groups. The imbalance $V_{r,r'}$ is calculated as:

$$V_{r,r'} = \frac{m_{r',r}^o (\sum_{k \in r'} X_{kt} n_k^o (1 - u_k^o \kappa))}{m_{r,r'}^o (\sum_{k \in r} X_{kt} n_k^o (1 - u_k^o \kappa))}$$

The mixing matrix is then adjusted by this degree of imbalance V for each pair:

$$m_{r,r'}^o \rightarrow m_{r,r'}^o {V_{r,r'}}^{\theta}$$

$$m_{r',r}^o \rightarrow m_{r',r}^o {V_{r,r'}}^{(\theta - 1)}$$

The parameter θ describes the degree of compromise between the two sexes and is set to 0.5 to equalize the compromise between males and females[10].

We note that the number of sexual partners of individuals in compartment D_j, T_j or O_j is reduced by 68% (ε, range: 59%-76%) following diagnosis[236-239], and the probability of transmission is reduced by 91% (δ_{sex}, range: 79%-96%) when the partner is in compartment T_j receiving ART[7,164].

1.2.3 Transmission via homosexual contact: The sufficient contact rate between uninfected MSMs in compartment i and infected MSMs in compartment j is:

$$\beta_{ijt}^{s} = -n_i^s(1-u_i^s\kappa)\ln\left(1-m_{r,r'}^{s}\frac{X_{jt}}{\sum_{k\in r'}X_{kt}}\sigma_j\right), \qquad i\in r, j\in r'$$

Where i, j, k correspond to compartments of MSM (including MSM-PWID). Similarly, the partnership mixing between MSM is controlled by the mixing matrix $m_{r,r'}^{s}$ where r and r' are both subgroups of MSM that are also defined by race/ethnicity and risk level (**Table A4**).

$$m_{r,r'}^{s} = \varepsilon_r^s\delta_{r,r'} + (1-\varepsilon_r^s)\frac{\sum_{k\in r'}(1-\varepsilon_{r'}^s)X_{kt}n_k^s(1-u_k^s\kappa)}{\sum_{\forall k}(1-\varepsilon_{r_k}^s)X_{kt}n_k^s\,(1-u_k^s\kappa)}$$

We redistributed the mixing matrix among each subgroups in r' assuming the same proportional mixing described above, and also restricted mixing between high- and low-risk MSM to 1%. No adjustment is made to balance partnerships among MSM.

We note that the number of sexual partners of individuals in compartment D_j, T_j or O_j is reduced by 68% (ε, range: 59%-76%) following diagnosis[236-239], and the probability of transmission is reduced by 91% (δ_{sex}, range: 79%-96%) when the partner is in compartment T_j receiving ART[7,164]. Furthermore, we also adjusted the probability of transmission per partnership σ_j for high-risk MSM and MSM-PWID who are receiving PrEP by 60% (δ_{PrEP}, range: 56.3% - 61.9%)[240,241].

1.3 Population proportion adjustment

Given (i) potential individual behaviour change, i.e. transitions between risk group/risk level, despite no available data to track these transitions; and (ii) heterogeneous fluctuations in the proportion of risk group/risk level due to disparate population dynamics and risk of HIV infection, we maintained a constant proportion of each of the four risk groups (i.e. PWID, MSM, MSM-PWID, HET) among the susceptible (S_1) population. We adjusted these proportions among males and females at each time step while allowing for projected dynamics in population demographics according to race/ethnicity and sex. Furthermore, we also maintained the proportion of people in high- and low-risk strata constant among MSM (including MSM-PWID) and HET in both the susceptible and PLHIV groups respectively, with adjustment made between high- and low-risk group[10].

2. Model Parameterization

The primary basis for the development of the model was a comprehensive and extensive evidence synthesis that has been described elsewhere[229]. In the evidence synthesis, required data to populate the model were grouped in six categories: (i) initial susceptible and HIV-infected population estimates; (ii) parameters used to calculate the force of HIV infection; (iii) screening, diagnosis, treatment and HIV disease progression; (iv) HIV prevention programs, including SSP, OAT, and PrEP; (v) the costs of medical care for susceptible and HIV-infected individuals; and (vi) quality-adjusted life year (QALY) weights for each stage of HIV disease progression. Model parameters were also identified as those that should be consistent across, and those requiring context-specific data (e.g. HIV risk behaviours, population proportions). We identified the best possible data sources for each domain and explicitly ranked every piece of evidence entering the model on the basis of study design, study quality and recency, with additional data verification performed by our scientific advisory committee for some less than ideal data. Data for parameter estimates, as well as their ranges and prior distributions fitted, were collected and transparently reported using various search strategies from numerous data sources, including 59 peer-reviewed publications, 24 public health and surveillance reports and primary analyses using 11 data sets. Details on methods used to instantiate model and estimate disease progression are provided below.

2.1 Model instantiation

We simulated the HIV epidemic by first instantiating the population group size and HIV epidemic levels in each city based on 2011 data and population numbers derived from census data, surveillance reports and other data sources. Initial population estimates for each city capture overall population numbers (aged 15-64) stratified by sex, race/ethnicity risk group, high/low sexual risk among HET, MSM, MSM-PWID, and OAT status among PWID/MSM-PWID, resulting in 42 population subgroups. We distributed these 42 subgroups among 19 health states, including susceptible (HIV-negative) (screened and unscreened), infected (undiagnosed) (3 CD4 cell count strata and acute HIV), diagnosed (untreated) (3 CD4 strata and acute HIV), on-ART and off-ART (3 CD4 strata each). We also included PrEP states for HIV-susceptible, acute and asymptomatic HIV (CD4≥500) among infected but undiagnosed PLHIV (3 PrEP strata), although PrEP was modelled only among high-risk MSM and high-risk MSM-PWID. This resulted in 798 initial population values (42 subgroups x 19 health states).

While the basic demographic stratifications for the initial population estimates (i.e. sex and race/ethnicity) are directly available from cross-tabulated census data, risk group stratification was derived according to the corresponding proportions among the general population, as identified from population-level survey or surveillance studies[208,242-244]. In particular, we derived the MSM-PWID initial population by two means: (1) according to the proportion of MSM that inject drugs and (2) according to the proportion of male PWID that have sex with men, and then took the average of the two estimated population size. The initial numbers of PLHIV were a subset of the total population numbers. Derivations for sex, race/ethnicity and risk group stratified number of identified/diagnosed PLHIV (including D_i, T_i, and O_i), as well as the proportions currently on ART and ever on ART (off-ART proportion was then the difference), were rather complicated, with some available from surveillance database at the city level (i.e. D_i) while the rest triangulated from HIV Research Network (HIVRN) data[245], as detailed in the evidence synthesis paper[229]. With the supplement of the estimated proportion of PLHIV aware of their HIV status from surveillance, we were able to ascertain the initial number

of PLHIV that are infected but undiagnosed (I_i) by: $\frac{Diagnosed\ PLHIV}{\%\ aware\ of\ HIV\ status} - Diagnosed\ PLHIV$. We further stratified the initial population of PLHIV by HIV stages (acute HIV and 3 CD4 strata) according to the estimated CD4 count distribution from HIVRN data[245] (for diagnosed PLHIV) and the literature (for undiagnosed PLHIV), assuming a 1% (range: 0%-5%) of acute stage among I_i and D_i. The distribution of OAT recipients (stratified by sex and race/ethnicity in source data) across each health state was assumed proportional to the number of PWID in these states.

Proportions of individuals with high- and low-risk sexual intensity among susceptible HET was determined using behavioural surveys and surveillance data on individuals with 5 or more sexual partners in the past 12 months[160]. In contrast, the proportion of high- and low-risk Susceptible MSM and MSM-PWID were determined according to the proportion that are indicated for PrEP (25%) in accordance with CDC guidelines[208]. For HIV-infected HET, MSM and MSM-PWID, we used proportions of PLHIV individuals with STDs as a proxy for high-risk behavior based on literature sources[246,247]. Initial values for PrEP compartments were all set as 0 due to unavailability of PrEP in 2011. Data used to instantiate model can be found in our evidence synthesis paper published elsewhere[229] and **Table A5** presents the resulting initial population estimates for each of the 798 model compartments in 2011.

2.2 Entry, maturation and mortality

We calculated entry, maturation and mortality rates for each of the study risk groups according to the numbers of individuals who enter or mature out of the model population each month, as well as published mortality estimates for non-PWID and PWID. The entry probability was the proportion of the 15 year-olds within the study population (population aged 15-64), and converted to a rate, incorporating growth in this proportion during the study period (projected population dynamics for each city were detailed in our evidence synthesis). The maturation probability was the proportion of 65 year-olds within the study population, and converted to a rate, incorporating mortality, as baseline mortality drawn from life tables for each city. Both baseline entry and maturation rates were derived from the United States Census Bureau. Entry rates were confined to S1 state, while maturation and mortality rates were applied all states. Mortality rates for PLHIV were differentiated by HIV progression stages (acute and three CD4 levels) and whether the individual is on ART. We note that complete data on all-cause mortality was incorporated into the model (See section 2.1).

$$Entry\ rate:\ \rho = -ln(1 - \frac{15\ year\ old\ population}{15 - 64\ year\ old\ population})/12 + growth$$

$$Mutuation + mortality\ rate:\ \mu = -ln(1 - \frac{64\ year\ old\ population}{15 - 64\ year\ old\ population})/12 + mortality$$

2.3 HIV Testing and Symptom-based Case-finding Rates

The best available evidence for the percentage of individuals in each subgroup receiving an HIV test in the past 12 months identified in our evidence synthesis, necessary to determine monthly testing rates, were derived from sample-based studies, including National HIV Behavioral Surveillance (NHBS)[208,244,248], Behavioral Risk Factor Surveillance System

(BRFSS)[209] and the New York City Community Health Survey (NYC-CHS)[249]. However, selection bias inherent to sample-based studies resulted in testing rates that were likely overestimated and provided a very poor fit during calibration of our model to the observed number of new diagnoses in each city. In the absence of alternative high-quality sources for population-level HIV testing rate estimates, we applied a preliminary model calibration using the same Nelder-Mead algorithm to back-calculate baseline testing rates against the observed number of new diagnoses for each population group in 2012 [229]. We back-calculated testing rates for each population group in the low-risk category as well as a testing rate ratio for individuals with high sexual intensity (compared to low-risk) and symptom-based case finding rates for PLHIV with more advanced HIV stages (200⩽CD4<499, CD4<200). Screening rates for the unscreened susceptible individuals (S_1) were assumed equal to the infected of the same population group. Monthly testing rates for individuals on PrEP were assumed to be 0.333 (the reciprocal of 3 months), consistent with the PrEP prescription guidelines[159].

In this preliminary testing rate calibration, we informed all other parameters with their point estimate and calibrated only against the first year's new diagnoses in order to reduce the influences of uncertainty from other parameters. Only one set of baseline testing and symptom-based case-finding rates was derived from this process and was held fixed in the later formal model calibration and validation. The prior values for the baseline testing rates were back-calculated according to the initial size of the infected but undiagnosed compartments (I_i, Section 2.1) and the observed new diagnoses in 2012, and we assumed a prior of 2.6 (range: 1-5) testing rate ratio for individuals with high sexual intensity level[156,196], while the priors for the symptom-based case finding rates were derived from the published literature[250]. Due to the small number of new diagnoses for some subgroups in some cities, e.g. female Hispanic HET in Seattle, and the associated estimation uncertainty, we adjusted extreme values of back-calculated testing rate estimates to maintain all testing rates within a reasonable range: (1) for PWID and low-risk MSM-PWID, subgroups whose average duration between tests (calculated by 1/testing_rate/12) greater than 15 years or shorter than 1 year were adjusted to a level of 15 years and 1 year respectively (rate = 1/duration/12); (2) for low-risk HET, male subgroups whose average duration between tests greater than 20 years (16 for female) or shorter than 6 years (5 for female) were adjusted to a level of 20 years (16 for female) and 6 years (5 for female) respectively; (3) corresponding high-risk subgroups were adjusted according to their counterparts in the low-risk and the testing rate ratio. These adjustments were based on a CDC analysis of national health data surveys[251] a national health survey for the ratio between male and female HET[251] and on a published modeling study in US[252]. Although these adjustments had minimal impact on model calibration/validation in this study, we believe they were still necessary to ensure face validity. Resulted annual probability of testing for each population group and symptom-based case finding, as transformed from their monthly rates, as well as the testing rate ratio between high-risk and low-risk subgroup of the same kind are presented in **Table A6**. To further validate these testing rate estimates, we also calculated the total number of HIV tests conducted in 2015 (including tests given to both HIV positive and negative individuals) from our model and compare it with a few externally estimates based on some plausible scenarios (**Table A7**).

In order to reflect potential changes in health services delivery, we also allowed for an annual change in the HIV testing rate, ψ_{slope}, assuming a prior of 0.05 (range: 0-0.1), that was subject to calibration, i.e. $\psi_t = \psi_0 * (1 + \psi_{slope})^t$, where ψ_t denotes the resulted testing rate in year t and ψ_0 denotes the baseline testing rate derived from the preliminary

testing rate calibration. This annual change was only applied in the calibration period (2012-2015) and testing rates remained constant in the prospective projections (2016 and onwards).

2.4 ART initiation, re-initiation and dropout rates

ART initiation, re-initiation and dropout from ART were mainly estimated from nationwide collaborative longitudinal HIV cohort data (HIV Research Network, HIVRN)[245] (estimation methods described in Section 2.5). For ART initiation, we differentiated individuals who initiated ART within 30 days of HIV diagnosis and individuals initiating ART more than 30-days post-diagnosis. Given that HIVRN only contains data for a selected PLHIV cohort that are receiving HIV care, and to obtain ART initiation rates applicable to general PLHIV, we adjusted initiation rates using the proportion of PLHIV linked to HIV care following diagnosis (p_1), as derived from city-/state-level surveillance database[253-258]. The proportion of immediate ART initiators (φ_i, i for different CD4 levels, denoted as φ in this section), stratified by sex, race/ethnicity, risk group and CD4 level, was estimated by multiplying the proportion of immediate ART initiation (within 30 days of diagnosis) among newly diagnosed PLHIV on HIV care (φ') with p_1. Similarly, ART initiation rates for PLHIV excluding those who immediately started ART (α_i, denoted as α in this section), also stratified by sex, race/ethnicity, risk group and CD4 level, were the product of two parts: ART initiation rate among diagnosed PLHIV on HIV care (α') and the proportion of diagnosed but untreated PLHIV (i.e. D_i) that are linked to care (p_2). We derived α' by dividing observed number of ART initiations in the cohort by the total person-months of ART-eligible PLHIV in the diagnosed but untreated state. Specifically,

$$\varphi = \varphi' * p_1$$

$$\alpha = \alpha' * p_2$$

$$p_2 = \frac{proportion\ linked\ to\ care\ following\ diagosis\ (but\ untreated)}{proportion\ in\ the\ diagnosed\ but\ untreated\ staus\ following\ diagosis} = \frac{p_1(1-\varphi')}{1-p_1\varphi'}$$

ART dropout rates and re-initiation rates, all stratified by sex, race/ethnicity and risk group, were derived from HIVRN data and were estimated using a continuous-time multi-state Markov model, along with the derivation of disease progression rates (Section 2.1). Full details on the model and estimations are described elsewhere[259,260]. As HIVRN data for CD4 count measurements were not always available for those not on ART, we only differentiated the rates of ART dropout by CD4 category. In addition, we accounted for increased ART adherence associated with OAT receipt by reducing the ART dropout rate for PWID (including MSM-PWID) receiving OAT[261].

2.5 In-migration rates

The number of diagnosed PLHIV migrating into a given city was derived by reconciling the difference between the total number of diagnosed PLHIV reported in surveillance reports and the estimated counterpart according to the reported

number of new diagnoses and all-cause deaths for each year between 2012-2015. Specifically, the estimated diagnosed PLHIV in year t $Diag_t^{est}$ was calculated by:

$$Diag_t^{est} = Diag_{t-1}^{rep} + New\_diag_t^{rep} - Deaths_t^{rep} - Diag_{t-1}^{rep} * Maturation\ rate$$

Where, $Diag_t^{rep}$ denotes the number of reported diagnosed PLHIV in year t

$New\_diag_t^{rep}$ denotes the number of reported new diagnoses in year t

$Deaths_t^{rep}$ denotes the number of reported all-cause deaths among PLHIV in year t

The in-migration rate, which was applied to both diagnosed and undiagnosed PLHIV, was then derived by estimating the average of the proportion of the in-migration population among total observed cases and transforming the yearly probability into corresponding monthly rate. The in-migration rate ρ_m is estimated by:

$$\rho_m = \{-\ln\left(1 - mean(\frac{Diag_t^{rep} - Diag_t^{est}}{Diag_t^{obs}})\right)\}/12$$

The in-migration rates were set to 0 during the projection period (2016-2040) due to a lack of supporting evidence.

2.6 PrEP entry and exit rates

We allowed for growth in PrEP uptake among high-risk MSM and MSM-PWID following the Food and Drug Administration (FDA)'s approval of Truvada for use as PrEP in July 2012[262], before which entry rates were set to 0. Time-varying PrEP entry rates were determined according to the total number of unique PrEP users who had at least one day of PrEP in a year from 2012 to 2015 in each jurisdiction[263], as well as its stratification by race/ethnicity to account for ethnic disparities in PrEP prescriptions[264,265], and we converted this annual probability to a monthly entry rate. The PrEP exit rates, on the other hand, were estimated as the reciprocal of the average duration that individuals remain on PrEP (20.6 months, range: 13.1-49.6)[159].

2.7 OAT entry and exit rates

OAT was available to all PWID and MSM-PWID. The OAT exit rate (one common rate across cities, sex and race/ethnicity) was derived from a systematic review on OAT retention[266] while the entry rates (π) among each PWID and MSM-PWID group were back-calculated according to the exit rate ($\bar{\pi}$) and the initial coverage of OAT among each group assuming the number of OAT entries to equalize exits:

$$N_{PWID\ not\ on\ OAT} * \pi = N_{PWID\ on\ OAT} * \bar{\pi}$$

Such that

$$\pi = \frac{Coverage_{\ OAT}}{1 - Coverage_{\ OAT}} * \bar{\pi}, \qquad where, Coverage_{\ OAT} = \frac{N_{PWID\ on\ OAT}}{N_{PWID\ on\ OAT} + N_{PWID\ not\ on\ OAT}}$$

2.8 Disease progression

Region-specific rates of transitioning between on-ART health states were estimated from a parametric, continuous-time, Multi-state Markov model using HIVRN cohort data, and corresponding regional estimates were used for each city. We estimated the impact of prognostic factors on CD4 disease progression and simultaneously estimated CD4 state transition probabilities during treatment over time, as well as mortality, ART dropout, and ART re-initiation rates. The estimation was operationalized by a matrix with 14 possible instantaneous transitions among 5 states (3 CD4 strata, off ART and death). Sex, race/ethnicity and risk group have all been accounted for as confounding factors in estimating these transition probabilities. Markov chains constitute a common way of modeling the progression of a chronic disease through various severity states. For these models, a transition matrix with the probabilities of moving from one state to another for a specific time interval is usually estimated from observational cohort data. The time between CD4 measurements is inherently controlled for in this methodology. These models efficiently handle heavily censored data, such as when the exact time of disease onset is unknown or when a subject is observed over a portion of his/her disease history[267-272]. This work has been detailed in a prior publication[259,260], and was used to derive monthly transition probabilities between CD4 states, as well as ART dropout and re-initiation rates and mortality. We note that due to a lack of CD4 count records for ART-discontinued PLHIV, estimation for ART re-initiation rates was not stratified by CD4 strata.

We estimated off-ART disease progression (assuming equivalent for any PLHIV not on ART, i.e. I_i, D_i and O_i) from other sources[250,273-275]. Particularly, the disease progression rate for acute stage (from acute to CD4>500 stratum) was calculated as the reciprocal of the estimated mean duration of the acute stage (1.7 months, range: 1-6.8 months[161]). We assumed equivalent mortality rates between HIV-susceptible and untreated PLHIV in acute stage or with CD4 count ≥ 500. For untreated PLHIV in the remaining CD4 strata (200≤CD4<499 and CD4<200), we fitted the model with two baseline mortality rates for non-PWID individuals, as well as two mortality rate multipliers for PWID/MSM-PWID groups (estimates based on HIVRN analysis), one for each CD4 stratum respectively, all constituting candidates for model calibration. In addition, given the protective effect of OAT in reducing overdose and other injected-related risk of death[276], we also allowed for a reduced mortality rate for PWID receiving OAT.

3. Model calibration and validation

3.1 Model calibration

Calibration of model inputs to observed epidemiological endpoints ensures the credibility of model results and thus strengthens our confidence in model inferences. In this study, we adopted a direct-search algorithm, Nelder-Mead algorithm (using R package '*dfoptim*'[277]), to iteratively calibrate key uncertain parameters against three sets of observed calibration endpoints for each city. A total of 17 individual targets composed the three sets of calibration endpoint, including the number of diagnosed PLHIV at each year end (stratified by sex, race/ethnicity and risk group), the annual

number of new HIV diagnoses (separately for the overall estimate, African/American (Black) population, and MSM), and the annual number of all-cause mortality deaths among PLHIV (separately for the overall estimate, African/American (Black) population, and MSM). Specifications for the model calibration process can be found in the manuscript and conformed with methodological guidelines[61], including those for the selection of calibration targets, free parameters, Goodness-of-fit (GoF) metric, search algorithm, acceptance criteria and stopping rule. Our calibration computations (10,000 iterations for each city) was performed on the platform of Compute Canada WestGrid HPC Cluster infrastructure (www.computecanada.ca). The selection of initial free parameters for calibration and the determination of target weight for a multi-target GoF metric are two fundamental components in model calibration; however, this selection has typically been based on subjective decisions in previous modeling studies[61]. In the following sections, we present two methods we adopted to determine the set of calibration parameters and target weights to reduce such subjectivity. The full breadth of model calibration results are presented in **Figure A2**.

3.1.1 Morris method and parameter selection

The list of free parameters were determined by adopting a one-at-a-time (OAT) factor screening approach - Morris method[169]. Given the high dimensionality of data space, calibrating all of them are computationally infeasible, entailing a screening process throughout the uncertain parameter space prior to model calibration[278]. Morris method employs individually randomized one-factor-at-a-time experiments to characterize the impact of the change in an input parameter on a model output, i.e. elementary effect[169], intending to isolate the parameters that have either biggest linear (additive) effects, or non-linear (interaction) effects on the model outcomes (calibration targets)[279]. All 140 parameters ($\boldsymbol{X} = x_1, x_2, x_i, \dots, x_{140}$) determining model dynamics were identified to enter the parameter selection process, and their plausible ranges were specified in **Table A1**. Detailed process for the Morris method is presented below:

Before proceeding, the parameter space $\boldsymbol{X}$ is discretized into a p-level grid Ω such that x_i can only take values from the set ${x_i}^{min} + \{0, \frac{1}{\mathrm{p}-1}, \frac{2}{\mathrm{p}-1}, \dots, 1\}({x_i}^{max} - {x_i}^{min})$, where ${x_i}^{max}$ and ${x_i}^{min}$ denote the minimum and maximum possible values for parameter x_i, resulting in a 140-dimensional p-level grid.

The Morris design starts by randomly selecting a 'base' value $\boldsymbol{x}^*$ for the vector $\boldsymbol{X}$ such that each component is sampled from Ω. The first sampling point $\boldsymbol{x}^{(1)}$ is derived from $\boldsymbol{x}^*$ by increasing one or more components by Δ while $\boldsymbol{x}^{(1)}$ remaining in Ω, where Δ is a predetermined multiple of $1/(\mathrm{p}-1)$ assuming each x_i is scaled to the interval [0, 1]. The second sampling point $\boldsymbol{x}^{(2)} = (\boldsymbol{x}^{(1)} \pm \boldsymbol{e_i}\Delta)$, whichever remains in Ω, where $\boldsymbol{e_i}$ is a vector of zeros but with a unit as its i^{th} component (i is randomly selected from {1, 2, …, k}). The third sampling point $\boldsymbol{x}^{(3)} = (\boldsymbol{x}^{(2)} \pm \boldsymbol{e_j}\Delta)$, whichever remains in Ω, where j is randomly selected from the remaining {1, 2, …, k} that $j \neq i$. This procedure proceeds until all the components have been changed once, producing a succession of k+1 sampling points, with two consecutive points differ in only one component by the same Δ. This process will be repeated r times, each with a new set of randomly generated 'base' value, to create $(k+1)r$ sampling points (excluding the 'base' set) on which model was evaluated.

A convenient choice for the parameter p and Δ is that p is even and Δ equals to $p/[2(p-1)]$[169,280]. We chose $p = 8$ (and thus $\Delta = 4/7$) and $r = 10$.

The elementary effect associated with the parameter x_i (assuming x_i as the component in which current sampling point differs from the previous) in the j^{th} iteration on target t is estimated by:

$d_j^t(x_i) = \frac{y^t(x_1+x_2+\cdots+x_{i-1}+x_i+\Delta+x_{i+1}\ldots+x_k)-y^t(x_1+x_2+\cdots+x_k)}{\Delta}$, if x_i has been increase by Δ, or

$d_j^t(x_i) = \frac{y^t(x_1+x_2+\cdots+x_k)-y^t(x_1+x_2+\cdots+x_{i-1}+x_i+\Delta+x_{i+1}\ldots+x_k)}{\Delta}$, if x_i has been decrease by Δ.

where $y^t(\boldsymbol{X})$ denotes the model outcome (in respect of calibration target t) by inputting $\boldsymbol{X}$.

The sensitivity measures, μ and σ, are respectively the mean and standard deviation of the distribution of elementary effects and are estimated by:

$$\boldsymbol{\mu_i^t} = \sum_{j=1}^{r} d_j^t(x_i)/r$$

$$\boldsymbol{\sigma_i^t} = \sqrt{\sum_{j=1}^{r} (d_j^t(x_i) - \boldsymbol{\mu_i^t})^2/r}$$

Campolongo et al. recommended the use of $\boldsymbol{\mu_i^{t^*}} = |\boldsymbol{\mu_i^t}|$ as to reduce the Type II error[279]. A higher μ^* indicates a larger overall elementary (or first-order) effect (linear effect) on the output. A larger standard deviation σ implies possible interaction effects (non-linear effects) with other parameters on the output. While there's no explicit guidelines for the cutoff values[278], we classified parameters with either μ^* or σ greater than 7.5% of any calibration targets as influential and included them in the subsequent model calibration. **Table A1** presented results of the selected key uncertain parameters for each city from the Morris method, together with their prior and post-calibration values before/after calibration.

3.1.2 Best-worst method and target weight determination

To estimate the weights for each target in the overall weighted 'goodness of fit', we adopted a novel best-worst method (BWM)[179,180] that has been applied in the field of operations research[281-284]. BWM is a multi-criteria decision-making method that relies on structured pairwise comparison to identify optimal weight for each decision criterion (i.e. calibration target) according to the preferences (i.e. relative importance) between each criterion with the best and worst criterion. This approach possesses advantages in requiring less comparison data than a full pairwise comparison matrix and generating more consistent results[281]. BWM requires decision makers to first select the best criterion that has the most important role in decision making, and the worst criterion (least important) and then place their preferences of the best criterion over each of the other criteria and also preferences of each of the other criteria over the worst criterion using a

number from a predefined scale (e.g. 1 to 9). These two sets of pairwise comparison results are then used to determine the optimal weight for each criterion by solving:

$$\text{Minimize } \xi^L \text{ , such that}$$

$$\left|w_B - a_{Bj} w_j\right| \leq \xi^L, \text{ for all j}$$

$$\left|w_j - a_{jW} w_W\right| \leq \xi^L, \text{ for all j}$$

$$\sum_j w_j = 1$$

$$w_j \geq 0, \text{ for all j}$$

where, w_B and w_W: the weight for the best and worst criterion respectively

w_j: the weight for criterion j (i.e. j^{th} target)

a_{Bj}: the preference of the best criterion over criterion j

a_{jW}: the preference of criterion j over the worst criterion

We designed a brief survey for our SAC members according to the essential steps of BWM. Specifically, each SAC member was asked to provide responses in choosing the calibration target they think is most important (Best) and the target that is least important (Worst) for the model to accurately reproduce. Pairwise comparisons were then performed to rate their preferences (interpreted as relative importance for calibration) of each target against the most and the least important target on a scale of 1-9 in integers. The optimization problem was solved by using R package '*nloptr*'[285]. The ultimate weight for each target was then determined by averaging the weight derived from each SAC member's survey result. **Figure A3** shows an example of the survey we distributed among our SAC members. **Table A8** shows the resulted weight vector. The three targets with the highest weights (i.e. greatest importance), as selected by our SAC, were (1) Annual number of new HIV diagnoses (Total); (2) Annual number of new HIV diagnoses (MSM); (3) Annual number of new HIV diagnoses (Black). Adjustments to weights were made for cities with unique microepidemics or missing target data (see more details in the legend of **Table A8**).

3.2 Model Validation

Model validation is another tool to ensure the accuracy of a model in making relevant predictions. We performed model validation to assess the face, internal and external validity of the model. In particular, model projections (on the basis of calibrated parameter sets) were externally validated against the empirically estimated annual number of HIV incident cases (separately for the overall estimate and MSM population) between 2012-2015 and evaluated according to the proportion of projections fallen within the confidence intervals. More details about the process of model validation can be found in the manuscript and the external validation results are available in **Figure A4**. To assess the internal validity

of our model, we performed extreme value analyses on a few hypothetical extreme scenarios to help us determine whether the model performed as expected. **Table A9** presents these scenarios in comparison with our anticipated results.

For face validation, we provided a survey to our Scientific Advisory Committee with 25-year status quo projections (2016-2040) for each microepidemic assuming no changes in HIV treatment, care and prevention service provision from 2015 levels (except PrEP up until 2017 levels). In the survey, we detailed our projections for each city on (1) population dynamics, stratified by race/ethnicity; (2) cascades of HIV care; (3) rate of new incidence, overall and stratified by race/ethnicity and risk group; (4) rate of new diagnoses, overall and stratified by race/ethnicity and risk group; (5) and rate of new incidence and new diagnoses among MSM, overall and stratified by race/ethnicity. We distributed the survey and performed individual follow-up with our SAC members to gather their expert opinion on the face validity of our model outcomes for each city. While most of the feedback we received was consistent with on our projections, two major concerns were raised during the consultation. The first concern was a general concern regarding the scale-up of PrEP during the first few years of projection period: new evidence came out showing that most cities were undergoing rapid growth in PrEP uptake in more recent years, while our previous modeling protocol only allowed PrEP growth up until 2015 and remained fixed at that level from 2016 and onwards. The important difference of PrEP uptake between 2015 and 2017 could lead to an overestimation of the projected epidemic during this period and thus result in an overly optimistic evaluation for the cost-effectiveness of further PrEP expansion. To address this concern, we modified our modeling protocol to incorporate the new PrEP data (up to 2017) for our status quo scenario. The second major concern was raised by our local experts from Seattle where our projected epidemic exceeded their expectations/known figures. We reviewed our model and evidence inputted for Seattle and identified two factors that might have caused the discrepancy. First, data from HIVRN that were used to inform ART initiation, re-initiation and dropout rates for Seattle may not have been representative given that HIVRN data for the western region did not include any study sites from Washington state. We hypothesized that this may have resulted in a projected cascade of HIV care that did not accurately represent local epidemiological data. We collected additional information from Seattle's annual surveillance reports and conducted further back-calculation for the new ART engagement estimates. Second, we also noticed a change in Seattle's latest surveillance report with respect to the definition of the counts of new diagnoses - now excluding people who had been diagnosed elsewhere[286]. While Seattle experts' judgement was based on the estimates in their new report, our model was calibrated to the old targets from previous surveillance reports (which were significantly higher). We updated our target data with the new estimates and recalibrated our model to this new set of targets. With the above modifications, our model yielded outcomes that were confirmed by our Seattle SAC members (MG, JD). **Figure A4** presents figures we included in the face validation survey following the conclusion of the face validation process.

Table A1. Free parameters for calibration

COMMON PARAMETERS - Prior: point estimates (range); Post-calibration: median (95% credible interval)						
CITY	***Atlanta***	***Baltimore***	***Los Angeles***	***Miami***	***New York City***	***Seattle***
Monthly mortality rate for PLHIV (CD4: 200-499), except PWID						
Prior	6.00E-4 (3.06E-4, 4.7E-3)					
Post	3.06E-4 (3.06E-4, 3.06E-4)	3.11E-4 (3.06E-4, 1.22E-3)	3.06E-4 (3.06E-4, 3.07E-4)	4.57E-4 (3.06E-4, 1.31E-3)	3.45E-4 (3.06E-4, 4.96E-4)	3.06E-4 (3.06E-4, 3.08E-4)
Monthly mortality rate for PLHIV (CD4<200), except PWID						
Prior	0.0072 (0.0038, 0.0128)					
Post	0.0038 (0.0038, 0.0038)	0.0101 (0.0084, 0.0104)	0.0038 (0.0038, 0.0038)	0.0046 (0.0038, 0.0059)	0.0038 (0.0038, 0.0042)	0.0038 (0.0038, 0.0038)
Multiplier of mortality rate for PLHIV that inject drugs (CD4: 200-499)						
Prior	1.59 (1.18, 6.10)					
Post	1.18 (1.18, 1.20)	1.18 (1.18, 1.21)	1.18 (1.18, 1.54)	2.12 (1.18, 6.10)	5.77 (1.18, 6.10)	1.18 (1.18, 1.29)
Multiplier of mortality rate for PLHIV that inject drugs (CD4<200)						
Prior	1.59 (1.18, 6.10)					
Post	1.18 (1.18, 1.18)	1.18 (1.18, 1.18)	1.18 (1.18, 1.22)	1.43 (1.18, 3.29)	5.41 (4.75, 6.10)	1.18 (1.18, 1.20)
Multiplier for number of sexual partners for PWID, relative to HET*						
Prior	0.4 (0.1, 2)					
Post	0.102 (0.100, 2.00)		0.101 (0.100, 0.207)			0.154 (0.100, 2.00)
Decreased number of sexual partners post-diagnosis						
Prior	68% (59%, 76%)					
Post	76.0% (75.2%, 76.0%)	76.0% (75.8%, 76.0%)	74.5% (59.0%, 76.0%)	73.1% (59.0%, 76.0%)	75.1% (69.2%, 76.0%)	59.3% (59.0%, 71.6%)
Injection frequency per month						
Prior	30 (15, 60)					
Post		15.0 (15.0, 15.33)	41.7 (21.9, 60.0)		15.8 (15.0, 59.4)	29.3 (15.1, 59.9)
Decreased probability of injection sharing post-diagnosis						
Prior	50% (10%, 90%)					
Post		90.0% (89.4%, 90.0%)	57.9% (10.0%, 76.7%)		89.1% (51.8%, 90.0%)	26.9% (10.0%, 89.9%)
SSP effect on reducing injection sharing						
Prior	42% (22%, 81%)					
Post						30.8% (22.0%, 81.0%)
Probability of transmission per heterosexual partnership (CD4⩾500), female to male						
Prior	0.015 (0.005, 0.07)					

Post	0.0050 (0.0050, 0.012)		0.0050 (0.0050, 0.0056)	0.0055 (0.0050, 0.0293)	0.0078 (0.0050, 0.0329)	0.0698 (0.0361, 0.070)
Probability of transmission per heterosexual partnership (CD4: 200-499), female to male						
Prior	0.025 (0.005, 0.07)					
Post	0.0593 (0.0050, 0.070)					
Probability of transmission per heterosexual partnership (CD4<200), female to male						
Prior	0.05 (0.0125, 0.14)					
Post	0.0376 (0.0125, 0.140)			0.0545 (0.0125, 0.140)		
Probability of transmission per heterosexual partnership (CD4≥500), male to female						
Prior	0.03 (0.02, 0.07)					
Post	0.0201 (0.020, 0.070)	0.0200 (0.20, 0.0204)	0.0211 (0.020, 0.070)	0.0695 (0.0454, 0.070)	0.0202 (0.020, 0.0315)	0.0641 (0.020, 0.070)
Probability of transmission per heterosexual partnership (CD4:200-499), male to female						
Prior	0.05 (0.02, 0.07)					
Post	0.0222 (0.20, 0.070)					
Probability of transmission per heterosexual partnership (CD4<200), male to female						
Prior	0.1 (0.05, 0.14)					
Post	0.0501 (0.0500, 0.140)					
Probability of transmission per homosexual partnership (CD4≥500)						
Prior	0.045 (0.025, 0.1)					
Post	0.0251 (0.0250, 0.0433)	0.0477 (0.0250, 0.100)	0.0674 (0.0250, 0.100)	0.0582 (0.0253, 0.100)	0.0635 (0.0251, 0.100)	0.0352 (0.0250, 0.0995)
Probability of transmission per homosexual partnership (CD4: 200-499)						
Prior	0.065 (0.025, 0.1)					
Post	0.0483 (0.0250, 0.0710)	0.100 (0.0254, 0.100)	0.0996 (0.0741, 0.100)	0.0990 (0.0444, 0.100)	0.0935 (0.0285, 0.100)	0.0629 (0.0250, 0.100)
Probability of transmission per homosexual partnership (CD4<200)						
Prior	0.125 (0.05, 0.2)					
Post	0.0500 (0.050, 0.0524)	0.050 (0.050, 0.0557)	0.137 (0.050, 0.200)	0.0504 (0.050, 0.143)	0.103 (0.0561, 0.177)	0.1697 (0.0501, 0.200)
Probability of transmission per shared injection (CD4≥500)						
Prior	0.003 (0.0014, 0.0092)					
Post	0.0092 (0.0091, 0.0092)	0.0014 (0.0014, 0.0092)		0.0092 (0.0014, 0.0092)		0.0082 (0.0014, 0.0092)
Probability of transmission per shared injection (CD4: 200-499)						
Prior	0.004 (0.0014, 0.0092)					
Post		0.0014 (0.0014, 0.0092)				
Probability of transmission per shared injection (CD4<200)						
Prior	0.006 (0.0041, 0.020)					

Post		0.0041 (0.0041, 0.0045)				
Multiplier of transmission probability for acute stage						
Prior			5.3 (0.79, 10)			
Post	2.39 (0.790, 9.06)	1.04 (0.790, 4.12)	0.838 (0.790, 2.637)	9.34 (4.35, 10.0)	2.55 (0.790, 9.95)	1.24 (0.790, 5.08)
ART effect in reducing probability of sexual transmission						
Prior			91% (79%, 96%)			
Post		96.0% (79.0%, 96.0%)	91.7% (79.0%, 96.0%)	80.4% (79.0%, 96.0%)	94.8% (84.7%, 96.0%)	79.4% (79.0%, 90.7%)
ART effect in reducing probability of injection-sharing transmission						
Prior			50% (10%, 90%)			
Post		90.0% (10.0%, 90.0%)				
Condom effectiveness in reducing heterosexual transmission						
Prior			80% (57%, 91%)			
Post	90.4% (57.0%, 91.0%)		89.8% (57.0%, 91.0%)			57.4% (57.0%, 91.0%)
Condom effectiveness in reducing homosexual transmission						
Prior			70.5% (58.2%, 79.2%)			
Post	79.1% (58.2%, 79.2%)	77.4% (58.2%, 79.2%)	66.9% (58.2%, 79.2%)	68.7% (58.2%, 79.2%)	75.3% (58.3%, 79.2%)	65.2% (58.2%, 79.2%)
Annual change in HIV testing rate*						
Prior			0.05 (0, 0.1)			
Post	0.100 (0.0933, 0.100)	0.00 (0.00, 0.00057)	0.00 (0.00, 0.010)	0.0814 (0.0001, 0.100)	0.100 (0.0859, 0.100)	0.0008 (0.00, 0.0220)
Transition rate from acute to chronic HIV (1 / acute stage duration)						
Prior			0.588 (0.147, 1)			
Post	0.147 (0.147, 0.197)	0.147 (0.147, 0.185)	0.150 (0.147, 0.998)	0.148 (0.147, 0.223)	0.797 (0.159, 1.00)	0.162 (0.147, 1.00)

CITY-SPECIFIC PARAMETERS - Prior: point estimates (range); Post: median (95% credible interval)

CITY	***Atlanta***	***Baltimore***	***Los Angeles***	***Miami***	***New York City***	***Seattle***
Monthly number of heterosexual partners for White, low-risk MSM						
Prior	0.0219 (0.0143, 0.0298)					
Post	0.0143 (0.0143, 0.0152)					
Monthly number of heterosexual partners for White, high-risk MSM						
Prior				0.0264 (0.0094, 0.0595)		0.0419 (0.0086, 0.0663)
Post				0.0183 (0.0094, 0.0595)		0.00866 (0.0086, 0.0632)
Monthly number of heterosexual partners for Black, high-risk MSM						
Prior	0.0795 (0.0150, 0.150)					

Post	0.149 (0.0150, 0.150)					
Monthly number of heterosexual partners for Hispanic, high-risk MSM						
Prior				0.0719 (0.0123, 0.160)		
Post				0.159 (0.0962, 0.160)		
Monthly number of heterosexual partners for male, White, high-risk HET						
Prior	0.670 (0.549, 0.791)					
Post	0.553 (0.549, 0.791)					
Monthly number of heterosexual partners for male, Black, high-risk HET						
Prior	0.633 (0.213, 1.05)		0.814 (0.486, 1.14)			
Post	1.048 (0.213, 1.05)		0.491 (0.486, 1.14)			
Monthly number of heterosexual partners for female, White, high-risk HET						
Prior	0.657 (0.567, 0.747)				0.581 (0.402, 0.760)	
Post	0.567 (0.567, 0.747)				0.408 (0.402, 0.760)	
Monthly number of heterosexual partners for female, Black, high-risk HET						
Prior	0.545 (0.0750, 1.02)					
Post	1.018 (0.999, 1.02)					
Monthly number of heterosexual partners for female, Hispanic, high-risk HET						
Prior			0.626 (0.485, 0.767)			0.626 (0.485, 0.767)
Post			0.767 (0.486, 0.767)			0.767 (0.488, 0.767)
Monthly number of homosexual partners for White, low-risk MSM						
Prior		0.174 (0.144, 0.203)				0.174 (0.144, 0.203)
Post		0.145 (0.144, 0.203)				0.151 (0.144, 0.203)
Monthly number of homosexual partners for Black, low-risk MSM						
Prior		0.213 (0.132, 0.294)	0.213 (0.132, 0.294)		0.213 (0.132, 0.294)	
Post		0.132 (0.132, 0.294)	0.292 (0.167, 0.294)		0.291 (0.145, 0.294)	
Monthly number of homosexual partners for White, high-risk MSM						
Prior	0.802 (0.203, 1.80)	0.904 (0.203, 3.02)	0.857 (0.203, 1.87)	1.30 (0.203, 3.02)	0.907 (0.203, 2.08)	0.669 (0.203, 1.49)
Post	0.203 (0.203, 0.204)	0.203 (0.203, 0.230)	0.226 (0.203, 0.325)	0.207 (0.203, 0.322)	0.212 (0.203, 0.319)	0.220 (0.203, 0.656)
Monthly number of homosexual partners for Black, high-risk MSM						
Prior	0.457 (0.294, 1.80)	0.665 (0.294, 1.50)	0.633 (0.294, 1.52)	1.06 (0.294, 2.30)	0.603 (0.294, 1.49)	0.558 (0.294, 1.67)
Post	1.800 (1.40, 1.80)	1.49 (1.39, 1.49)	1.50 (1.08, 1.52)	0.753 (0.316, 1.25)	1.44 (0.986, 1.49)	0.517 (0.295, 1.22)
Monthly number of homosexual partners for Hispanic, high-risk MSM						
Prior	0.720 (0.208, 1.67)	0.932 (0.208, 1.67)	0.725 (0.208, 1.45)	1.04 (0.208, 2.46)	0.817 (0.208, 1.67)	0.757 (0.208, 1.82)

Post	0.475 (0.208, 0.498)	0.362 (0.263, 0.540)	0.392 (0.208, 0.528)	0.528 (0.222, 0.950)	0.925 (0.544, 1.25)	0.694 (0.470, 1.47)
Condom use probability in heterosexual partnership for male, White, high-risk HET						
Prior	0.315 (0.128, 0.502)					
Post	0.501 (0.128, 0.502)					
Condom use probability in homosexual partnership for White, low-risk MSM						
Prior						0.333 (0.229, 0.437)
Post						0.392 (0.229, 0.437)
Condom use probability in homosexual partnership for Black, low-risk MSM						
Prior		0.574 (0.230, 0.919)	0.574 (0.230, 0.919)	0.574 (0.230, 0.919)	0.574 (0.230, 0.919)	
Post		0.917 (0.230, 0.919)	0.238 (0.230, 0.918)	0.331 (0.230, 0.918)	0.351 (0.230, 0.914)	
Condom use probability in homosexual partnership for Hispanic, low-risk MSM						
Prior			0.642 (0.396, 0.888)	0.642 (0.396, 0.888)	0.642 (0.396, 0.888)	
Post			0.580 (0.396, 0.888)	0.398 (0.396, 0.817)	0.696 (0.396, 0.888)	
Condom use probability in homosexual partnership for White, high-risk MSM						
Prior		0.435 (0.350, 0.519)	0.366 (0.321, 0.411)	0.435 (0.350, 0.520)	0.466 (0.418, 0.513)	0.318 (0.281, 0.355)
Post		0.519 (0.350, 0.519)	0.399 (0.321, 0.411)	0.487 (0.350, 0.520)	0.505 (0.419, 0.513)	0.336 (0.281, 0.355)
Condom use probability in homosexual partnership for Black, high-risk MSM						
Prior		0.472 (0.360, 0.583)		0.477 (0.411, 0.543)	0.543 (0.466, 0.619)	0.466 (0.351, 0.580)
Post		0.360 (0.360, 0.583)		0.509 (0.411, 0.543)	0.542 (0.466, 0.619)	0.499 (0.351, 0.580)
Condom use probability in homosexual partnership for Hispanic, high-risk MSM						
Prior		0.379 (0.250, 0.508)		0.377 (0.339, 0.416)	0.412 (0.361, 0.462)	0.289 (0.211, 0.368)
Post		0.428 (0.250, 0.508)		0.388 (0.339, 0.416)	0.443 (0.361, 0.462)	0.318 (0.211, 0.368)
Assortativeness of heterosexual partnership paring for high-risk Black						
Prior	0.668 (0.560, 0.775)					
Post	0.775 (0.771, 0.775)					
Proportion of PLHIV linked to HIV care following diagnosis (CD4⩾500) for male, Black PWID						
Prior					0.560 (0.226, 0.848)	
Post					0.241 (0.226, 0.329)	
Proportion of PLHIV linked to HIV care following diagnosis (CD4⩾500) for female, Black PWID						
Prior		0.610 (0.273, 0.867)				
Post		0.867 (0.856, 0.867)				

Table for complete model parameters and the evidence sources for the above selected parameters can be found in the previously published evidence synthesis paper[229]. * Data prior values (range/distribution) based on assumptions.

Table A2. Assumptions regarding HIV contact between HIV-infected and uninfected individuals, by risk group

		MSM	MSM/PWID	PWID		HETERO	
				M*	F*	M*	F*
MSM		Homosexual sex	Homosexual sex		Heterosexual sex		Heterosexual sex
MSM/PWID		Homosexual sex	Needle sharing, Homosexual sex	Needle sharing	Needle sharing, Heterosexual sex		Heterosexual sex
PWID	M*		Needle sharing	Needle sharing	Needle sharing, Heterosexual sex		Heterosexual sex
	F*	Heterosexual sex	Needle sharing, Heterosexual sex	Needle sharing, Heterosexual sex	Needle sharing	Heterosexual sex	
HETERO	M*				Heterosexual sex		Heterosexual sex
	F*	Heterosexual sex	Heterosexual sex	Heterosexual sex		Heterosexual sex	

MSM: Men who have sex with men; PWID: injection drug users; HETERO: heterosexual individuals (non-injection drug users). *In the model, we differentiated males and females (denoted as M and F respectively) to take into account their distinct HIV contacts with other risk group. Corresponding to the sex distribution among PWID and HETERO group, the ratio of proportion of male to female was assumed to be 1:1 among heterosexual group and 2:1 among PWID group.

Table A3. Assortative mixing matrix for heterosexual partnership

	PE (range)	***Risk level for r'***	***Low-risk***			***High-risk***		
Region	*Risk level for r*	**Ethnicity**	White	Black	Hispanic	White	Black	Hispanic
Northeast: ***BAL*** ***NYC***		White	0.72 (0.65, 0.78)					
	Low-risk	Black		0.64 (0.54, 0.73)				
		Hispanic			0.51 (0.41, 0.60)			
		White				0.48 (0.25, 0.72)		
	High-risk	Black					0.74 (0.53, 0.96)	
		Hispanic						0.36 (0.08, 0.64)
Southeast: ***ATL*** ***MIA***		White	0.69 (0.65, 0.73)					
	Low-risk	Black		0.76 (0.73, 0.80)				
		Hispanic			0.62 (0.55, 0.68)			
		White				0.54 (0.42, 0.66)		
	High-risk	Black					0.67 (0.56, 0.78)	
		Hispanic						0.49 (0.31, 0.67)
West: ***LA*** ***SEA***		White	0.54 (0.48, 0.60)					
	Low-risk	Black		0.63 (0.52, 0.73)				
		Hispanic			0.53 (0.47, 0.59)			
		White				0.54 (0.35, 0.73)		
	High-risk	Black					0.63 (0.52, 0.73)	
		Hispanic						0.57 (0.38, 0.76)

Northeast region, including Baltimore (BAL) and New York City (NYC); Southeast region, including Atlanta (ATL) and Miami (MIA); West region, including Los Angeles (LA) and Seattle (SEA). PE: point estimate

Table A4. Assortative mixing matrix for homosexual partnership

Region	*PE (range)*	*Risk level for r'*	*Low-risk*			*High-risk*		
	Risk level for r	**Ethnicity**	White	Black	Hispanic	White	Black	Hispanic
Northeast: ***BAL*** ***NYC***		White	0.35 (0.32, 0.38)					
	Low-risk	Black		0.50 (0.46, 0.53)				
		Hispanic			0.06 (0.02, 0.10)			
		White				0.35 (0.32, 0.38)		
	High-risk	Black					0.50 (0.46, 0.53)	
		Hispanic						0.06 (0.02, 0.10)
Southeast: ***ATL*** ***MIA***		White	0.35 (0.32, 0.38)					
	Low-risk	Black		0.50 (0.46, 0.53)				
		Hispanic			0.06 (0.02, 0.10)			
		White				0.35 (0.32, 0.38)		
	High-risk	Black					0.50 (0.46, 0.53)	
		Hispanic						0.06 (0.02, 0.10)
West: ***LA*** ***SEA***		White	0.11 (0.07, 0.15)					
	Low-risk	Black		0.23 (0.17, 0.28)				
		Hispanic			0.06 (0.02, 0.09)			
		White				0.11 (0.07, 0.15)		
	High-risk	Black					0.23 (0.17, 0.28)	
		Hispanic						0.06 (0.02, 0.09)

Northeast region, including Baltimore (BAL) and New York City (NYC); Southeast region, including Atlanta (ATL) and Miami (MIA); West region, including Los Angeles (LA) and Seattle (SEA). PE: point estimate

Table A5. Initial values for population subgroups used to instantiate the model

Atlanta				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{1P}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	31861	4584	0	13	510	204	548	0	0	16	495	643	463	943	754	206	530	382	206
			Black	8616	2821	0	26	1028	411	1105	0	0	38	1040	1795	886	1622	1408	497	785	831	456
			Hispanic	4435	3097	0	2	90	36	97	0	0	3	82	146	113	136	134	27	64	82	29
	High-risk		White	3774	8375	0	5	189	75	203	0	0	6	183	238	171	349	279	76	196	141	76
			Black	982	2830	0	10	380	152	409	0	0	14	385	664	328	600	521	184	290	307	169
			Hispanic	1358	1152	0	1	33	13	36	0	0	1	30	54	42	50	50	10	24	30	11
MSM-PWID	Low-risk	Off-OAT	White	2556	368	0	0	17	7	18	0	0	2	73	55	40	65	59	21	29	34	21
			Black	433	142	0	1	27	11	29	0	0	3	131	98	72	97	88	31	43	51	32
			Hispanic	211	148	0	0	3	1	3	0	0	0	12	9	7	9	8	3	4	5	3
		On-OAT	White	303	672	0	0	7	3	8	0	0	1	31	23	17	28	25	9	12	15	9
			Black	49	142	0	0	12	5	13	0	0	1	56	42	31	42	38	13	19	22	14
			Hispanic	65	55	0	0	1	0	1	0	0	0	5	4	3	4	3	1	2	2	1
	High-risk	Off-OAT	White	105	15	0	0	1	0	1	0	0	0	3	2	2	3	2	1	1	1	1
			Black	7	2	0	0	0	0	0	0	0	0	2	2	1	2	1	0	1	1	1
			Hispanic	7	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		On-OAT	White	12	28	0	0	0	0	0	0	0	0	1	1	1	1	1	0	1	1	0
			Black	1	2	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
			Hispanic	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PWID	Male	Off-OAT	White	4558	2486	0	0	9	4	10	0	0	1	36	36	46	36	32	11	16	19	12
			Black	6160	7150	0	1	52	21	56	0	0	7	217	213	275	181	163	57	81	95	59
			Hispanic	1049	1049	0	0	3	1	3	0	0	0	12	12	15	9	8	3	4	5	3
		On-OAT	White	188	102	0	0	0	0	0	0	0	0	1	1	2	1	1	0	1	1	0
			Black	98	114	0	0	1	0	1	0	0	0	3	3	4	3	3	1	1	2	1
			Hispanic	37	37	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	Female	Off-OAT	White	2817	2504	0	0	10	4	10	0	0	1	42	41	53	45	41	14	20	24	15
			Black	3152	3796	0	1	32	13	35	0	0	5	153	151	194	139	126	44	62	73	46
			Hispanic	632	632	0	0	2	1	2	0	0	0	10	10	13	9	8	3	4	5	3
		On-OAT	White	217	193	0	0	1	0	1	0	0	0	3	3	4	3	3	1	2	2	1
			Black	109	132	0	0	1	0	1	0	0	0	5	5	7	5	4	2	2	3	2
			Hispanic	33	33	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0
HET	Low-risk	Male	White	778225	111972	0	0	12	5	12	0	0	0	4	10	17	18	15	3	12	7	2
			Black	333174	109066	0	3	113	45	122	0	0	4	64	134	150	138	133	57	44	86	62
			Hispanic	101669	70990	0	0	12	5	13	0	0	0	5	11	24	13	17	5	6	8	6
		Female	White	10633	31899	0	0	1	0	1	0	0	0	0	1	2	2	1	0	1	1	0
			Black	29941	22882	0	1	31	12	33	0	0	1	17	36	41	38	36	16	12	23	17
			Hispanic	7730	1933	0	0	1	1	2	0	0	0	1	1	3	2	2	1	1	1	1
	High-risk	Male	White	929822	69926	0	1	35	14	37	0	0	1	45	53	32	101	59	15	55	36	12
			Black	498796	128307	0	9	359	143	385	0	0	16	492	580	504	918	561	190	445	380	155
			Hispanic	157276	4569	0	1	23	9	24	0	0	1	27	43	35	60	35	7	25	23	11
		Female	White	10188	6792	0	0	1	0	1	0	0	0	2	2	1	3	2	1	2	1	0
			Black	7723	5467	0	0	15	6	17	0	0	1	21	25	22	39	24	8	19	16	7
			Hispanic	713	1070	0	0	1	0	1	0	0	0	1	1	1	1	1	0	1	1	0

Baltimore				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{IP}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	21581	1781	0	1	57	23	61	0	0	1	27	23	9	183	91	9	101	59	17
			Black	5478	1536	0	5	205	82	221	0	0	4	131	169	60	484	368	74	241	235	104
			Hispanic	1550	306	0	0	9	4	10	0	0	0	5	7	2	22	17	3	14	10	2
	High-risk		White	2476	5311	0	1	21	8	23	0	0	0	10	8	3	68	34	3	37	22	6
			Black	743	1594	0	2	76	30	82	0	0	1	49	62	22	179	136	27	89	87	39
			Hispanic	197	422	0	0	3	1	4	0	0	0	2	3	1	8	6	1	5	4	1
MSM-PWID	Low-risk	Off-OAT	White	2143	177	0	0	3	1	3	0	0	0	5	4	3	14	13	4	7	8	5
			Black	737	207	0	0	11	4	11	0	0	1	28	21	15	51	46	16	24	29	18
			Hispanic	87	17	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	1
		On-OAT	White	246	527	0	0	1	0	1	0	0	0	2	2	1	6	5	2	3	3	2
			Black	100	214	0	0	5	2	5	0	0	0	12	9	7	22	20	7	10	12	8
			Hispanic	11	24	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0
	High-risk	Off-OAT	White	336	28	0	0	0	0	0	0	0	0	1	1	0	2	2	1	1	1	1
			Black	28	8	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	1
			Hispanic	6	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		On-OAT	White	39	83	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0
			Black	4	8	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
			Hispanic	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PWID	Male	Off-OAT	White	2740	6185	0	0	19	8	21	0	0	1	39	39	50	104	94	33	49	58	36
			Black	4612	10410	0	2	78	31	84	0	0	7	200	196	253	377	341	120	180	212	132
			Hispanic	189	426	0	0	3	1	4	0	0	0	8	8	10	16	15	5	8	9	6
		On-OAT	White	430	970	0	0	3	1	3	0	0	0	6	6	8	16	15	5	8	9	6
			Black	177	400	0	0	3	1	3	0	0	0	8	8	10	14	13	5	7	8	5
			Hispanic	14	32	0	0	0	0	0	0	0	0	1	1	1	1	1	0	1	1	0
	Female	Off-OAT	White	2874	5704	0	0	6	2	6	0	0	1	18	18	23	34	30	11	16	19	12
			Black	4011	7963	0	1	50	20	54	0	0	6	183	179	231	259	234	82	124	146	91
			Hispanic	190	377	0	0	1	0	1	0	0	0	4	4	5	6	5	2	3	3	2
		On-OAT	White	585	1160	0	0	1	0	1	0	0	0	4	4	5	7	6	2	3	4	2
			Black	146	290	0	0	2	1	2	0	0	0	7	7	8	9	9	3	4	5	3
			Hispanic	20	41	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0
HET	Low-risk	Male	White	499979	41272	0	2	79	32	85	0	0	2	80	84	24	130	85	41	88	41	31
			Black	147219	41271	0	6	245	98	264	0	0	7	234	283	190	331	272	120	161	172	120
			Hispanic	34959	6910	0	0	12	5	13	0	0	0	9	13	11	18	15	3	10	9	4
		Female	White	14947	10913	0	0	8	3	9	0	0	0	8	8	2	13	9	4	9	4	3
			Black	13013	9501	0	2	67	27	72	0	0	2	64	77	51	90	74	33	44	47	33
			Hispanic	1354	989	0	0	1	1	2	0	0	0	1	2	1	2	2	0	1	1	1
	High-risk	Male	White	558900	49667	0	1	38	15	41	0	0	1	40	24	11	156	66	5	72	37	33
			Black	191943	76075	0	7	272	109	293	0	0	8	280	314	193	875	461	158	489	286	160
			Hispanic	32741	6972	0	0	7	3	7	0	0	0	7	6	4	20	12	4	10	9	4
		Female	White	4868	5468	0	0	1	1	1	0	0	0	1	1	0	5	2	0	2	1	1
			Black	2655	2982	0	0	12	5	13	0	0	0	12	13	8	38	20	7	21	12	7
			Hispanic	206	232	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Los Angeles				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{1P}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	55457	4582	0	15	613	245	659	0	0	16	641	596	326	3758	2331	590	858	750	375
			Black	6689	1514	0	6	250	100	269	0	0	14	438	649	341	993	830	282	214	264	148
			Hispanic	62557	5851	0	15	586	235	630	0	0	16	360	662	539	3235	2353	745	627	861	393
	High-risk		White	5298	14715	0	6	227	91	244	0	0	6	237	220	121	1390	862	218	317	278	139
			Black	377	2357	0	2	92	37	99	0	0	5	162	240	126	367	307	104	79	98	55
			Hispanic	6421	16381	0	5	217	87	233	0	0	6	133	245	200	1197	870	276	232	318	145
MSM-PWID	Low-risk	Off-OAT	White	3431	283	0	0	18	7	20	0	0	2	72	54	40	201	179	64	45	53	33
			Black	183	41	0	0	11	5	12	0	0	2	79	60	44	96	86	31	22	26	16
			Hispanic	2582	242	0	0	16	6	17	0	0	2	65	49	36	175	156	56	39	46	29
		On-OAT	White	328	910	0	0	8	3	8	0	0	1	31	23	17	86	77	27	19	23	14
			Black	10	65	0	0	5	2	5	0	0	1	34	26	19	41	37	13	9	11	7
			Hispanic	265	676	0	0	7	3	7	0	0	1	28	21	15	75	67	24	17	20	12
	High-risk	Off-OAT	White	771	64	0	0	4	2	4	0	0	0	16	12	9	45	40	14	10	12	7
			Black	9	2	0	0	1	0	1	0	0	0	4	3	2	5	4	1	1	1	1
			Hispanic	280	26	0	0	2	1	2	0	0	0	7	5	4	19	17	6	4	5	3
		On-OAT	White	74	205	0	0	2	1	2	0	0	0	7	5	4	19	17	6	4	5	3
			Black	0	3	0	0	0	0	0	0	0	0	2	1	1	2	2	1	0	1	0
			Hispanic	29	73	0	0	1	0	1	0	0	0	3	2	2	8	7	3	2	2	1
PWID	Male	Off-OAT	White	4350	2900	0	0	8	3	8	0	0	0	14	14	18	101	90	32	23	27	17
			Black	3642	4270	0	0	10	4	11	0	0	2	46	46	59	106	95	34	24	28	18
			Hispanic	8207	8549	0	0	9	4	10	0	0	1	19	18	23	125	111	40	28	33	21
		On-OAT	White	978	652	0	0	2	1	2	0	0	0	3	3	4	23	20	7	5	6	4
			Black	174	203	0	0	0	0	1	0	0	0	2	2	3	5	5	2	1	1	1
			Hispanic	889	927	0	0	1	0	1	0	0	0	2	2	3	14	12	4	3	4	2
	Female	Off-OAT	White	2702	1564	0	0	5	2	5	0	0	0	14	14	18	67	59	21	15	18	11
			Black	1114	2088	0	0	7	3	8	0	0	1	43	42	54	82	73	26	18	22	14
			Hispanic	3962	4267	0	0	7	3	7	0	0	1	21	21	27	98	87	31	22	26	16
		On-OAT	White	1246	721	0	0	2	1	2	0	0	0	6	6	8	31	27	10	7	8	5
			Black	86	162	0	0	1	0	1	0	0	0	3	3	4	6	6	2	1	2	1
			Hispanic	452	486	0	0	1	0	1	0	0	0	2	2	3	11	10	4	3	3	2
HET	Low-risk	Male	White	1255794	103758	0	0	13	5	14	0	0	0	5	19	13	50	47	17	15	12	6
			Black	189088	42790	0	1	23	9	25	0	0	1	20	61	44	60	75	23	10	24	13
			Hispanic	1311463	122653	0	1	34	14	37	0	0	1	9	26	66	92	140	68	20	31	38
		Female	White	31770	5957	0	0	1	0	1	0	0	0	0	1	1	3	3	1	1	1	0
			Black	7199	3600	0	0	2	1	2	0	0	0	2	6	4	6	7	2	1	2	1
			Hispanic	55026	10352	0	0	3	1	4	0	0	0	1	3	6	9	13	7	2	3	4
	High-risk	Male	White	1396789	94702	0	1	31	13	34	0	0	2	35	75	55	252	107	24	48	33	33
			Black	236339	58895	0	1	59	23	63	0	0	5	121	217	181	306	188	63	98	58	9
			Hispanic	1373279	196660	0	2	87	35	93	0	0	5	156	122	191	578	400	74	132	126	54
		Female	White	7868	17309	0	0	1	0	1	0	0	0	1	3	2	9	4	1	2	1	1
			Black	2702	1673	0	0	2	1	2	0	0	0	4	7	5	9	6	2	3	2	0
			Hispanic	20580	7221	0	0	3	1	3	0	0	0	6	4	7	21	14	3	5	5	2

Miami				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{IP}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	4936	373	0	2	87	35	94	0	0	4	126	164	118	235	188	51	200	144	78
			Black	2550	329	0	5	197	79	212	0	0	10	271	468	231	479	416	147	352	372	204
			Hispanic	16207	3363	0	8	301	121	324	0	0	14	322	576	443	767	756	151	545	697	248
	High-risk		White	688	1082	0	1	32	13	35	0	0	2	47	61	44	87	69	19	74	53	29
			Black	299	661	0	2	73	29	78	0	0	4	100	173	86	177	154	54	130	138	76
			Hispanic	2500	4023	0	3	111	45	120	0	0	5	119	213	164	284	280	56	202	258	92
MSM-PWID	Low-risk	Off-OAT	White	433	33	0	0	2	1	2	0	0	0	11	8	6	11	10	3	7	9	5
			Black	152	20	0	0	4	2	5	0	0	1	26	19	14	24	22	8	16	19	12
			Hispanic	884	183	0	0	7	3	7	0	0	1	35	27	20	38	34	12	26	30	19
		On-OAT	White	60	95	0	0	1	0	1	0	0	0	5	3	2	5	4	1	3	4	2
			Black	18	39	0	0	2	1	2	0	0	0	11	8	6	10	9	3	7	8	5
			Hispanic	136	219	0	0	3	1	3	0	0	0	15	11	8	16	15	5	11	13	8
	High-risk	Off-OAT	White	16	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Black	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Hispanic	24	5	0	0	0	0	0	0	0	0	1	1	1	1	1	0	1	1	1
		On-OAT	White	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Black	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Hispanic	4	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PWID	Male	Off-OAT	White	518	477	0	0	3	1	3	0	0	1	16	15	20	18	17	6	12	15	9
			Black	1221	2341	0	0	7	3	8	0	0	1	38	37	47	41	37	13	28	33	21
			Hispanic	2877	3940	0	0	11	4	12	0	0	2	53	52	67	65	59	21	44	52	33
		On-OAT	White	19	18	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	1	0
			Black	18	34	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
			Hispanic	77	105	0	0	0	0	0	0	0	0	1	1	2	2	2	1	1	1	1
	Female	Off-OAT	White	215	537	0	0	1	0	1	0	0	0	5	5	6	6	5	2	4	5	3
			Black	369	983	0	0	11	4	12	0	0	2	66	65	83	70	63	22	48	56	35
			Hispanic	1597	2129	0	0	3	1	4	0	0	1	20	19	25	24	21	8	16	19	12
		On-OAT	White	15	39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Black	12	32	0	0	0	0	0	0	0	0	2	2	3	2	2	1	2	2	1
			Hispanic	93	124	0	0	0	0	0	0	0	0	1	1	1	1	1	0	1	1	1
HET	Low-risk	Male	White	130698	9887	0	1	36	15	39	0	0	1	19	49	80	85	68	15	86	47	16
			Black	103185	13310	0	2	71	28	76	0	0	3	56	118	131	135	129	56	65	127	92
			Hispanic	406584	84381	0	3	123	49	133	0	0	5	57	131	293	216	279	88	152	210	157
		Female	White	2239	4478	0	0	4	1	4	0	0	0	2	5	8	8	7	2	9	5	2
			Black	7917	5998	0	0	19	8	21	0	0	1	15	32	36	37	35	15	18	35	25
			Hispanic	18318	9159	0	0	15	6	16	0	0	1	7	15	35	26	33	10	18	25	19
	High-risk	Male	White	134437	8590	0	0	18	7	19	0	0	1	38	45	27	69	40	10	57	37	13
			Black	113984	34947	0	5	211	85	227	0	0	14	432	509	442	769	469	159	565	482	197
			Hispanic	521646	49930	0	2	71	28	76	0	0	4	107	173	142	292	167	33	185	170	83
		Female	White	810	1619	0	0	1	0	1	0	0	0	1	2	1	2	1	0	2	1	0
			Black	1748	1385	0	0	9	4	10	0	0	1	19	22	19	33	20	7	24	21	8
			Hispanic	3937	2362	0	0	2	1	2	0	0	0	2	4	3	7	4	1	4	4	2

New York City				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{1P}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	40069	18264	0	10	417	167	448	0	0	33	1481	1268	477	5330	2657	270	100	59	17
			Black	14540	7218	0	8	308	123	331	0	0	25	907	1164	412	3039	2311	462	136	132	59
			Hispanic	20411	11242	0	7	291	117	313	0	0	20	738	987	294	3057	2405	412	136	105	21
	High-risk		White	4065	15380	0	4	154	62	166	0	0	12	548	469	176	1971	983	100	37	22	6
			Black	2152	5101	0	3	114	46	123	0	0	9	336	430	152	1124	855	171	50	49	22
			Hispanic	2157	8394	0	3	108	43	116	0	0	8	273	365	109	1131	889	152	50	39	8
MSM-PWID	Low-risk	Off-OAT	White	2727	1243	0	0	5	2	5	0	0	1	49	37	27	98	88	31	2	2	1
			Black	658	327	0	0	10	4	10	0	0	2	95	71	52	175	158	56	7	9	6
			Hispanic	2049	1128	0	0	10	4	11	0	0	2	89	67	49	196	177	62	7	8	5
		On-OAT	White	277	1047	0	0	2	1	2	0	0	0	21	16	12	42	38	13	1	1	0
			Black	97	231	0	0	4	2	4	0	0	1	41	31	22	75	68	24	3	4	2
			Hispanic	216	843	0	0	4	2	5	0	0	1	38	29	21	84	76	27	3	3	2
	High-risk	Off-OAT	White	633	289	0	0	1	0	1	0	0	0	11	9	6	23	20	7	0	0	0
			Black	22	11	0	0	0	0	0	0	0	0	3	2	2	6	5	2	0	0	0
			Hispanic	194	107	0	0	1	0	1	0	0	0	8	6	5	19	17	6	1	1	0
		On-OAT	White	64	243	0	0	1	0	1	0	0	0	5	4	3	10	9	3	0	0	0
			Black	3	8	0	0	0	0	0	0	0	0	1	1	1	2	2	1	0	0	0
			Hispanic	21	80	0	0	0	0	0	0	0	0	4	3	2	8	7	3	0	0	0
PWID	Male	Off-OAT	White	2059	3088	0	0	15	6	16	0	0	5	143	140	181	263	238	84	4	5	3
			Black	4437	9367	0	2	60	24	65	0	0	19	586	575	741	1042	941	331	45	53	33
			Hispanic	6426	19401	0	2	66	26	71	0	0	21	640	628	809	1151	1039	365	39	46	29
		On-OAT	White	478	718	0	0	3	1	4	0	0	1	33	33	42	61	55	19	1	1	1
			Black	145	306	0	0	2	1	2	0	0	1	19	19	24	34	31	11	1	2	1
			Hispanic	608	1836	0	0	6	2	7	0	0	2	61	59	77	109	98	35	4	4	3
	Female	Off-OAT	White	201	904	0	0	3	1	3	0	0	1	30	29	38	61	55	19	1	1	1
			Black	584	1753	0	1	29	12	31	0	0	10	313	307	395	613	553	195	26	31	19
			Hispanic	1496	5022	0	1	23	9	25	0	0	8	248	244	314	492	445	156	17	20	12
		On-OAT	White	361	1625	0	0	5	2	5	0	0	2	54	53	68	109	99	35	2	2	1
			Black	63	190	0	0	3	1	3	0	0	1	34	33	43	66	60	21	3	3	2
			Hispanic	259	870	0	0	4	2	4	0	0	1	43	42	54	85	77	27	3	3	2
HET	Low-risk	Male	White	833582	379955	0	4	146	58	157	0	0	9	391	410	117	1306	857	408	30	14	11
			Black	306604	152204	0	10	409	164	440	0	0	26	854	1030	692	3194	2626	1156	139	149	104
			Hispanic	398711	219604	0	6	239	96	257	0	0	15	416	594	495	2019	1716	387	81	69	34
		Female	White	15891	31783	0	0	12	5	13	0	0	1	32	34	10	107	70	33	2	1	1
			Black	29770	28563	0	3	119	48	128	0	0	8	249	300	202	930	765	337	41	43	30
			Hispanic	45216	41986	0	2	79	31	84	0	0	5	137	195	163	663	564	127	27	23	11
	High-risk	Male	White	1040706	376642	0	2	60	24	65	0	0	5	280	168	75	1066	451	36	17	9	8
			Black	456509	243159	0	11	438	175	471	0	0	39	1360	1524	938	6422	3382	1159	322	189	105
			Hispanic	462112	291407	0	5	190	76	205	0	0	17	697	563	402	2620	1617	582	92	87	36
		Female	White	4579	9159	0	0	1	0	1	0	0	0	5	3	1	21	9	1	0	0	0
			Black	3647	3064	0	0	8	3	9	0	0	1	26	30	18	124	66	22	6	4	2
			Hispanic	34507	36664	0	1	40	16	43	0	0	4	145	117	84	547	337	121	19	18	8

Seattle				Susceptible			Infected						Diagnosed				On-ART			Off-ART		
				S_1	S_2	S_p	I_A	I_1	I_2	I_3	I_{AP}	I_{1P}	D_A	D_1	D_2	D_3	T_1	T_2	T_3	O_1	O_2	O_3
MSM	Low-risk		White	27964	2014	0	4	180	72	193	0	0	3	137	127	70	1221	757	192	93	81	41
			Black	1658	496	0	0	18	7	20	0	0	0	11	17	9	103	86	29	7	9	5
			Hispanic	3134	151	0	1	22	9	24	0	0	1	12	22	18	132	96	30	9	12	5
	High-risk		White	3562	6430	0	2	67	27	72	0	0	1	51	47	26	452	280	71	34	30	15
			Black	359	359	0	0	7	3	7	0	0	0	4	6	3	38	32	11	3	3	2
			Hispanic	373	722	0	0	8	3	9	0	0	0	4	8	7	49	35	11	3	4	2
MSM-PWID	Low-risk	Off-OAT	White	2048	148	0	0	8	3	9	0	0	1	25	19	14	98	87	31	7	9	5
			Black	127	38	0	0	1	0	1	0	0	0	2	2	1	9	8	3	1	1	0
			Hispanic	129	6	0	0	1	0	1	0	0	0	3	2	2	9	8	3	1	1	1
		On-OAT	White	261	471	0	0	3	1	4	0	0	0	11	8	6	42	37	13	3	4	2
			Black	28	28	0	0	0	0	0	0	0	0	1	1	1	4	3	1	0	0	0
			Hispanic	15	30	0	0	0	0	0	0	0	0	1	1	1	4	4	1	0	0	0
	High-risk	Off-OAT	White	222	16	0	0	1	0	1	0	0	0	3	2	2	11	9	3	1	1	1
			Black	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Hispanic	9	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
		On-OAT	White	28	51	0	0	0	0	0	0	0	0	1	1	1	5	4	1	0	0	0
			Black	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Hispanic	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PWID	Male	Off-OAT	White	2746	2863	0	0	3	1	3	0	0	0	9	9	11	32	29	10	2	3	2
			Black	1413	983	0	0	1	1	1	0	0	0	5	5	6	17	15	5	1	1	1
			Hispanic	424	349	0	0	1	0	1	0	0	0	3	3	3	9	8	3	1	1	0
		On-OAT	White	298	311	0	0	0	0	0	0	0	0	1	1	1	4	3	1	0	0	0
			Black	59	41	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
			Hispanic	31	26	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
	Female	Off-OAT	White	2734	2161	0	0	1	1	1	0	0	0	6	6	7	19	17	6	1	2	1
			Black	700	840	0	0	1	0	1	0	0	0	3	3	4	9	8	3	1	1	0
			Hispanic	370	208	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
		On-OAT	White	506	400	0	0	0	0	0	0	0	0	1	1	1	3	3	1	0	0	0
			Black	34	41	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			Hispanic	39	22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HET	Low-risk	Male	White	494313	35597	0	0	16	6	17	0	0	0	2	7	5	75	71	25	8	6	3
			Black	28143	8419	0	0	20	8	21	0	0	0	3	10	7	81	101	31	4	11	6
			Hispanic	53064	2550	0	0	7	3	7	0	0	0	1	2	6	22	33	16	2	2	3
		Female	White	12137	2567	0	0	1	0	1	0	0	0	0	0	0	4	4	1	0	0	0
			Black	1329	374	0	0	2	1	2	0	0	0	0	1	1	8	10	3	0	1	1
			Hispanic	1950	585	0	0	1	0	1	0	0	0	0	0	1	2	3	2	0	0	0
	High-risk	Male	White	546932	33868	0	0	11	4	12	0	0	0	4	9	6	114	48	11	7	5	5
			Black	32757	5765	0	0	16	6	17	0	0	0	7	13	11	136	83	28	15	9	1
			Hispanic	48260	5563	0	0	2	1	3	0	0	0	2	1	2	20	14	3	2	1	1
		Female	White	5650	4154	0	0	0	0	0	0	0	0	0	0	0	4	2	0	0	0	0
			Black	378	193	0	0	0	0	1	0	0	0	0	0	0	4	3	1	0	0	0
			Hispanic	635	318	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0

Table A6. HIV testing rates estimated from back-calculation following adjustment

Annual HIV testing probability				*Atlanta*	*Baltimore*	*Los Angeles*	*Miami*	*New York City*	*Seattle*
MSM	**Low-risk**		White	7.0%	17.3%	13.5%	14.6%	20.4%	11.3%
			Black	10.8%	22.7%	22.1%	25.2%	36.2%	20.9%
			Hispanic	7.7%	36.6%	28.9%	15.4%	39.5%	21.6%
	High-risk		White	10.9%	24.2%	19.1%	20.2%	28.5%	18.2%
			Black	16.7%	31.4%	30.6%	34.0%	48.3%	32.3%
			Hispanic	12.0%	48.5%	39.2%	21.3%	52.1%	33.3%
MSM-PWID	**Low-risk**		White	6.9%	6.4%	15.3%	6.4%	19.6%	38.5%
			Black	7.2%	6.7%	18.7%	11.2%	24.4%	63.2%
			Hispanic	6.5%	14.0%	25.4%	6.4%	32.1%	63.2%
	High-risk		White	10.7%	9.3%	21.5%	9.1%	27.4%	55.5%
			Black	11.2%	9.6%	26.0%	15.6%	33.6%	81.1%
			Hispanic	10.1%	19.7%	34.7%	9.1%	43.3%	81.1%
PWID		**Male**	White	39.7%	6.4%	26.1%	6.4%	14.4%	34.7%
			Black	6.4%	6.4%	46.7%	6.4%	6.4%	32.4%
			Hispanic	22.1%	15.5%	31.9%	6.4%	6.4%	9.5%
		Female	White	56.9%	22.2%	41.6%	45.3%	6.4%	63.2%
			Black	20.3%	9.8%	63.2%	6.6%	6.4%	63.2%
			Hispanic	40.6%	44.2%	53.4%	35.4%	6.4%	9.5%
HET	**Low-risk**	**Male**	White	15.3%	4.9%	4.9%	17.5%	15.4%	15.4%
			Black	8.9%	4.9%	4.9%	21.5%	12.9%	6.9%
			Hispanic	12.7%	6.7%	4.9%	17.7%	12.4%	4.9%
		Female	White	23.2%	7.0%	7.0%	24.0%	21.8%	24.2%
			Black	13.7%	7.0%	7.0%	29.2%	18.4%	11.3%
			Hispanic	19.5%	9.6%	7.0%	24.3%	17.6%	8.0%
	High-risk	**Male**	White	14.1%	9.1%	18.1%	15.4%	18.1%	15.4%
			Black	12.3%	6.1%	18.1%	6.5%	18.1%	18.1%
			Hispanic	6.0%	18.1%	18.1%	18.1%	15.6%	6.1%
		Female	White	21.5%	13.0%	25.3%	21.2%	25.4%	24.2%
			Black	18.9%	9.5%	25.3%	9.1%	25.4%	28.3%
			Hispanic	9.4%	25.3%	25.3%	24.9%	22.0%	9.9%
Symptom-based case finding (CD4: 200-499)				9.5%	9.6%	8.7%	9.5%	6.6%	3.5%
Symptom-based case finding (CD4 < 200)				19.9%	15.5%	12.5%	16.7%	19.9%	9.2%
HIV testing rate ratio (high-risk / low-risk)				1.59	1.46	1.46	1.43	1.47	1.67

Table A7. Validation for HIV testing rate estimates

City	*Number of new diagnoses (2015)*	*Population size*	*Externally estimated*						*Model estimated*	
			Publicly funded testing scenario*			**Positivity rate scenario^**			**Number of tests in 2015**	**Percentage tested in 2015**
			Reported #	**Lower**	**Upper**	**0.1%**	**0.2%**	**0.5%**		
Atlanta	1,842	3,586,253	42,506	91,027	153,798	1,841,696	920,848	368,339	**590,058**	16.5%
Baltimore	529	1,871,812	53,730	62,492	197,459	529,203	264,601	105,841	**133,725**	7.1%
Los Angeles	1,984	6,850,378	126,733	199,713	292,031	1,984,000	992,000	396,800	**789,880**	11.5%
Miami	1,314	1,756,032	332,649	143,823	328,245	1,314,364	657,182	262,873	**285,175**	16.2%
New York	2,407	5,787,014	121,284	295,803	501,646	2,407,226	1,203,613	481,445	**1,123,533**	19.4%
Seattle	228	1,401,600	13,382	24,024	40,681	228,000	114,000	45,600	**200,638**	14.1%

* Public funded test scenario was triangulated from the reported number of public-funded tests in each city or state[287] (data was only available at the state-level for Miami (Florida) and Seattle (Washington)) multiplying the ratio between the total number of new diagnoses in 2015 over the reported number of new HIV cases diagnosed through public-funded testing services. ^Positivity rate scenario were constructed by back-calculating the number of tests according to the number of new diagnoses and three different levels for the positivity rate, 0.1%, 0.2% and 0.5%.

Table A8. Target weights derived from the BWM survey

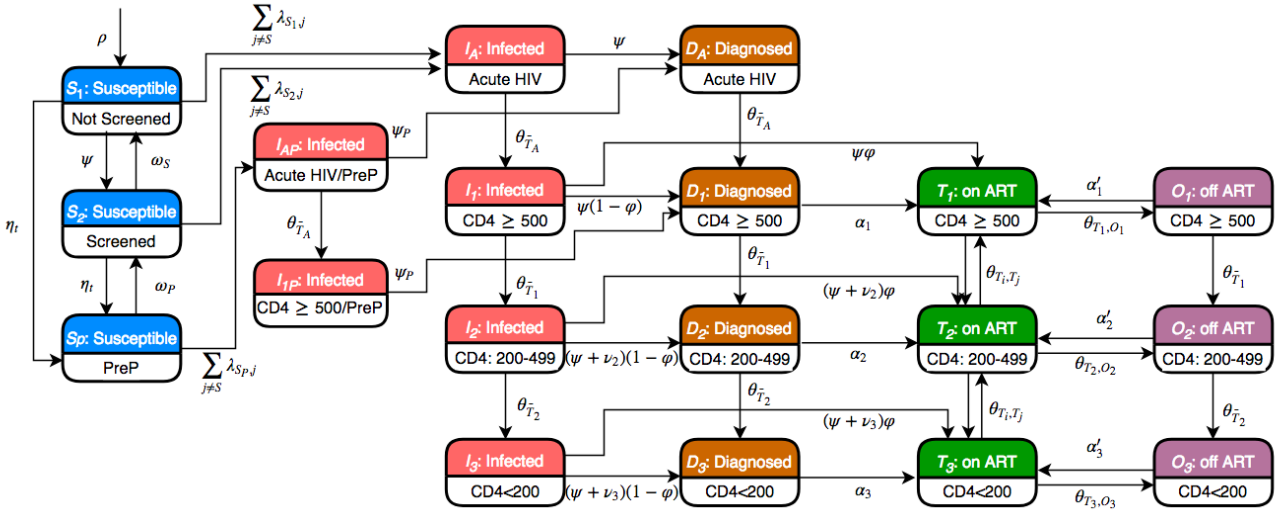
Target	*Other cities*	*Seattle**	*Miami^*
Total number diagnosed PLHIV (White MSM)	0.0576	0.0643	0.0597
Total number diagnosed PLHIV (Black MSM)	0.0713	0.0796	0.0739
Total number diagnosed PLHIV (Hispanic MSM)	0.0716	0.0800	0.0743
Total number diagnosed PLHIV (PWID)	0.0495	0.0553	0.0513
Total number diagnosed PLHIV (MSM/PWID)	0.0644	0.0720	0.0668
Total number diagnosed PLHIV (White male heterosexual)	0.0290	0.0324	0.0301
Total number diagnosed PLHIV (Black male heterosexual)	0.0344	0.0385	0.0357
Total number diagnosed PLHIV (Hispanic male heterosexual)	0.0234	0.0262	0.0243
Total number diagnosed PLHIV (White female heterosexual)	0.0307	0.0343	0.0319
Total number diagnosed PLHIV (Black female heterosexual)	0.0344	0.0385	0.0357
Total number diagnosed PLHIV (Hispanic female heterosexual)	0.0408	0.0456	0.0423
Annual number of new HIV diagnoses (Total)	0.1424	0.1591	0.1476
Annual number of new HIV diagnoses (Black)	0.1140	0.0363	0.1182
Annual number of new HIV diagnoses (MSM)	0.1313	0.1467	0.1362
Annual number of all-cause deaths among PLHIV (Total)	0.0372	0.0415	0.0385
Annual number of all-cause deaths among PLHIV (Black)	0.0325	0.0100	0.0336
Annual number of all-cause deaths among PLHIV (MSM)	0.0355	0.0397	

White: white/other. * Due to a much smaller proportion of HIV epidemics among black population, the weight for Annual number of new HIV diagnoses (Black) in Seattle was reassigned by the proportion of black PLHIV over total and the reduced weight was redistributed proportionally to other targets. ^ Since target data for Annual number of all-cause deaths among PLHIV (MSM) was unavailable in Miami, we redistributed its weight proportionally to other targets.

Table A9. Extreme scenario analysis

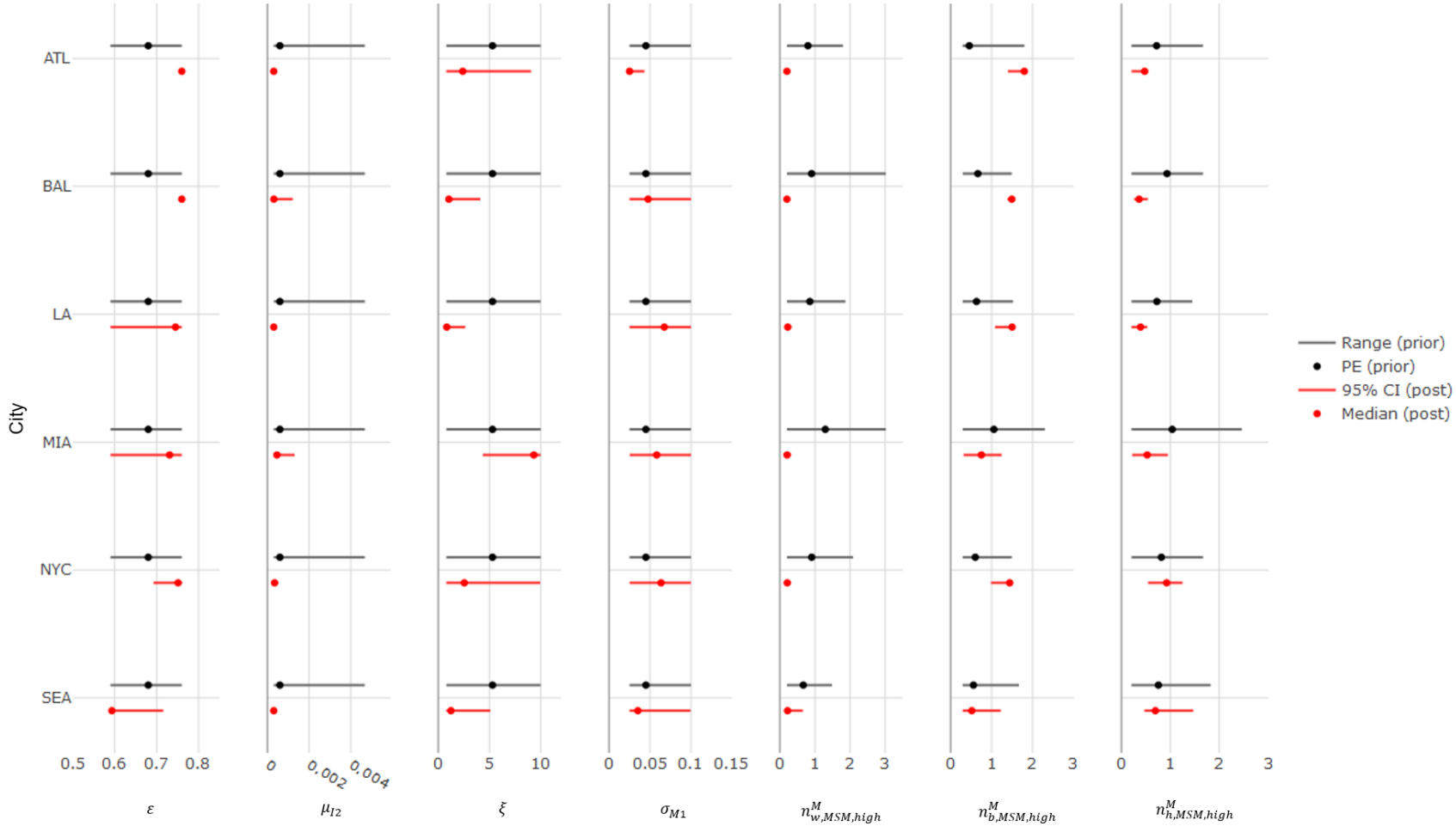
Extreme scenarios	Anticipated results		Check
	HIV incident cases	**HIV prevalence**	
Initial MSM population = 0	0 among MSM	0 among MSM	✓
Probability of transmission per heterosexual partnership = 0	0 among HET	Constant decrease among HET	✓
Probability of transmission per homosexual partnership = 0	0 among MSM Decrease among MSM/PWID	Constant decrease among MSM	✓
Probability of transmission per shared injection = 0	0 among PWID Decrease among MSM/PWID	Constant decrease among PWID	✓
Probability of transmission of all transmission routes = 0	0 among all risk groups	Constant decrease among all risk groups	✓
ART efficacy on sexual infectivity = 0	Slight increase among HET, MSM, MSM-PWID	Slight increase among HET, MSM, MSM-PWID	✓
ART efficacy on shared injection infectivity = 0	Increase among PWID	Increase among PWID	✓
HIV testing rates among all population = 0	Increase among all risk groups	Increase among all risk groups	✓
Number of shared injections = 0	≈ 0 among PWID	Constant decrease among PWID	✓
Probability of condom use for homosexual contacts = 100%	≈ 0 among MSM, MSM-PWID	Decrease among MSM, MSM-PWID	✓
Probability of condom use for heterosexual contacts = 100%	≈ 0 among HET	Decrease among HET	✓

Figure A1. Model schematic diagram



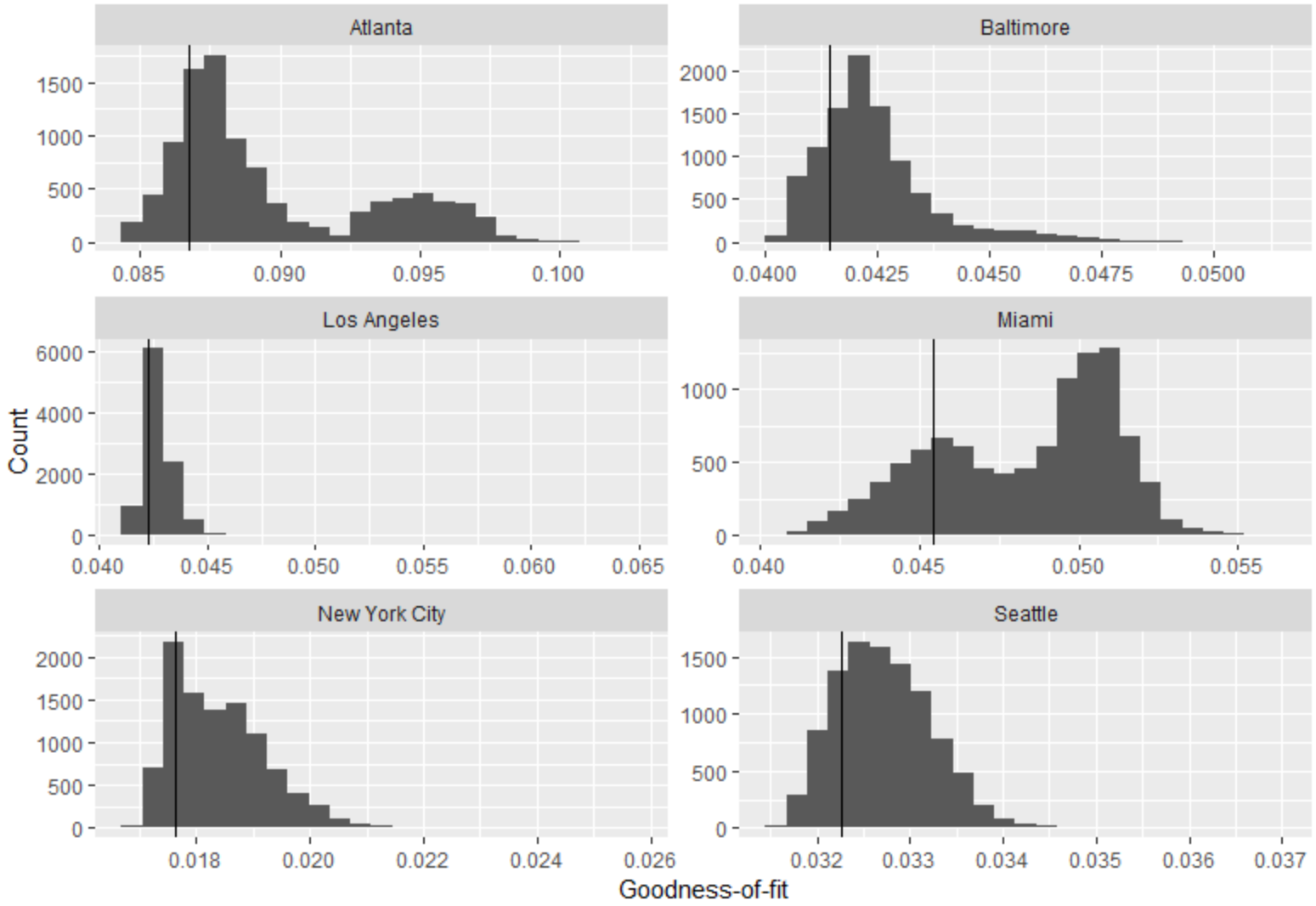
The schematic shows the 19 compartments that constitute each of the 42 population groups in the model.

Figure A2. Selected results for parameter values post calibration versus their prior values



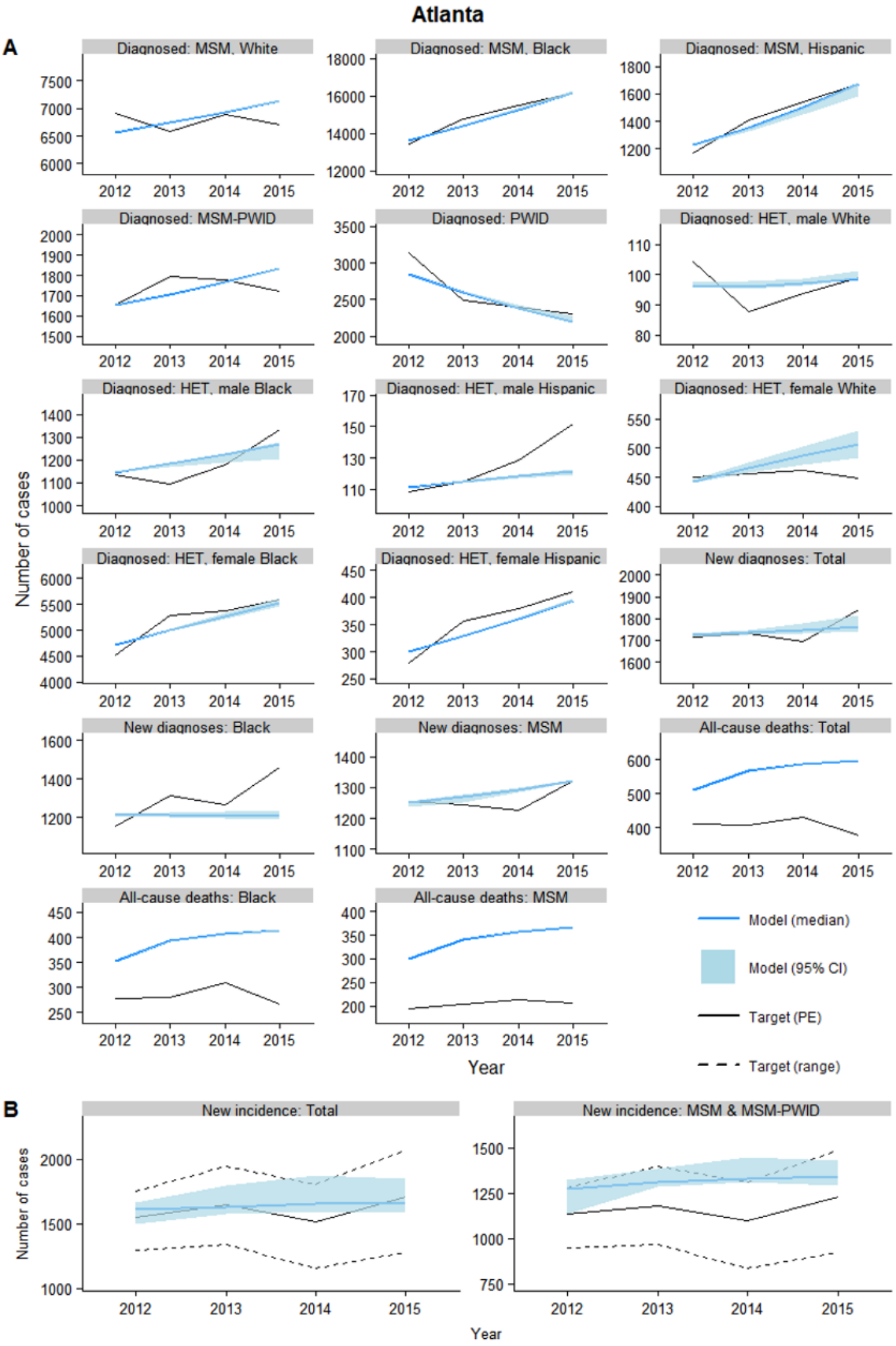
ATL: Atlanta; BAL: Baltimore; LA: Los Angeles; MIA: Miami; NYC: New York City; SEA: Seattle. PE: point estimate; 95% CI: 95% credible interval; post: post-calibration. ε: Decrease in sexual partners post-diagnosis; μ_{I2}: monthly mortality rate for PLHIV (CD4 200-499); ξ: transmission probability multiplier for acute stage; σ_{M1}: probability of transmission - male to male (CD4 $\geqslant$500); $n^M_{w,MSM,high}$: number of homosexual partners - White, high-risk MSM; $n^M_{b,MSM,high}$: number of homosexual partners - Black, high-risk MSM; $n^M_{h,MSM,high}$: number of homosexual partners - Hispanic, high-risk MSM

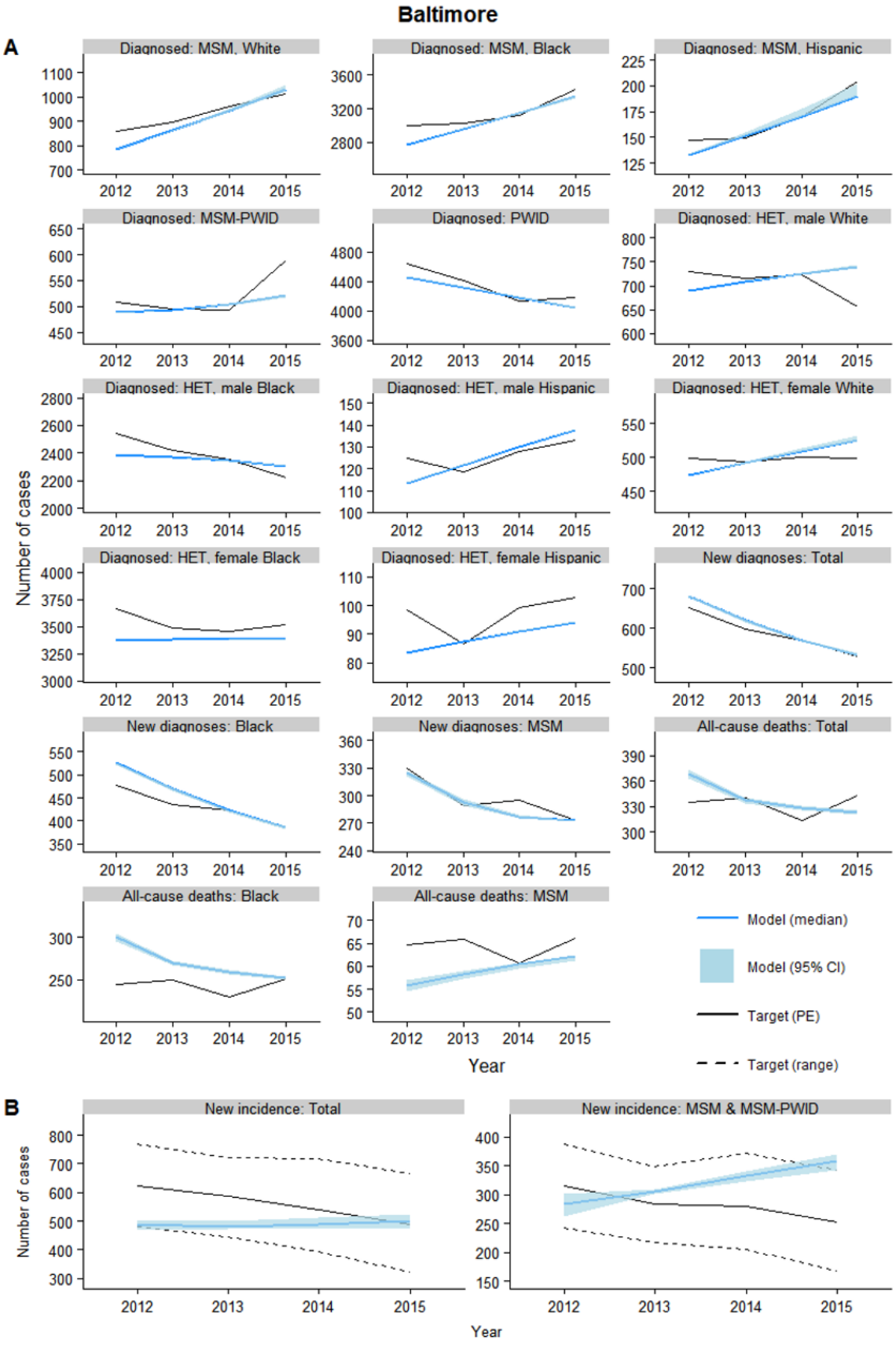
Figure A3. Distribution of goodness-of-fit following calibration

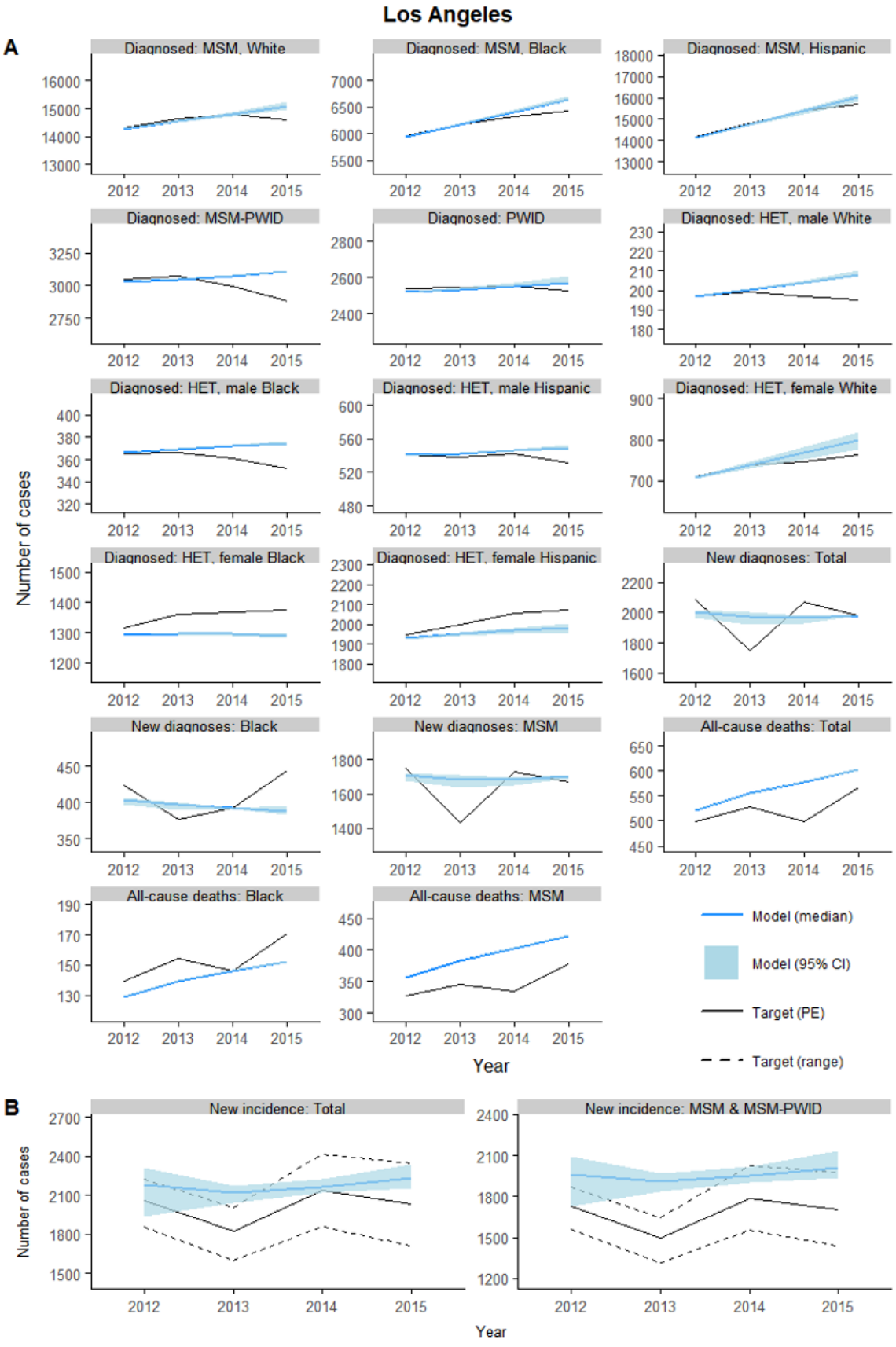


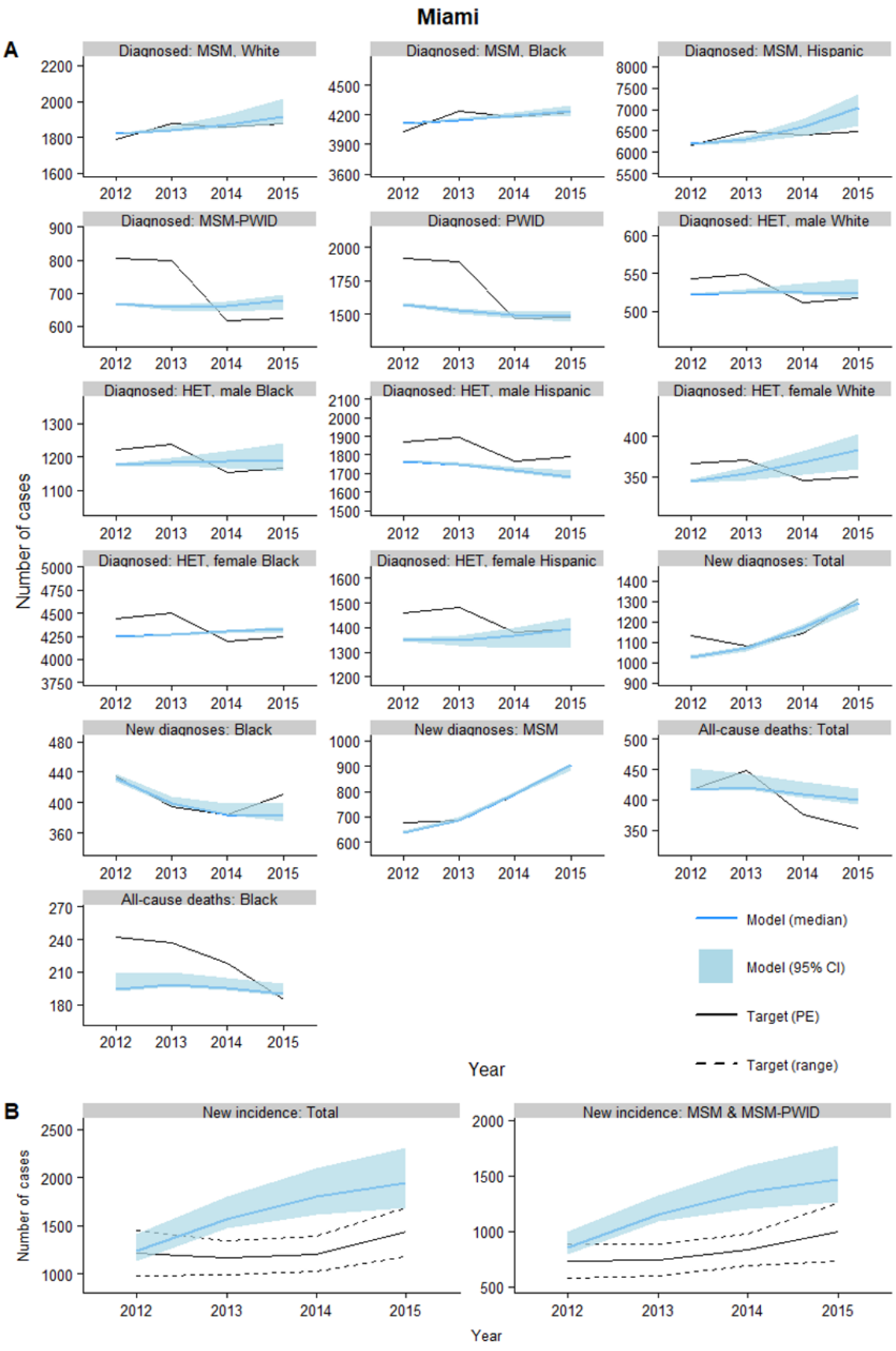
This histogram presents distribution of GOF in each city for all 10,000 calibration runs where the acceptable set was selected only for the 2,000 subsets with the smallest GOF. Vertical solid line represents the cut-off point (20th percentile).

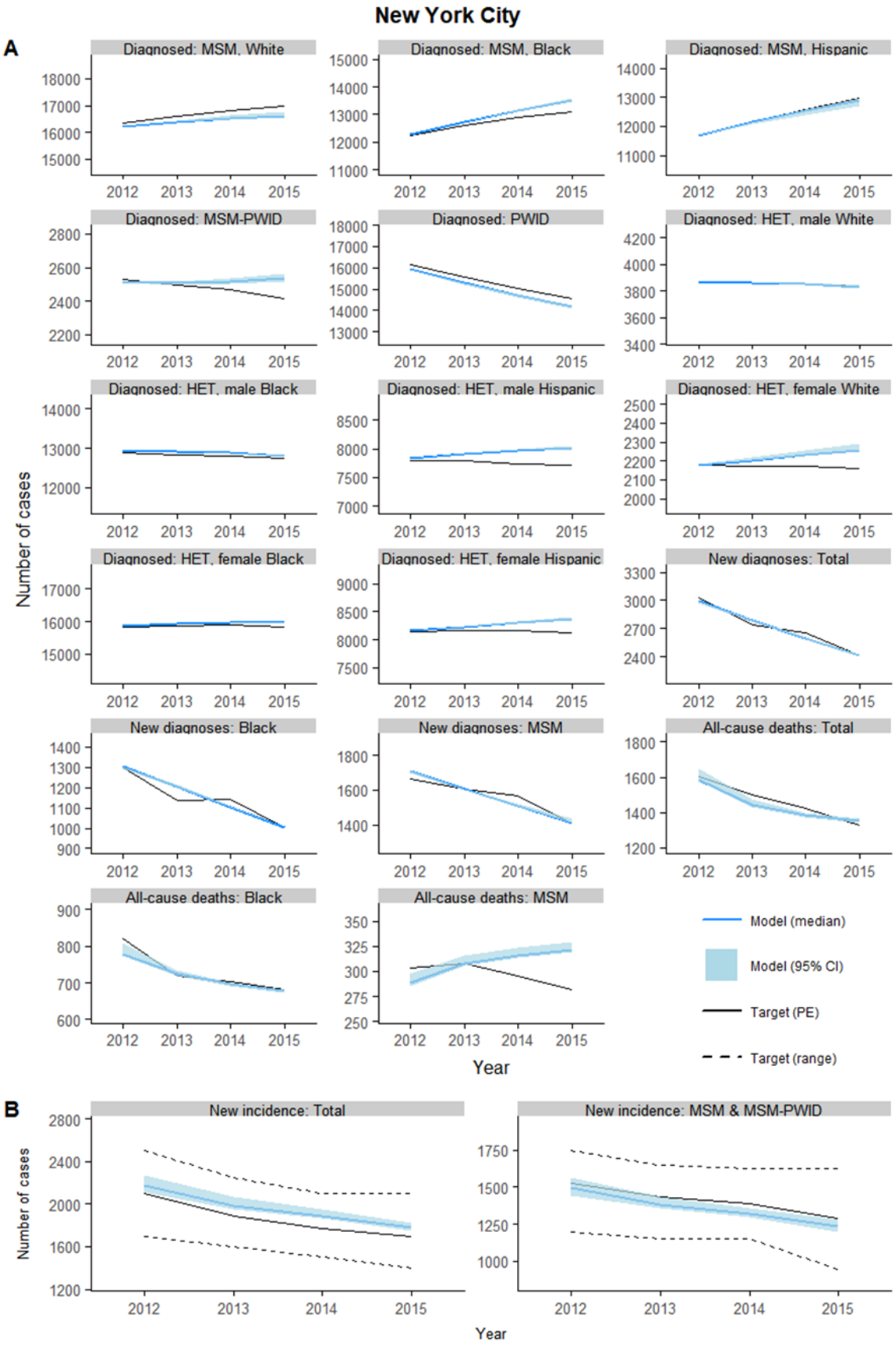
Figure A4. Results for model calibration and external validation

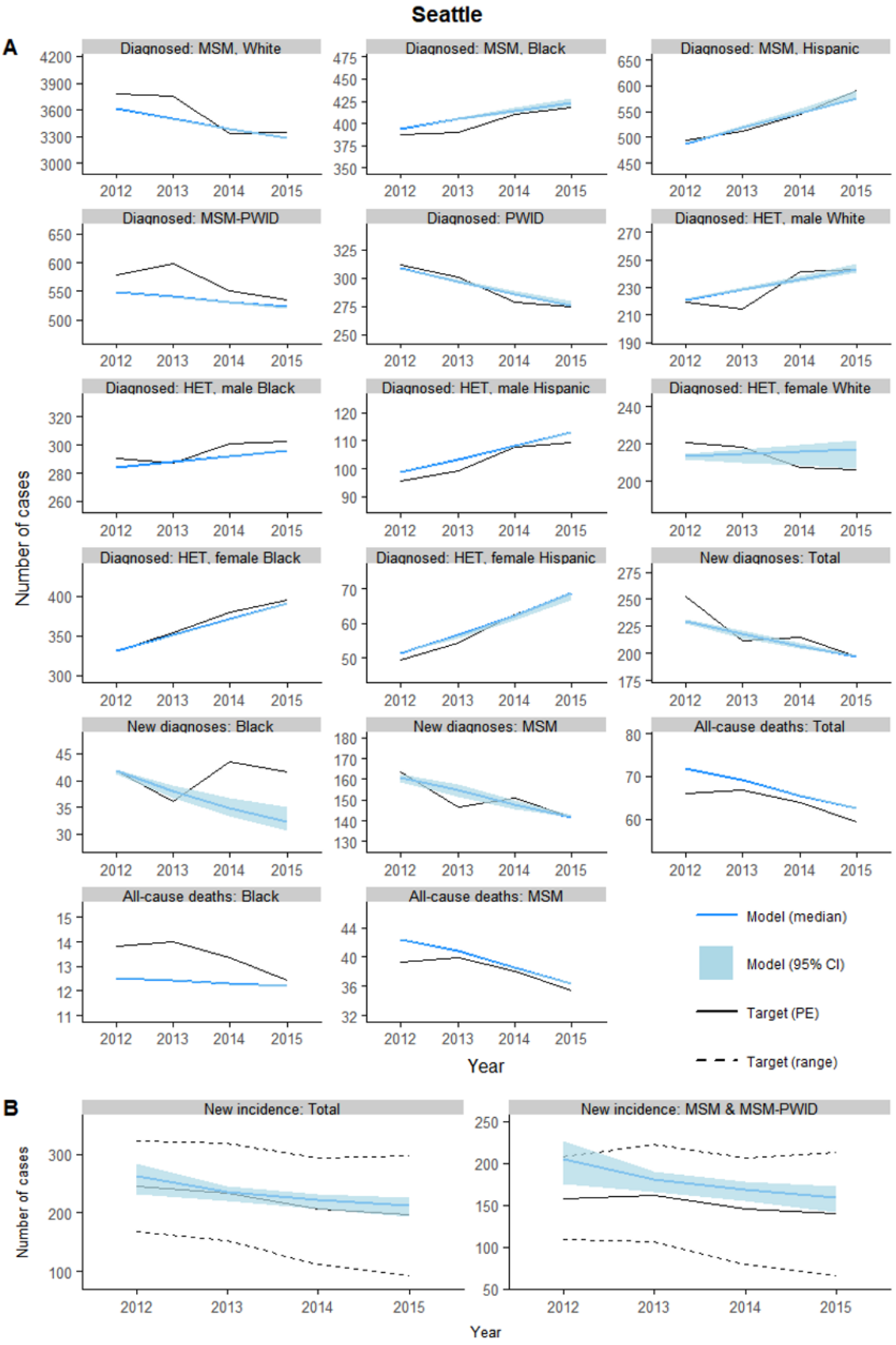



Baltimore
A
Diagnosed: MSM, White
Diagnosed: MSM, Black
Diagnosed: MSM, Hispanic
Diagnosed: MSM-PWID
Diagnosed: PWID
Diagnosed: HET, male White
Diagnosed: HET, male Black
Diagnosed: HET, male Hispanic
Diagnosed: HET, female White
Diagnosed: HET, female Black
Diagnosed: HET, female Hispanic
New diagnoses: Total
New diagnoses: Black
New diagnoses: MSM
All-cause deaths: Total
All-cause deaths: Black
All-cause deaths: MSM
Number of cases
Year
Model (median)
Model (95% CI)
Target (PE)
Target (range)
B
New incidence: Total
New incidence: MSM & MSM-PWID
Number of cases
Year


Los Angeles
A
Diagnosed: MSM, White
Diagnosed: MSM, Black
Diagnosed: MSM, Hispanic
Diagnosed: MSM-PWID
Diagnosed: PWID
Diagnosed: HET, male White
Diagnosed: HET, male Black
Diagnosed: HET, male Hispanic
Diagnosed: HET, female White
Diagnosed: HET, female Black
Diagnosed: HET, female Hispanic
New diagnoses: Total
New diagnoses: Black
New diagnoses: MSM
All-cause deaths: Total
All-cause deaths: Black
All-cause deaths: MSM
Number of cases
Year
Model (median)
Model (95% CI)
Target (PE)
Target (range)
B
New incidence: Total
New incidence: MSM & MSM-PWID
Number of cases
Year


Miami
A
Diagnosed: MSM, White
Diagnosed: MSM, Black
Diagnosed: MSM, Hispanic
Diagnosed: MSM-PWID
Diagnosed: PWID
Diagnosed: HET, male White
Diagnosed: HET, male Black
Diagnosed: HET, male Hispanic
Diagnosed: HET, female White
Diagnosed: HET, female Black
Diagnosed: HET, female Hispanic
New diagnoses: Total
New diagnoses: Black
New diagnoses: MSM
All-cause deaths: Total
All-cause deaths: Black
Number of cases
Year
Model (median)
Model (95% CI)
Target (PE)
Target (range)
B
New incidence: Total
New incidence: MSM & MSM-PWID
Number of cases
Year


New York City
A
Diagnosed: MSM, White
Diagnosed: MSM, Black
Diagnosed: MSM, Hispanic
Diagnosed: MSM-PWID
Diagnosed: PWID
Diagnosed: HET, male White
Diagnosed: HET, male Black
Diagnosed: HET, male Hispanic
Diagnosed: HET, female White
Diagnosed: HET, female Black
Diagnosed: HET, female Hispanic
New diagnoses: Total
New diagnoses: Black
New diagnoses: MSM
All-cause deaths: Total
All-cause deaths: Black
All-cause deaths: MSM
Number of cases
Year
Model (median)
Model (95% CI)
Target (PE)
Target (range)
B
New incidence: Total
New incidence: MSM & MSM-PWID
Number of cases
Year



PANEL A: Results for model calibration; PANEL B: Results for model external validation; PE: point estimate; 95% CI: 95% credible interval.

Figure A5. Sample BWM survey for determining weight vector

Introduction

The objective of this survey is to gain your opinions on the relative importance of the calibration targets we've set for our model. Model calibration represents the process of comparing the outputs of a simulation model with observed epidemiological outcomes (calibration "targets") to identify plausible ranges for uncertain model parameters that provide the best fit to available data[1]. ***Your insight will help us identify 'weights' for our calibration targets representing their relative importance to the overall calibration process for each city.***

We've selected 3 sets of calibration targets (17 targets in total), on the basis of data quality, and importance to the dynamics of the HIV epidemic, both overall and across ethnic and HIV risk groups: (i) the ***total number of diagnosed PLHIV*** at year end, stratified by risk group (MSM/PWID (1 target) and PWID (1 target)), with additional stratification by ethnic group and gender for MSM (3 targets: black, white and Hispanic males) and heterosexuals (6 targets: black, white and hispanic males and females); (ii) the ***annual number of new HIV diagnoses***, overall and for blacks and MSM (3 targets); and (iii) ***the annual number of all-cause deaths among PLHIV***, overall and for blacks and MSM (3 targets).

We've designed this brief survey to estimate weights for these targets adopting a '*Best-Worst Method*' from the field of operations research[2,3] to form the overall weighted 'goodness of fit' for our model in each city. The survey features 4 subtasks in which we ask you to rank the 17 targets according to the following scheme:

Best	Worst
Task 1: Select the calibration target you think is *most important* for the model to accurately reproduce.	**Task 2:** Select the calibration target you think is *least important* for the model to accurately reproduce.
Task 3: Perform a pairwise comparison between the *most important* target and each of the other targets by specifying their relative importance on a scale of 1-9.	**Task 4:** Perform a pairwise comparison between the *least important* target and each of the other targets by specifying their relative importance on a scale of 1-9.

Ultimately, we are concerned with trying to reproduce, to the best of our ability, the long-term course of the HIV epidemic in each of our demonstration cities. It is only on this basis that we can make realistic projects of the incremental costs and benefits of different combination implementation strategies to reduce the public health burden of HIV/AIDS.

References

1. Vanni T, Karnon J, Madan J, White RG, Edmunds WJ, Foss AM, Legood R. Calibrating models in economic evaluation. Pharmacoeconomics. 2011 Jan 1;29(1):35-49.
2. Rezaei J. Best-worst multi-criteria decision-making method. Omega. 2015 Jun 30;53:49-57.
3. Rezaei J. Best-worst multi-criteria decision-making method: Some properties and a linear model. Omega. 2016 Oct 31;64:126-30.

Your name: | **City:** Miami

Task 1: **In the following list of calibration targets, which one do you think is most important for the model to accurately reproduce?**
Your answer: 12 ← please give your answer with this pull-down menu

Index	Calibration targets
1	Total number diagnosed PLHIV (White MSM*)
2	Total number diagnosed PLHIV (Black MSM)
3	Total number diagnosed PLHIV (Hispanic MSM)
4	Total number diagnosed PLHIV (PWID)
5	Total number diagnosed PLHIV (MSM/PWID)
6	Total number diagnosed PLHIV (White male heterosexual*)
7	Total number diagnosed PLHIV (Black male heterosexual)
8	Total number diagnosed PLHIV (Hispanic male heterosexual)
9	Total number diagnosed PLHIV (White female heterosexual*)
10	Total number diagnosed PLHIV (Black female heterosexual)
11	Total number diagnosed PLHIV (Hispanic female heterosexual)
12	***Annual number of new HIV diagnoses (Total)***
13	Annual number of new HIV diagnoses (Black)
14	Annual number of new HIV diagnoses (MSM)
15	Annual number of all-cause deaths among PLHIV (Total)
16	Annual number of all-cause deaths among PLHIV (Black)
17	Annual number of all-cause deaths among PLHIV (MSM)

*White: Non-hispanic white and other races

Task 2: **In the following list of calibration targets, which one do you think is least important for the model to accurately reproduce?**
Your answer: 6 ← please give your answer with this pull-down menu

Index	Calibration targets
1	Total number diagnosed PLHIV (White MSM*)
2	Total number diagnosed PLHIV (Black MSM)
3	Total number diagnosed PLHIV (Hispanic MSM)
4	Total number diagnosed PLHIV (PWID)
5	Total number diagnosed PLHIV (MSM/PWID)
6	***Total number diagnosed PLHIV (White male heterosexual*)***
7	Total number diagnosed PLHIV (Black male heterosexual)
8	Total number diagnosed PLHIV (Hispanic male heterosexual)
9	Total number diagnosed PLHIV (White female heterosexual*)
10	Total number diagnosed PLHIV (Black female heterosexual)
11	Total number diagnosed PLHIV (Hispanic female heterosexual)
12	Annual number of new HIV diagnoses (Total)
13	Annual number of new HIV diagnoses (Black)
14	Annual number of new HIV diagnoses (MSM)
15	Annual number of all-cause deaths among PLHIV (Total)
16	Annual number of all-cause deaths among PLHIV (Black)
17	Annual number of all-cause deaths among PLHIV (MSM)

*White: Non-hispanic white and other races

Task 3: Pairwise comparison against the *most important target*

Please rate the relative importance of the most important target (also **bolded**) compared to *each of the other* 16 targets, on a scale of 1 (equally important) to 9 (much less important).

Comparison	Relative importance of	Over	Your answer:
1	Annual number of new HIV diagnoses (Total)	Total number diagnosed PLHIV (White MSM*)	5
2		Total number diagnosed PLHIV (Black MSM)	2
3		Total number diagnosed PLHIV (Hispanic MSM)	2
4		Total number diagnosed PLHIV (PWID)	4
5		Total number diagnosed PLHIV (MSM/PWID)	3
6		Total number diagnosed PLHIV (White male heterosexual*)	9
7		Total number diagnosed PLHIV (Black male heterosexual)	7
8		Total number diagnosed PLHIV (Hispanic male heterosexual)	7
9		Total number diagnosed PLHIV (White female heterosexual*)	8
10		Total number diagnosed PLHIV (Black female heterosexual)	6
11		Total number diagnosed PLHIV (Hispanic female heterosexual)	6
12		***Annual number of new HIV diagnoses (Total)***	1
13		Annual number of new HIV diagnoses (Black)	1
14		Annual number of new HIV diagnoses (MSM)	1
15		Annual number of all-cause deaths among PLHIV (Total)	5
16		Annual number of all-cause deaths among PLHIV (Black)	5
17		Annual number of all-cause deaths among PLHIV (MSM)	5

Task 4: Pairwise comparison against the least *important target*

Please rate the relative importance of the least important target (**bolded**) compared to *each of the other* 16 targets, on a scale of 1 (equally important) to 9 (much more important).

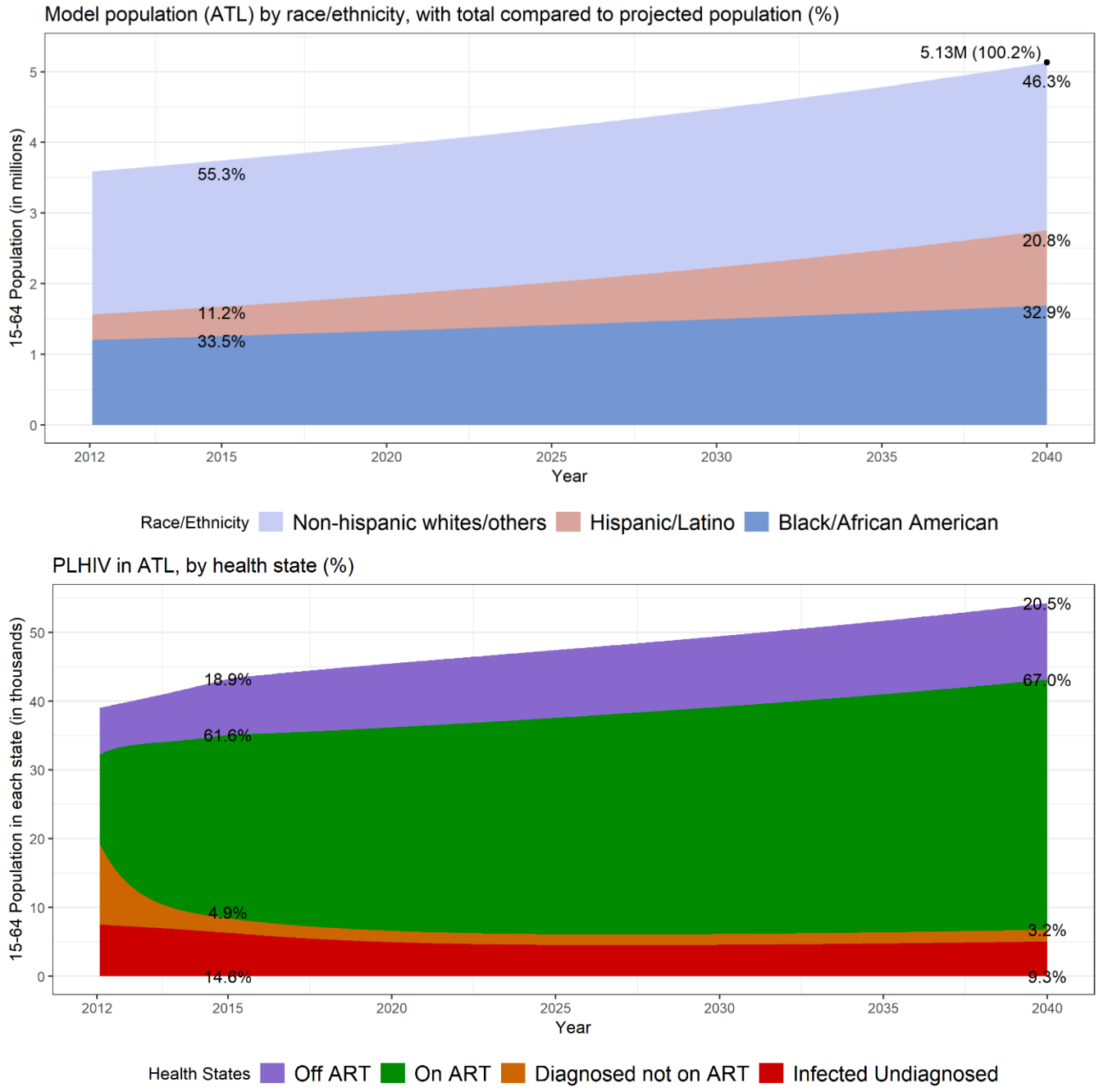
Comparison	Relative importance of	Over	Your answer:
1	Total number diagnosed PLHIV (White MSM*)	Total number diagnosed PLHIV (White male heterosexual*)	4
2	Total number diagnosed PLHIV (Black MSM)		9
3	Total number diagnosed PLHIV (Hispanic MSM)		9
4	Total number diagnosed PLHIV (PWID)		6
5	Total number diagnosed PLHIV (MSM/PWID)		7
6	***Total number diagnosed PLHIV (White male heterosexual*)***		1
7	Total number diagnosed PLHIV (Black male heterosexual)		4
8	Total number diagnosed PLHIV (Hispanic male heterosexual)		4
9	Total number diagnosed PLHIV (White female heterosexual*)		2
10	Total number diagnosed PLHIV (Black female heterosexual)		5
11	Total number diagnosed PLHIV (Hispanic female heterosexual)		5
12	Annual number of new HIV diagnoses (Total)		9
13	Annual number of new HIV diagnoses (Black)		8
14	Annual number of new HIV diagnoses (MSM)		8
15	Annual number of all-cause deaths among PLHIV (Total)		3
16	Annual number of all-cause deaths among PLHIV (Black)		5
17	Annual number of all-cause deaths among PLHIV (MSM)		4

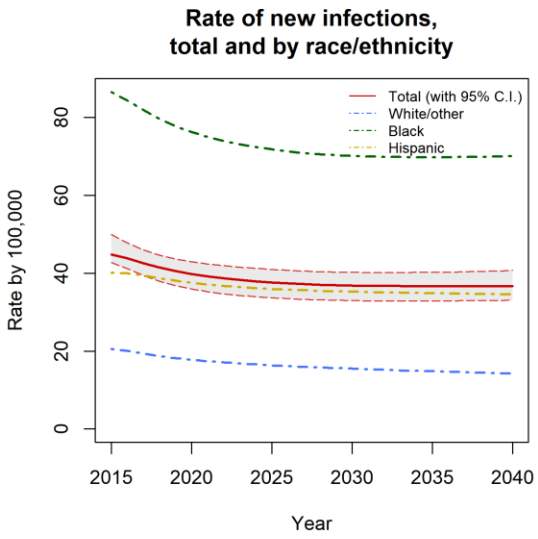
Thank you for taking the time to complete this survey!

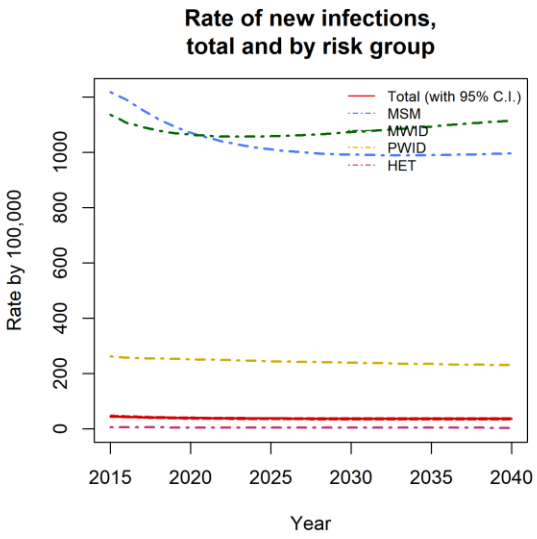
Filled answers present one example of responses we received from SAC

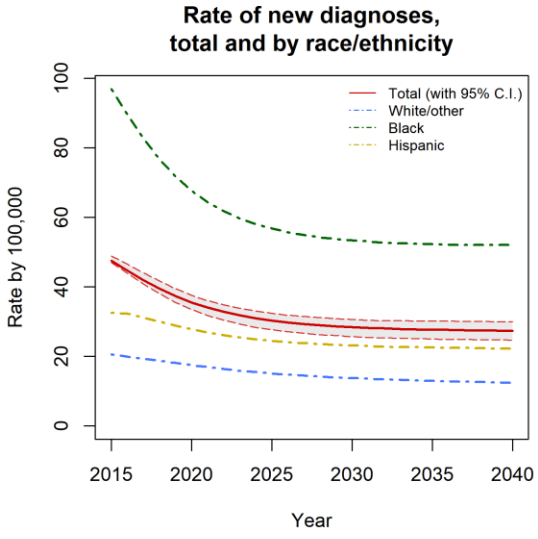
Figure A6. Model status quo scenario projections presented for qualitative face validity assessments

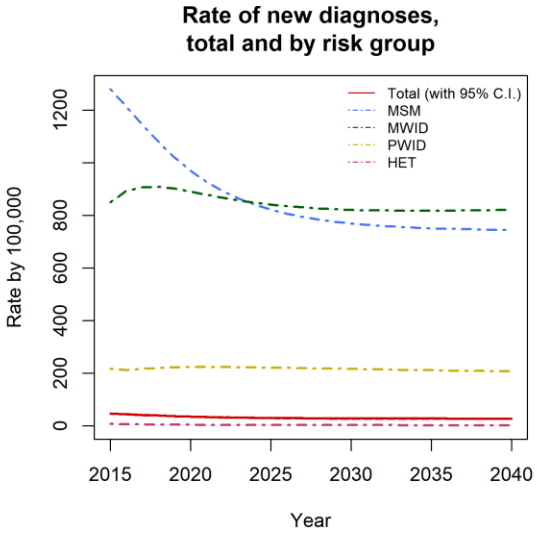
PANEL A. Atlanta

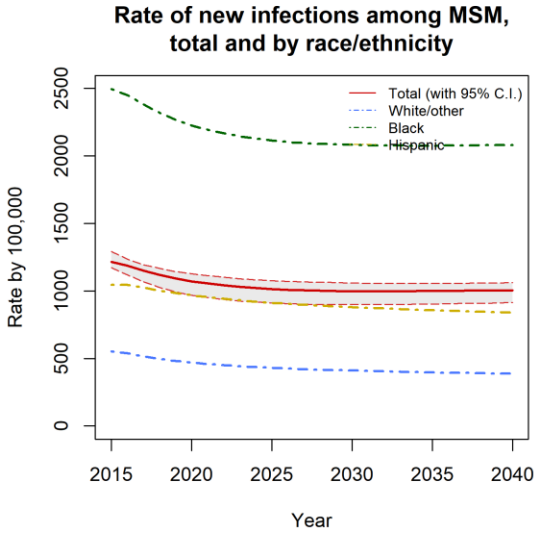


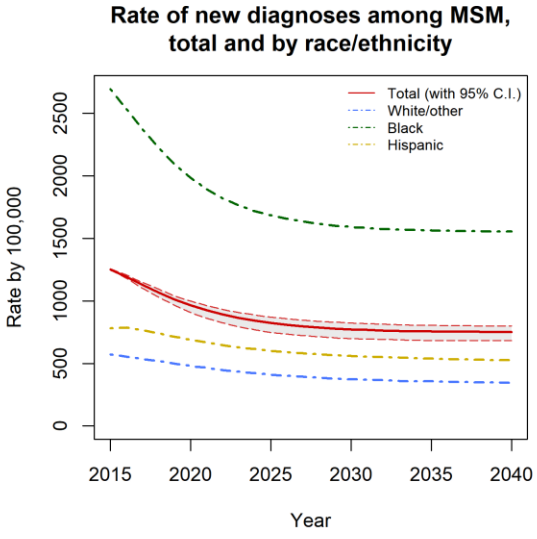

Rate of new infections,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
0
20
40
60
80
2015
2020
2025
2030
2035
2040
Year


Rate of new infections,
total and by risk group
Total (with 95% C.I.)
MSM
MWID
PWID
HET
Rate by 100,000
0
200
400
600
800
1000
2015
2020
2025
2030
2035
2040
Year


Rate of new diagnoses,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
0
20
40
60
80
100
2015
2020
2025
2030
2035
2040
Year


Rate of new diagnoses,
total and by risk group
Total (with 95% C.I.)
MSM
MWID
PWID
HET
Rate by 100,000
0
200
400
600
800
1200
2015
2020
2025
2030
2035
2040
Year


Rate of new infections among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
0
500
1000
1500
2000
2500
2015
2020
2025
2030
2035
2040
Year


Rate of new diagnoses among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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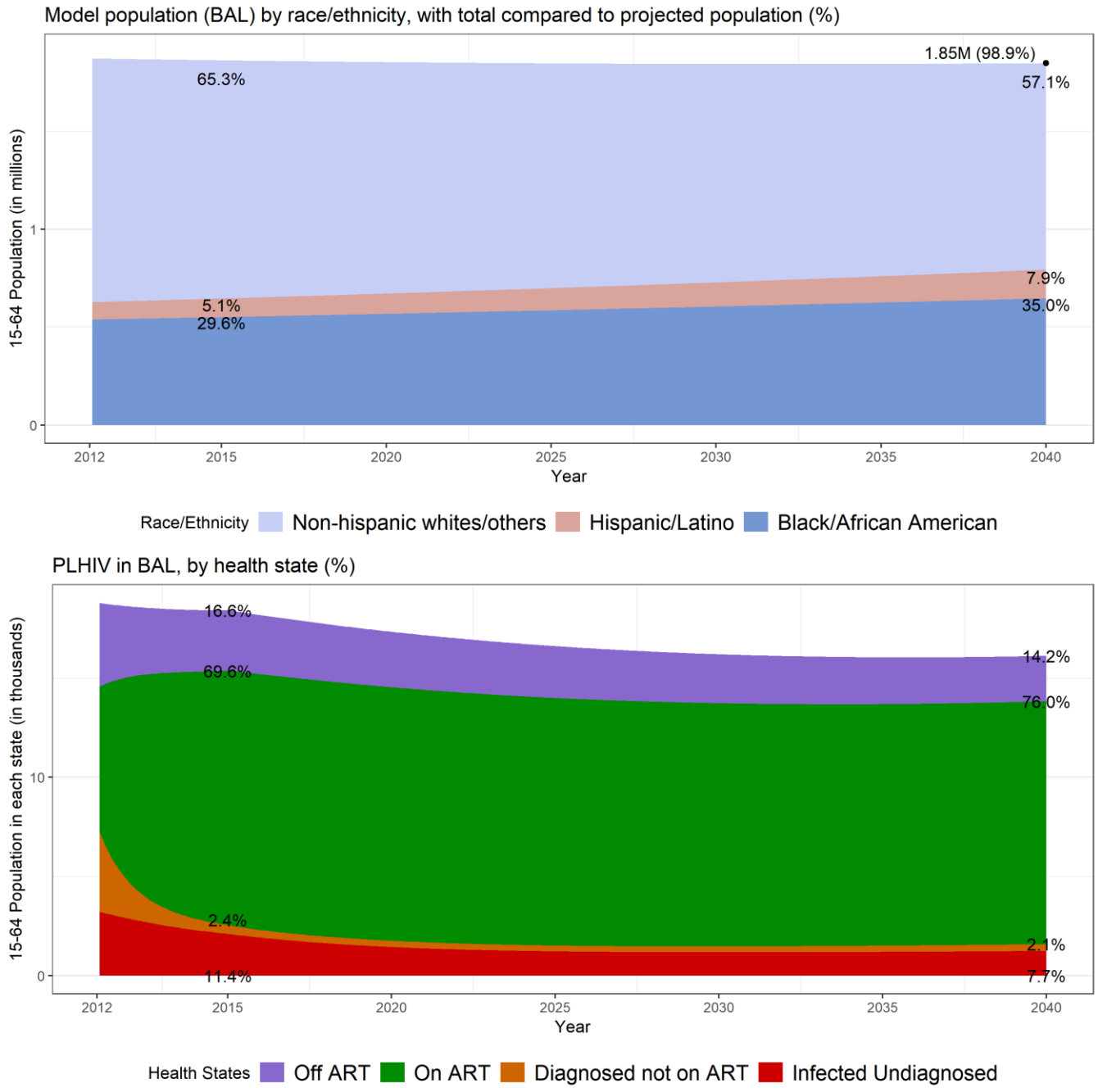
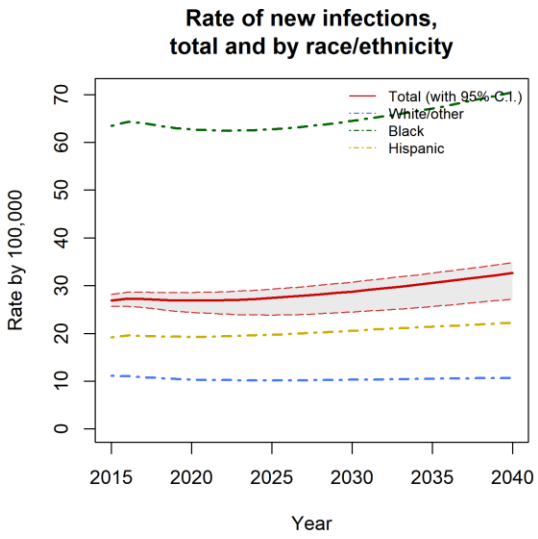
PANEL B. Baltimore




Rate of new infections,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Hispanic
Rate by 100,000
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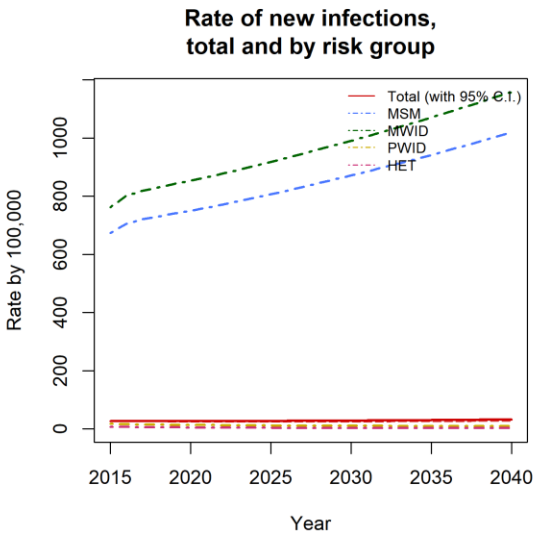
Rate of new infections,
total and by risk group
Total (with 95% C.I.)
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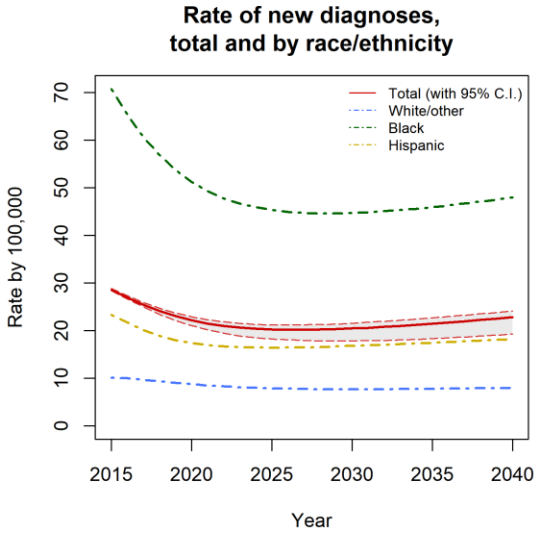
Rate of new diagnoses,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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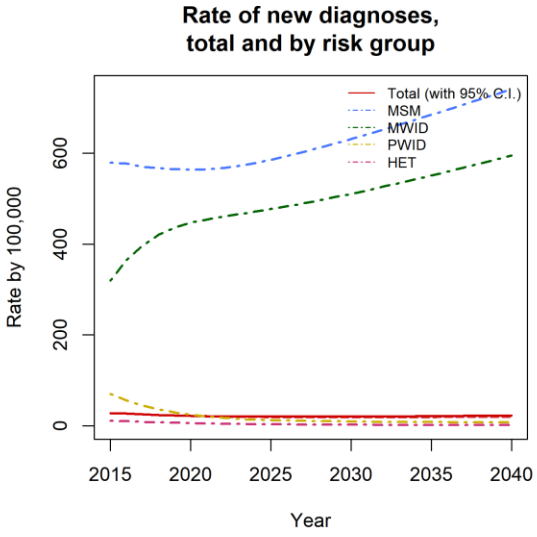
Rate of new diagnoses,
total and by risk group
Total (with 95% C.I.)
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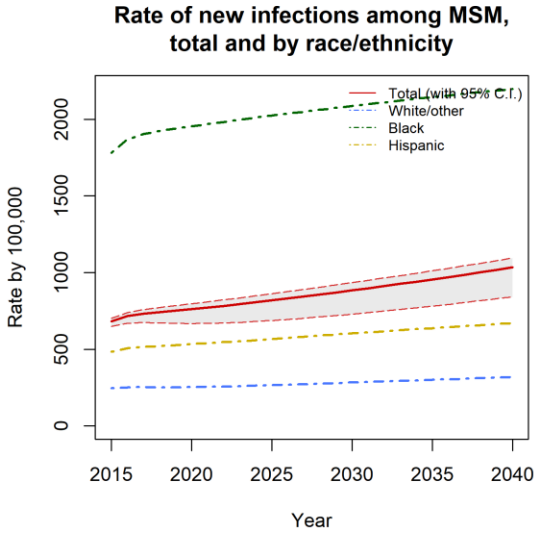
Rate of new infections among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Rate by 100,000
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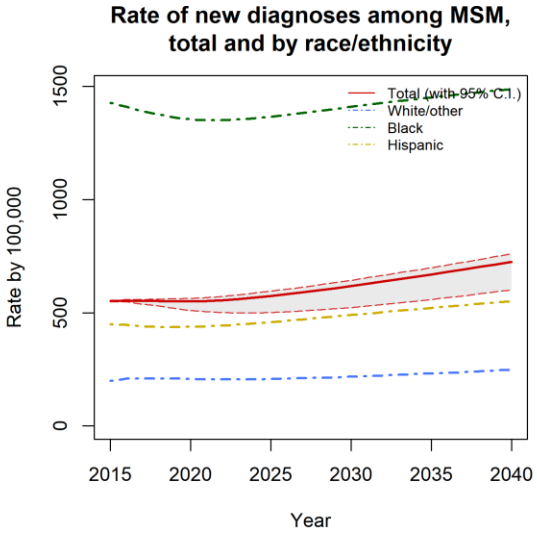
Rate of new diagnoses among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Hispanic
Rate by 100,000
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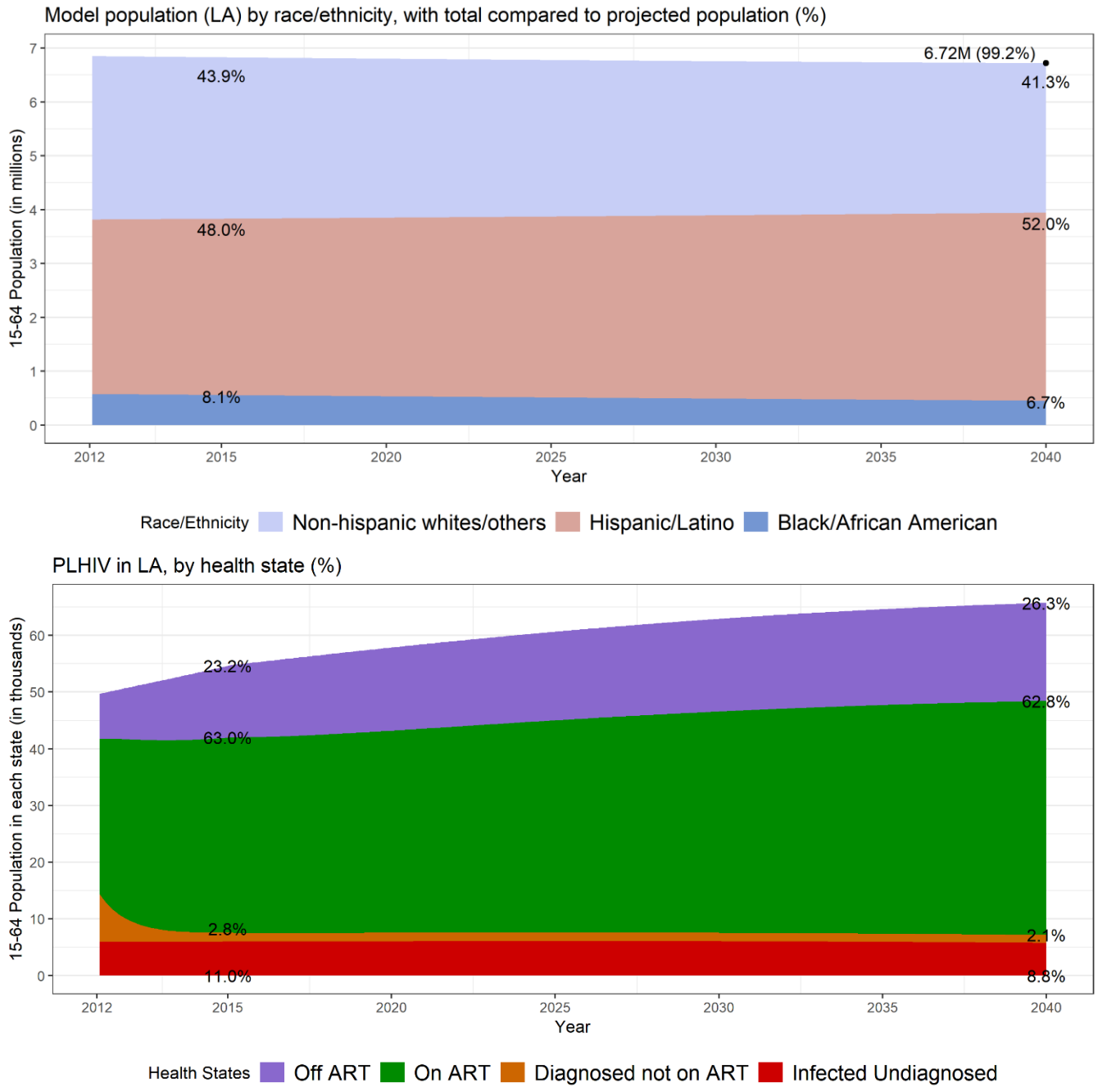
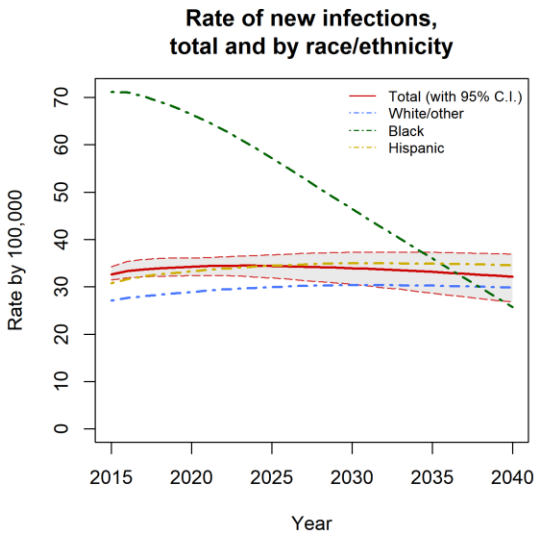
PANEL C. Los Angeles




Rate of new infections,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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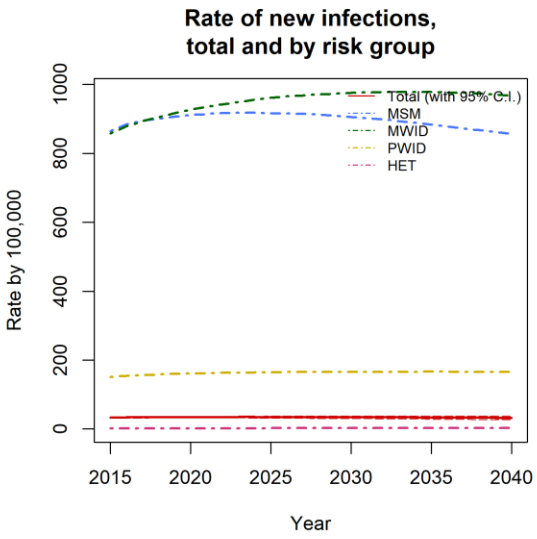
Rate of new infections,
total and by risk group
Total (with 95% C.I.)
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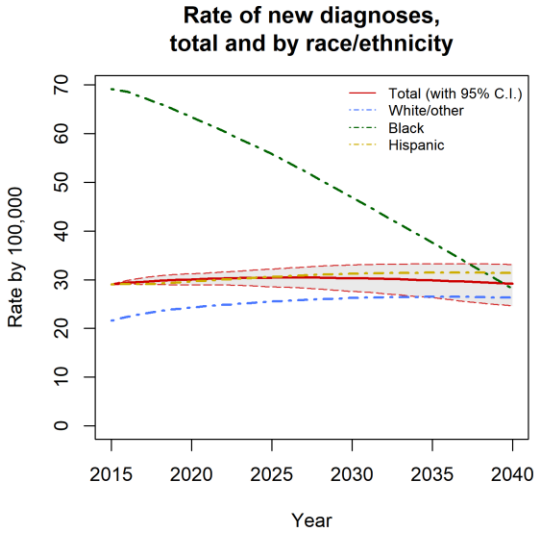
Rate of new diagnoses,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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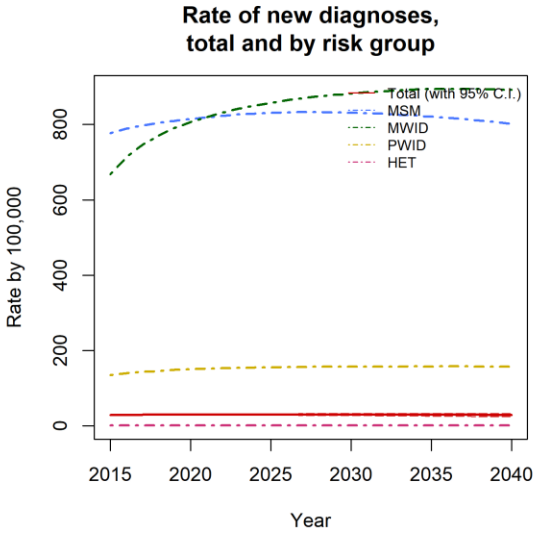
Rate of new diagnoses,
total and by risk group
Total (with 95% C.I.)
MSM
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Rate by 100,000
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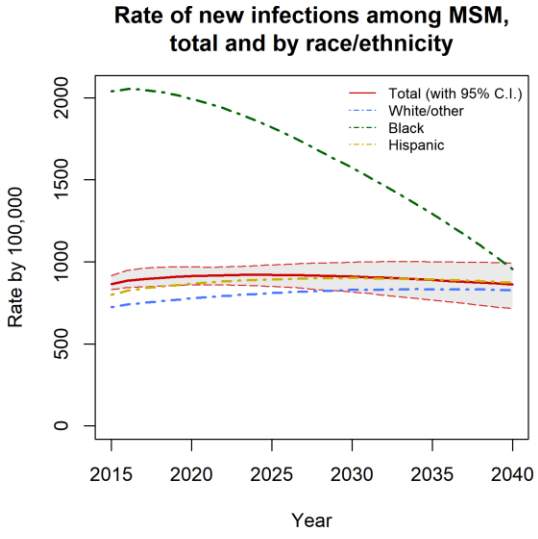
Rate of new infections among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Hispanic
Rate by 100,000
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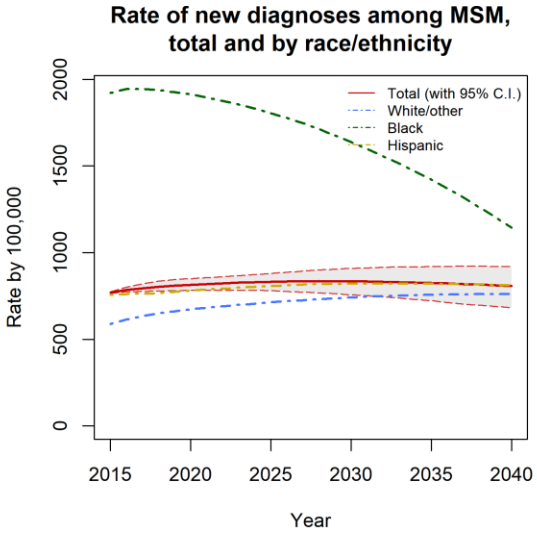
Year


Rate of new diagnoses among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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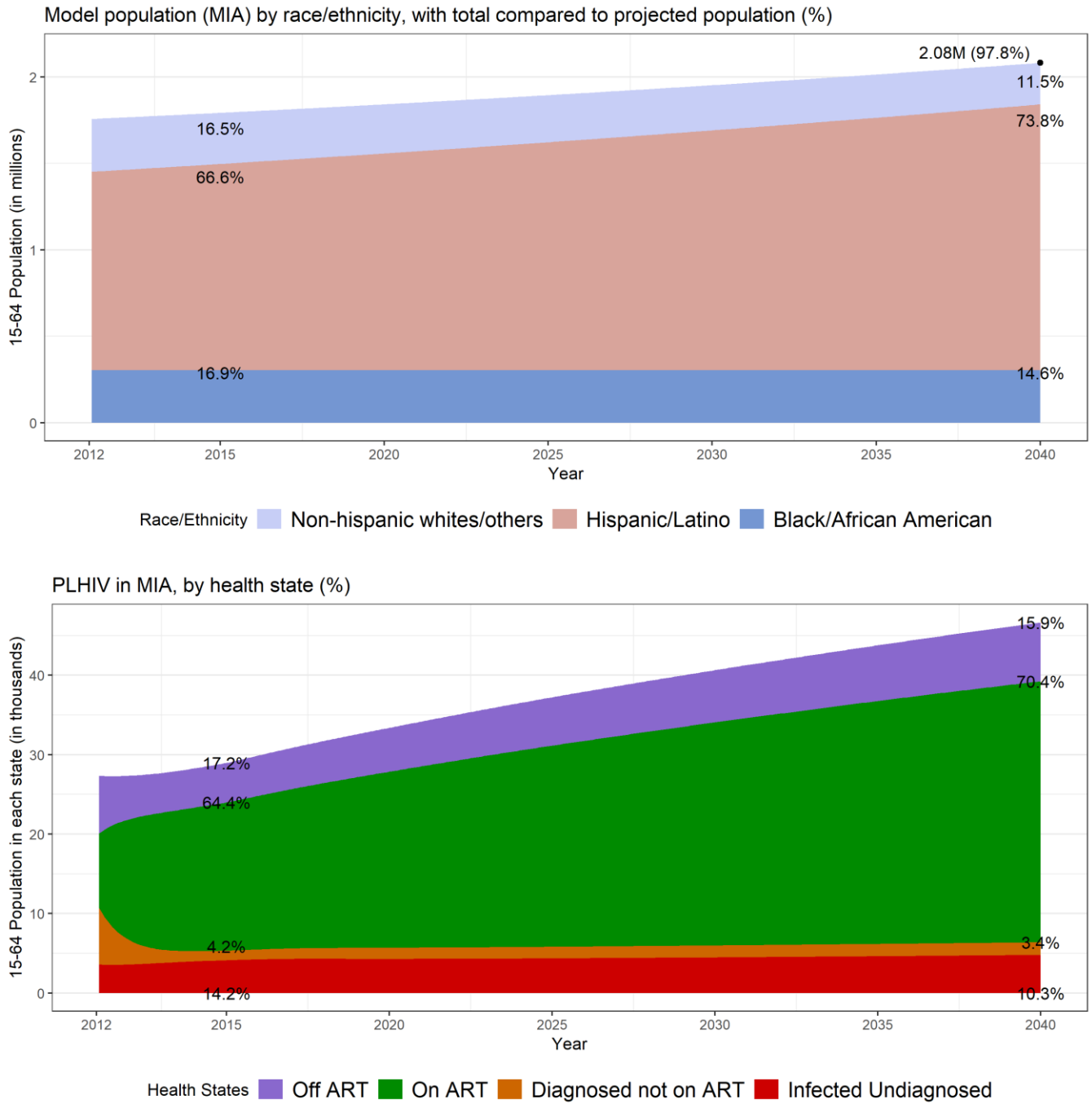
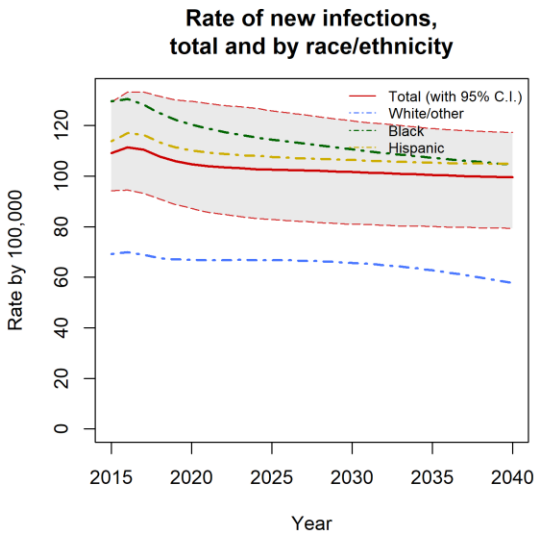
PANEL D. Miami




Rate of new infections,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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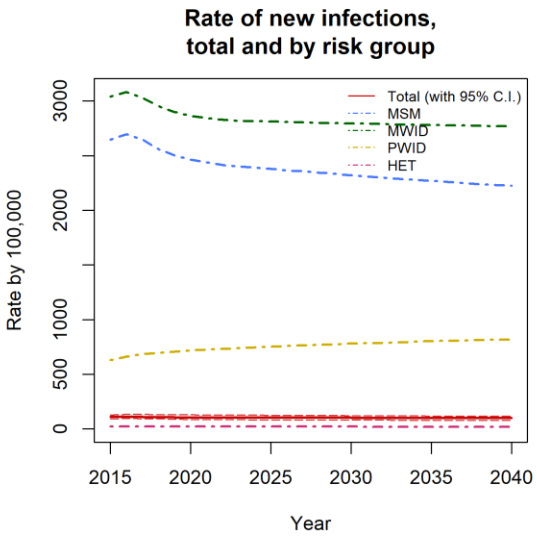
Rate of new infections,
total and by risk group
Total (with 95% C.I.)
MSM
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PWID
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Rate by 100,000
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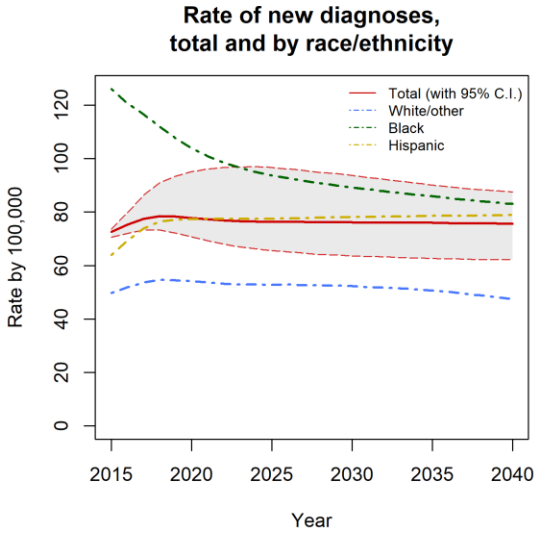
Year


Rate of new diagnoses,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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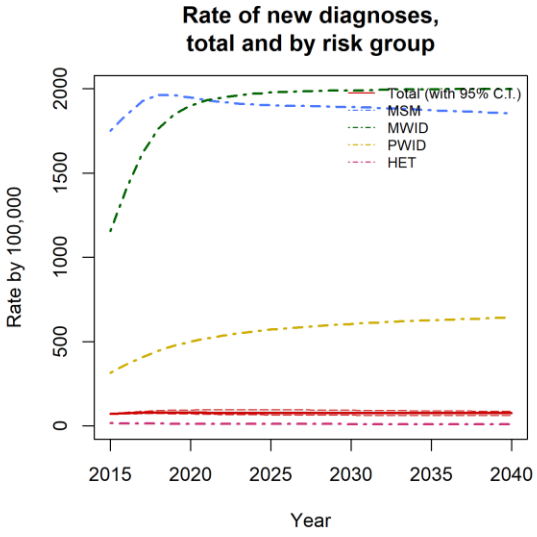
Rate of new diagnoses,
total and by risk group
Total (with 95% C.I.)
MSM
MWID
PWID
HET
Rate by 100,000
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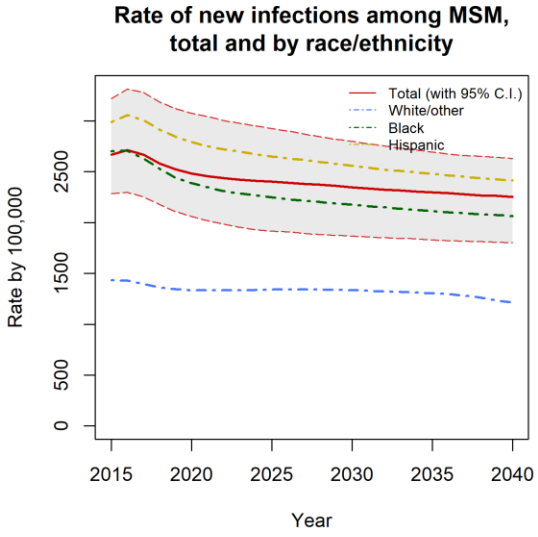
Year


Rate of new infections among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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2015
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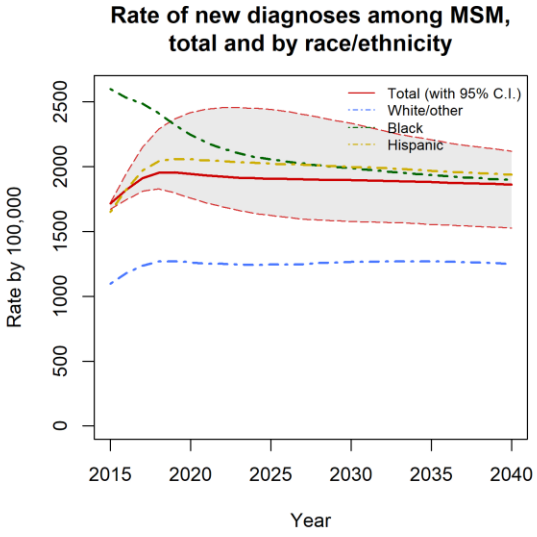
Year


Rate of new diagnoses among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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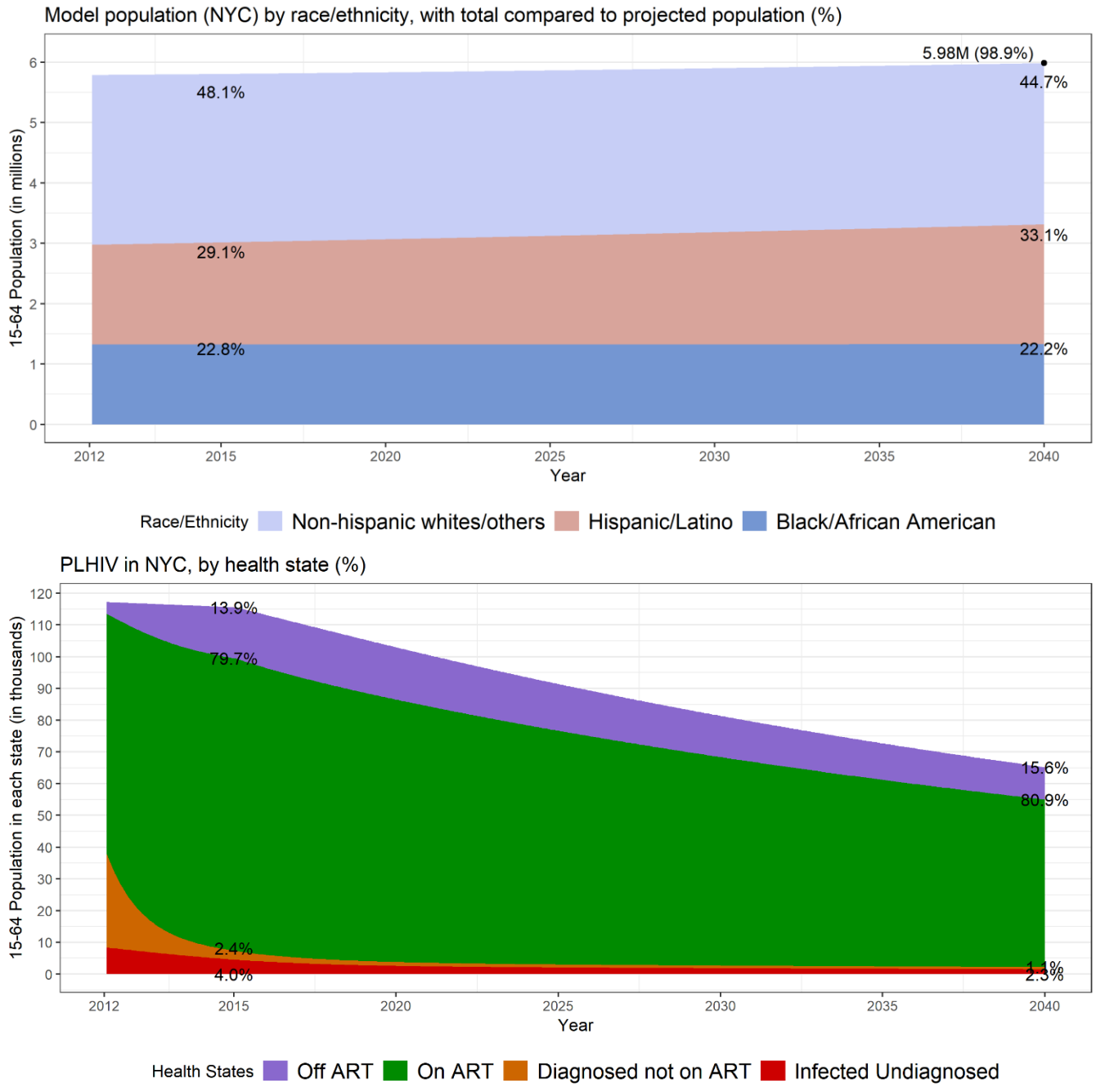
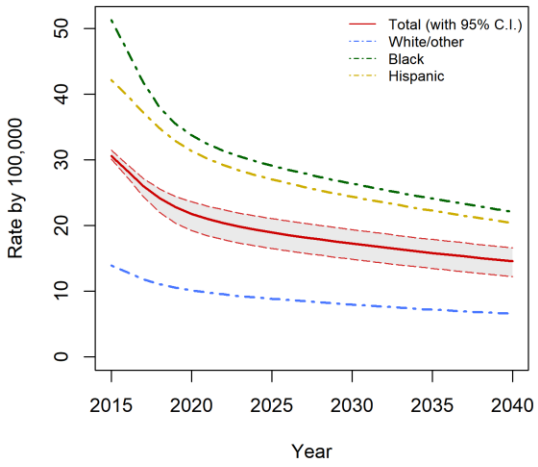
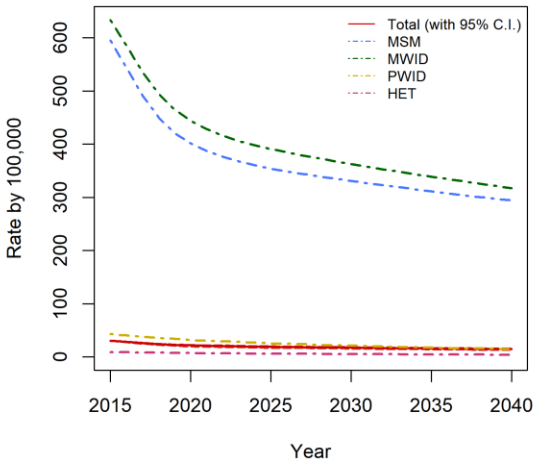
PANEL E. New York City



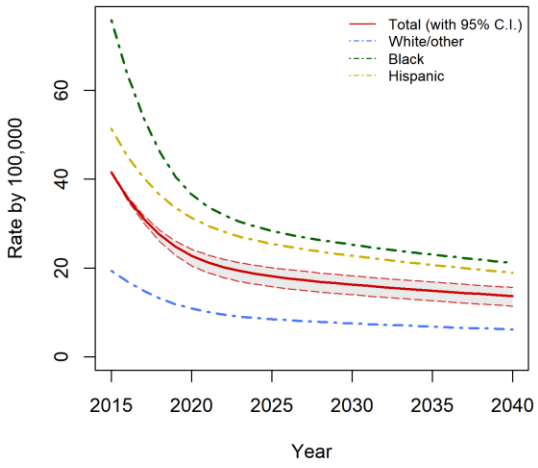
Rate of new infections, total and by race/ethnicity



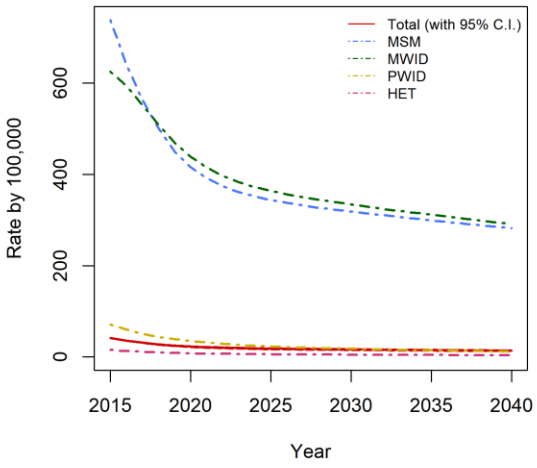
Rate of new infections, total and by risk group



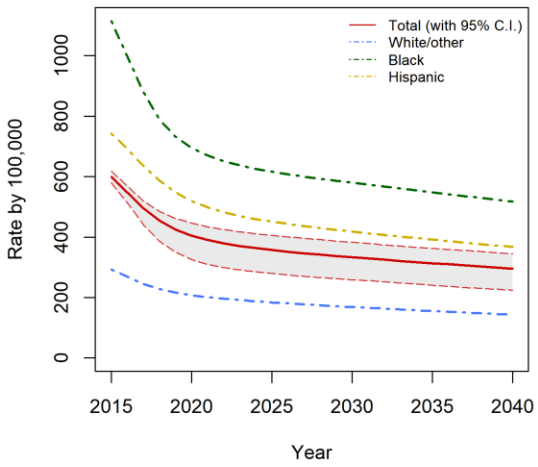
Rate of new diagnoses, total and by race/ethnicity



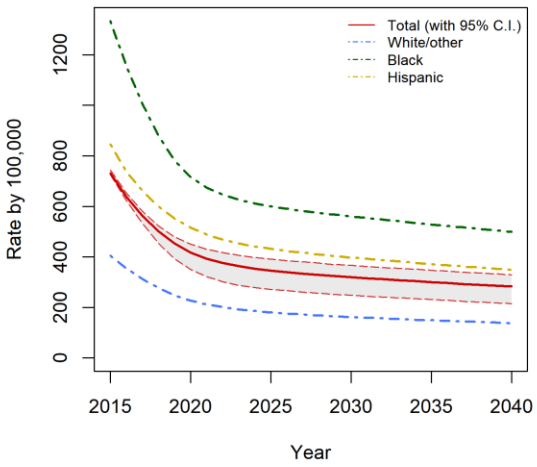
Rate of new diagnoses, total and by risk group



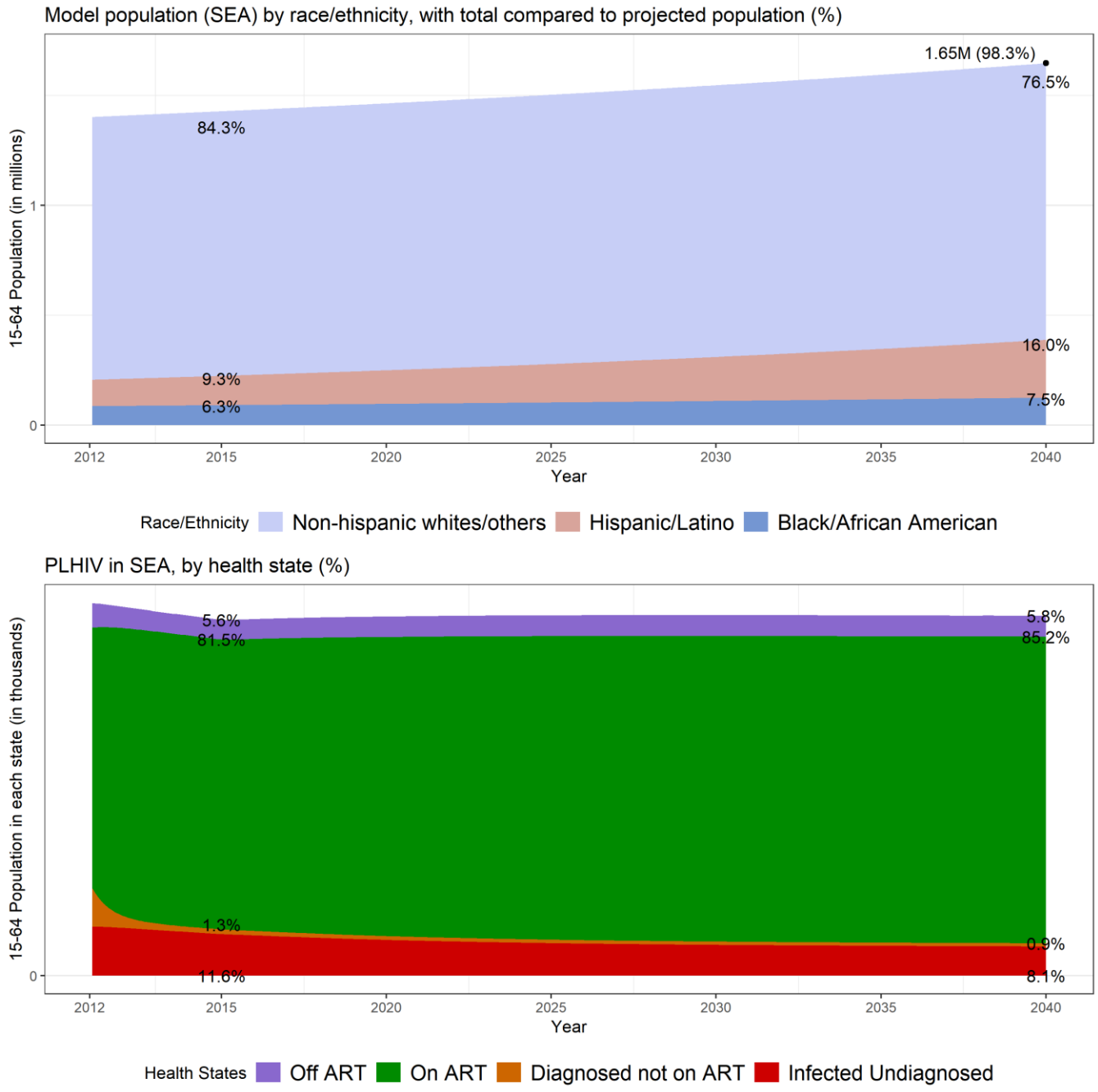
Rate of new infections among MSM, total and by race/ethnicity

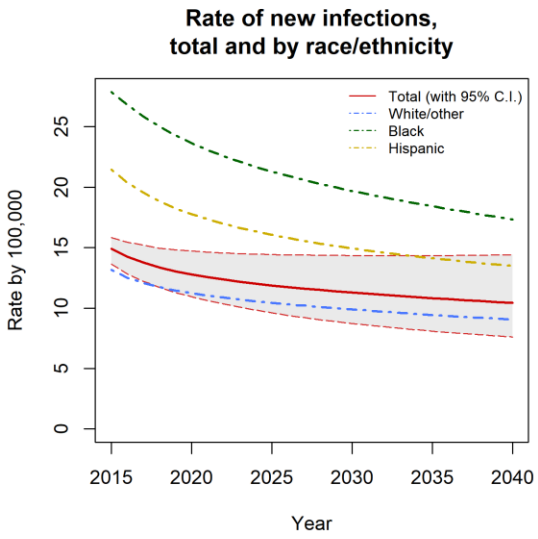


Rate of new diagnoses among MSM, total and by race/ethnicity



PANEL F. Seattle




Rate of new infections,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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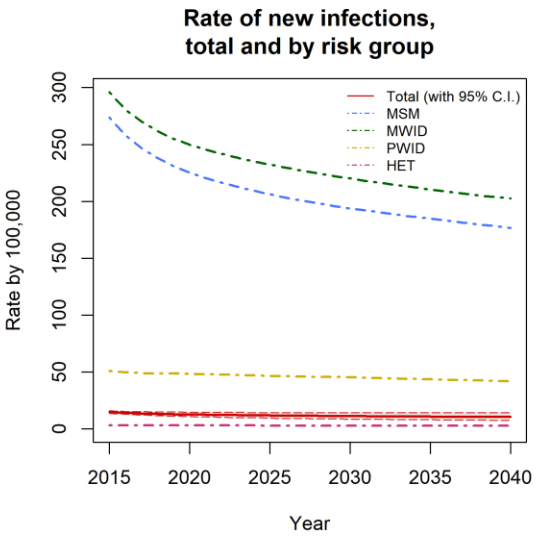
Rate of new infections,
total and by risk group
Total (with 95% C.I.)
MSM
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Rate by 100,000
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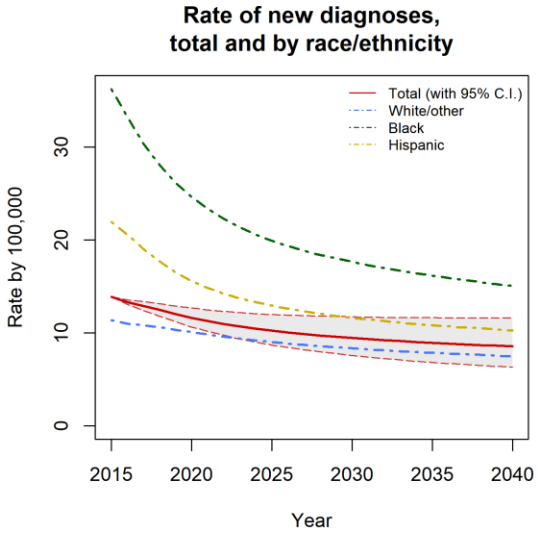
Rate of new diagnoses,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
Black
Hispanic
Rate by 100,000
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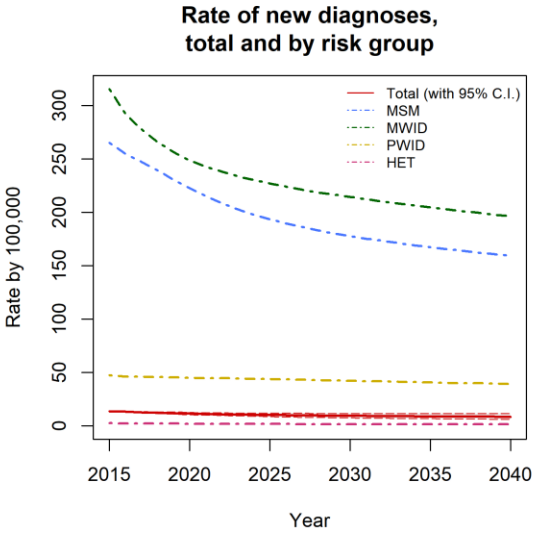
Rate of new diagnoses,
total and by risk group
Total (with 95% C.I.)
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Rate by 100,000
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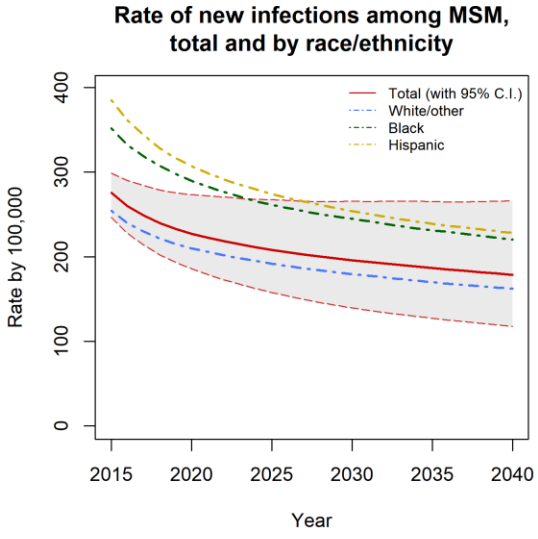
Rate of new infections among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Hispanic
Rate by 100,000
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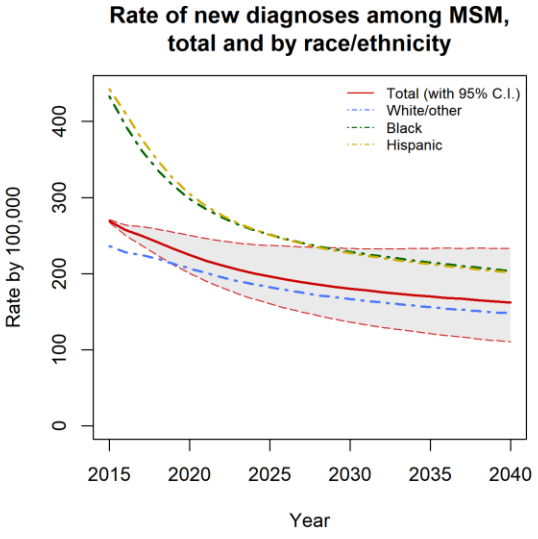
Rate of new diagnoses among MSM,
total and by race/ethnicity
Total (with 95% C.I.)
White/other
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Rate by 100,000
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Appendix C.

Supplementary Material for Chapter 4

This supplementary appendix presents the process of result validation and model tuning for the ANN model, as well as three additional figures and one table in supplementing the manuscript:

- Figure A1 presents the schematic diagram for the structure of the dynamic compartmental HIV transmission model we applied in this value of information analysis. It shows the 19 health states that individuals progress through in the model.
- Figure A2 shows the distribution of the expected value of partial perfect information (EVPPI) estimated for each individual model parameter using the generalized additive model at a threshold of $100,000/QALY. We then ranked these values accordingly and identified and grouped those with the greatest EVPPI as key groups of model parameters for further metamodel analysis with artificial neural network model.
- Figure A3 shows the validation result comparing the EVPPI estimates for the parameter group of HIV transmission probabilities per homosexual partnership using ANN model with GAM model and the two bounds.
- Table A1 presents the description, values and uncertainty distributions for the key groups of model parameters that were found most influential on decision uncertainty for each city.

Result validation and model tuning

Given the novelty of the ANN metamodel, we performed several checks to ensure the validity of its estimates of EVPPI for the key groups of parameters. First, given the extensive evidence for the precision and validation of the GAM approach, we treated the EVPPI estimates from the GAM as “gold standard” and compared the estimated EVPPI for HIV transmission probabilities per homosexual partnership (three parameters in the group) based on both the ANN and GAM approach. Second, we defined the lower bound of the EVPPI for a given parameter group as the maximum EVPPI value estimated for each single parameter (using GAM) within that group, while the upper bound was defined as the city-level EVPI which measured the decision uncertainty from all model parameters jointly. We compared the ANN metamodel results to ensure the EVPPI estimates for all the identified key groups of parameters fell within these bounds. Third, the variance of model predictions and resulting EVPPI from the ten repeated estimations can be a good sign of model fitting, i.e. large variance indicates poor fitting. We hand-tuned the model by varying the number of hidden layers and hidden nodes until the repeated estimated results were within a reasonable range while inside the two bounds. Figure A3 shows the result validation for the parameter group of HIV transmission probabilities per homosexual partnership.

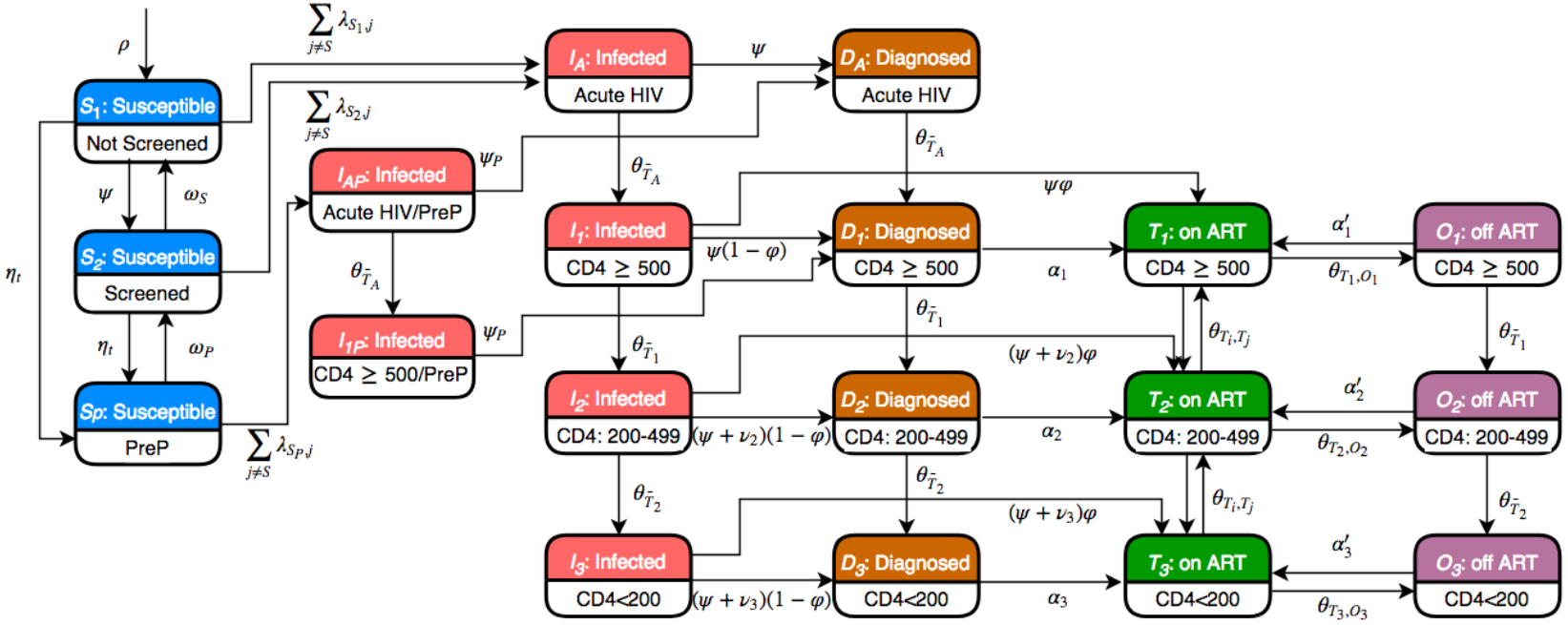

Fig. A1 – Model schematic diagram

Fig. A2 – Distribution of expected value of partial perfect information (EVPPI) for individual parameters

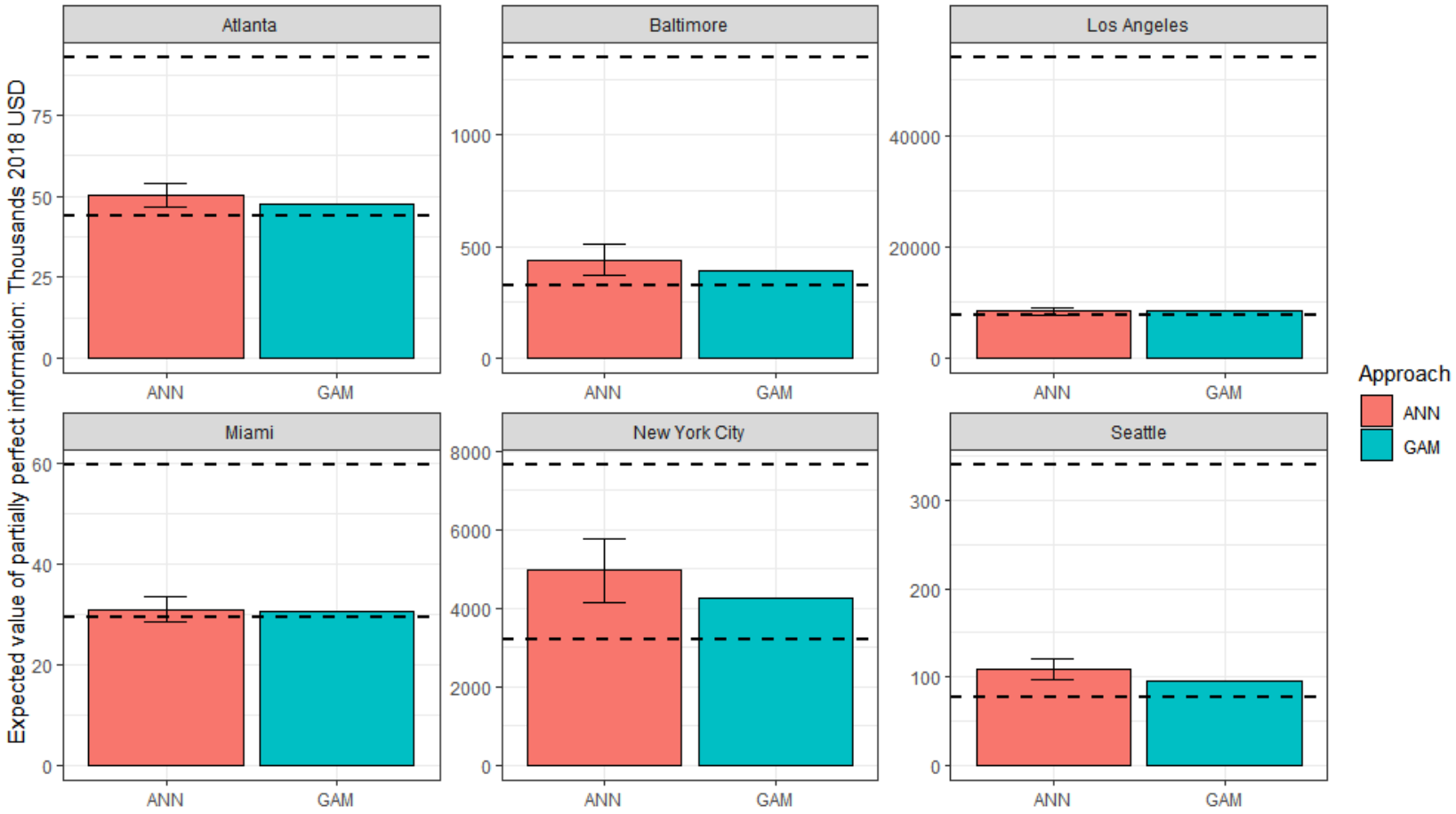

Fig. A3 – Result validation for the parameter group of HIV transmission probabilities per homosexual partnership

The error bars represent the mean ± 1.96 * standard deviation of the estimated values from the ten repeated estimations; two dashed lines represent the corresponding lower and upper bounds. ANN: artificial neural network; GAM: generalized additive model.

Table A1. Key groups of model parameters influential on decision uncertainty

CITY	*Atlanta*	*Baltimore*	*Los Angeles*	*Miami*	*New York City*	*Seattle*
MORTALITY RATES FOR PLHIV						
Monthly mortality rate for PLHIV (CD4: 200-499), except PWID						
PE	6.39E-04	6.39E-04	6.39E-04	6.39E-04	6.39E-04	6.39E-04
Distribution	Pert(1.13, 4.02)	Pert(1.13, 4.02)	Pert (1.13, 4.02)	Pert (1.13, 4.02)	Pert (1.13, 4.02)	Pert (1.13, 4.02)
Monthly mortality rate for PLHIV (CD4<200), except PWID						
PE	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072
Distribution	Pert (3.21, 4.53)	Pert (3.21, 4.53)	Pert (3.21, 4.53)	Pert (3.21, 4.53)	Pert (3.21, 4.53)	Pert (3.21, 4.53)
Multiplier of mortality rate for PLHIV that inject drugs (CD4: 200-499)						
PE	1.59	1.59	1.59	1.59	1.59	1.59
Distribution	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)
Multiplier of mortality rate for PLHIV that inject drugs (CD4<200)						
PE	1.59	1.59	1.59	1.59	1.59	1.59
Distribution	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)	Pert (1.16, 4.06)
Monthly mortality rate for PLHIV on ART (CD4>500), Male White PWID						
PE	0.000868	0.000798	0.000786	0.000868	0.000798	0.000748
Distribution	ln (-7.13, 0.246)	ln (-7.13, 0.246)	ln (-7.15, 0.288)	ln (-7.13, 0.246)	ln (-7.13, 0.246)	ln (-7.20, 0.316)
Monthly mortality rate for PLHIV on ART (CD4>500), Male White MSM						
PE	0.000303	0.000277	0.000273	0.000303	0.000277	0.000259
Distribution	ln (-8.10, 0.184)	ln (-8.19, 0.167)	ln (-8.21, 0.196)	ln (-8.10, 0.184)	ln (-8.19, 0.167)	ln (-8.26, 0.236)
Monthly mortality rate for PLHIV on ART (CD4>500), Male White MWID						
PE	0.000693	0.000636	0.000625	0.000693	0.000636	0.000617
Distribution	ln (-7.27, 0.237)	ln (-7.36, 0.221)	ln (-7.38, 0.241)	ln (-7.27, 0.237)	ln (-7.36, 0.221)	ln (-7.39, 0.29)
Monthly mortality rate for PLHIV on ART (CD4>500), Male White HET						
PE	0.000380	0.000348	0.000343	0.000380	0.000348	0.000314
Distribution	ln (-7.88, 0.234)	ln (-7.96, 0.236)	ln (-7.98, 0.279)	ln (-7.88, 0.234)	ln (-7.96, 0.236)	ln (-8.07, 0.304)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Black PWID						
PE	0.000759	0.000699	0.000688	0.000759	0.000699	0.000630
Distribution	ln (-7.18, 0.204)	ln (-7.27, 0.204)	ln (-7.28, 0.27)	ln (-7.18, 0.204)	ln (-7.27, 0.204)	ln (-7.37, 0.3)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Black MSM						
PE	0.000265	0.000242	0.000239	0.000265	0.000242	0.000218
Distribution	ln (-8.24, 0.198)	ln (-8.32, 0.193)	ln (-8.34, 0.244)	ln (-8.24, 0.198)	ln (-8.32, 0.193)	ln (-8.43, 0.287)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Black MWID						
PE	0.000606	0.000556	0.000548	0.000606	0.000556	0.000519
Distribution	ln (-7.41, 0.248)	ln (-7.49, 0.243)	ln (-7.51, 0.277)	ln (-7.41, 0.248)	ln (-7.49, 0.243)	ln (-7.56, 0.338)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Black HET						
PE	0.000332	0.000305	0.000301	0.000332	0.000305	0.000264
Distribution	ln (-8.01, 0.207)	ln (-8.10, 0.204)	ln (-8.11, 0.257)	ln (-8.01, 0.207)	ln (-8.10, 0.204)	ln (-8.24, 0.303)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Hispanic PWID						

PE	0.000439	0.000403	0.000398	0.000439	0.000403	0.000376
Distribution	ln (-7.73, 0.272)	ln (-7.82, 0.274)	ln (-7.83, 0.292)	ln (-7.73, 0.272)	ln (-7.82, 0.274)	ln (-7.89, 0.351)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Hispanic MSM						
PE	0.000153	0.000140	0.000138	0.000153	0.000140	0.000130
Distribution	ln (-8.78, 0.265)	ln (-8.87, 0.228)	ln (-8.89, 0.292)	ln (-8.78, 0.265)	ln (-8.87, 0.228)	ln (-8.95, 0.307)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Hispanic MWID						
PE	0.000351	0.000321	0.000316	0.000351	0.000321	0.000310
Distribution	ln (-7.96, 0.315)	ln (-8.04, 0.294)	ln (-8.06, 0.34)	ln (-7.96, 0.315)	ln (-8.04, 0.294)	ln (-8.08, 0.372)
Monthly mortality rate for PLHIV on ART (CD4>500), Male Hispanic HET						
PE	0.000192	0.000176	0.000174	0.000192	0.000176	0.000158
Distribution	ln (-8.56, 0.295)	ln (-8.65, 0.266)	ln (-8.66, 0.327)	ln (-8.56, 0.295)	ln (-8.65, 0.266)	ln (-8.75, 0.333)
Monthly mortality rate for PLHIV on ART (CD4>500), Female White PWID						
PE	0.000673	0.000616	0.000606	0.000673	0.000616	0.000597
Distribution	ln (-7.30, 0.267)	ln (-7.39, 0.241)	ln (-7.41, 0.288)	ln (-7.30, 0.267)	ln (-7.39, 0.241)	ln (-7.42, 0.307)
Monthly mortality rate for PLHIV on ART (CD4>500), Female White HET						
PE	0.000294	0.000269	0.000264	0.000294	0.000269	0.000250
Distribution	ln (-8.13, 0.232)	ln (-8.22, 0.228)	ln (-8.24, 0.263)	ln (-8.13, 0.232)	ln (-8.22, 0.228)	ln (-8.29, 0.294)
Monthly mortality rate for PLHIV on ART (CD4>500), Female Black PWID						
PE	0.000587	0.000539	0.000531	0.000587	0.000539	0.000502
Distribution	ln (-7.44, 0.217)	ln (-7.53, 0.226)	ln (-7.54, 0.282)	ln (-7.44, 0.217)	ln (-7.53, 0.226)	ln (-7.6, 0.309)
Monthly mortality rate for PLHIV on ART (CD4>500), Female Black HET						
PE	0.000257	0.000235	0.000232	0.000257	0.000235	0.000211
Distribution	ln (-8.27, 0.182)	ln (-8.36, 0.19)	ln (-8.37, 0.265)	ln (-8.27, 0.182)	ln (-8.36, 0.19)	ln (-8.46, 0.297)
Monthly mortality rate for PLHIV on ART (CD4>500), Female Hispanic PWID						
PE	0.000341	0.000311	0.000307	0.000341	0.000311	0.000300
Distribution	ln (-7.98, 0.289)	ln (-8.07, 0.286)	ln (-8.09, 0.318)	ln (-7.98, 0.289)	ln (-8.07, 0.286)	ln (-8.11, 0.356)
Monthly mortality rate for PLHIV on ART (CD4>500), Female Hispanic HET						
PE	0.000149	0.000136	0.000134	0.000149	0.000136	0.000126
Distribution	ln (-8.81, 0.274)	ln (-8.90, 0.251)	ln (-8.92, 0.302)	ln (-8.81, 0.274)	ln (-8.90, 0.251)	ln (-8.98, 0.328)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male White PWID						
PE	0.00132	0.00140	0.00165	0.00132	0.00140	0.00137
Distribution	ln (-6.63, 0.191)	ln (-6.57, 0.186)	ln (-6.41, 0.204)	ln (-6.63, 0.191)	ln (-6.57, 0.186)	ln (-6.6, 0.223)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male White MSM						
PE	0.000595	0.000628	0.000739	0.000595	0.000628	0.000613
Distribution	ln (-7.43, 0.14)	ln (-7.37, 0.151)	ln (-7.21, 0.145)	ln (-7.43, 0.14)	ln (-7.37, 0.151)	ln (-7.4, 0.183)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male White MWID						
PE	0.000936	0.000985	0.001158	0.000936	0.000985	0.000951
Distribution	ln (-6.97, 0.198)	ln (-6.92, 0.187)	ln (-6.76, 0.192)	ln (-6.97, 0.198)	ln (-6.92, 0.187)	ln (-6.96, 0.23)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male White HET						
PE	0.000844	0.000896	0.001054	0.000844	0.000896	0.000882
Distribution	ln (-7.08, 0.179)	ln (-7.02, 0.186)	ln (-6.85, 0.208)	ln (-7.08, 0.179)	ln (-7.02, 0.186)	ln (-7.03, 0.203)

Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Black PWID						
PE	0.00107	0.00113	0.00133	0.00107	0.00113	0.00104
Distribution	ln (-6.84, 0.158)	ln (-6.78, 0.16)	ln (-6.62, 0.192)	ln (-6.84, 0.158)	ln (-6.78, 0.16)	ln (-6.86, 0.226)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Black MSM						
PE	0.000481	0.000507	0.000597	0.000481	0.000507	0.000469
Distribution	ln (-7.64, 0.155)	ln (-7.59, 0.163)	ln (-7.42, 0.172)	ln (-7.64, 0.155)	ln (-7.59, 0.163)	ln (-7.67, 0.21)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Black MWID						
PE	0.000758	0.000796	0.000936	0.000758	0.000796	0.000728
Distribution	ln (-7.18, 0.206)	ln (-7.14, 0.193)	ln (-6.97, 0.223)	ln (-7.18, 0.206)	ln (-7.14, 0.193)	ln (-7.22, 0.266)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Black HET						
PE	0.000682	0.000723	0.000851	0.000682	0.000723	0.000674
Distribution	ln (-7.29, 0.14)	ln (-7.23, 0.158)	ln (-7.07, 0.196)	ln (-7.29, 0.14)	ln (-7.23, 0.158)	ln (-7.3, 0.205)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Hispanic PWID						
PE	0.000730	0.000768	0.000904	0.000730	0.000768	0.000733
Distribution	ln (-7.22, 0.196)	ln (-7.17, 0.185)	ln (-7.01, 0.213)	ln (-7.22, 0.196)	ln (-7.17, 0.185)	ln (-7.22, 0.256)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Hispanic MSM						
PE	0.000328	0.000344	0.000405	0.000328	0.000344	0.000329
Distribution	ln (-8.02, 0.195)	ln (-7.98, 0.177)	ln (-7.81, 0.191)	ln (-8.02, 0.195)	ln (-7.98, 0.177)	ln (-8.02, 0.226)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Hispanic MWID						
PE	0.000518	0.000540	0.000636	0.000518	0.000540	0.000512
Distribution	ln (-7.57, 0.239)	ln (-7.52, 0.219)	ln (-7.36, 0.25)	ln (-7.57, 0.239)	ln (-7.52, 0.219)	ln (-7.58, 0.261)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Male Hispanic HET						
PE	0.000464	0.000490	0.000577	0.000464	0.000490	0.000473
Distribution	ln (-7.68, 0.188)	ln (-7.62, 0.179)	ln (-7.46, 0.196)	ln (-7.68, 0.188)	ln (-7.62, 0.179)	ln (-7.66, 0.229)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female White PWID						
PE	0.00135	0.00142	0.00167	0.00135	0.00142	0.00140
Distribution	ln (-6.61, 0.198)	ln (-6.56, 0.205)	ln (-6.39, 0.238)	ln (-6.61, 0.198)	ln (-6.56, 0.205)	ln (-6.57, 0.249)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female White HET						
PE	0.000858	0.000908	0.001068	0.000858	0.000908	0.000903
Distribution	ln (-7.06, 0.187)	ln (-7.00, 0.193)	ln (-6.84, 0.194)	ln (-7.06, 0.187)	ln (-7.00, 0.193)	ln (-7.01, 0.224)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female Black PWID						
PE	0.00109	0.00115	0.00135	0.00109	0.00115	0.00107
Distribution	ln (-6.82, 0.169)	ln (-6.77, 0.182)	ln (-6.61, 0.213)	ln (-6.82, 0.169)	ln (-6.77, 0.182)	ln (-6.84, 0.243)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female Black HET						
PE	0.000694	0.000732	0.000862	0.000694	0.000732	0.000690
Distribution	ln (-7.27, 0.159)	ln (-7.22, 0.159)	ln (-7.06, 0.196)	ln (-7.27, 0.159)	ln (-7.22, 0.159)	ln (-7.28, 0.216)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female Hispanic PWID						
PE	0.000745	0.000780	0.000917	0.000745	0.000780	0.000752
Distribution	ln (-7.2, 0.215)	ln (-7.16, 0.206)	ln (-6.99, 0.236)	ln (-7.2, 0.215)	ln (-7.16, 0.206)	ln (-7.19, 0.26)
Monthly mortality rate for PLHIV on ART (CD4: 200-499), Female Hispanic HET						
PE	0.000473	0.000497	0.000585	0.000473	0.000497	0.000485
Distribution	ln (-7.66, 0.194)	ln (-7.61, 0.183)	ln (-7.44, 0.215)	ln (-7.66, 0.194)	ln (-7.61, 0.183)	ln (-7.63, 0.24)

Monthly mortality rate for PLHIV on ART (CD4<200), Male White PWID						
PE	0.00798	0.00426	0.00566	0.00798	0.00426	0.00575
Distribution	ln (-4.83, 0.15)	ln (-5.46, 0.156)	ln (-5.17, 0.168)	ln (-4.83, 0.15)	ln (-5.46, 0.156)	ln (-5.16, 0.196)
Monthly mortality rate for PLHIV on ART (CD4<200), Male White MSM						
PE	0.00556	0.00295	0.00393	0.00556	0.00295	0.00409
Distribution	ln (-5.19, 0.117)	ln (-5.82, 0.138)	ln (-5.54, 0.125)	ln (-5.19, 0.117)	ln (-5.82, 0.138)	ln (-5.5, 0.154)
Monthly mortality rate for PLHIV on ART (CD4<200), Male White MWID						
PE	0.00891	0.00475	0.00632	0.00891	0.00475	0.00649
Distribution	ln (-4.72, 0.148)	ln (-5.35, 0.148)	ln (-5.06, 0.148)	ln (-4.72, 0.148)	ln (-5.35, 0.148)	ln (-5.04, 0.181)
Monthly mortality rate for PLHIV on ART (CD4<200), Male White HET						
PE	0.00498	0.00265	0.00353	0.00498	0.00265	0.00363
Distribution	ln (-5.3, 0.136)	ln (-5.93, 0.15)	ln (-5.65, 0.16)	ln (-5.3, 0.136)	ln (-5.93, 0.15)	ln (-5.62, 0.169)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Black PWID						
PE	0.00718	0.00384	0.00510	0.00718	0.00384	0.00504
Distribution	ln (-4.94, 0.117)	ln (-5.56, 0.137)	ln (-5.28, 0.168)	ln (-4.94, 0.117)	ln (-5.56, 0.137)	ln (-5.29, 0.191)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Black MSM						
PE	0.00500	0.00266	0.00355	0.00500	0.00266	0.00359
Distribution	ln (-5.3, 0.107)	ln (-5.93, 0.129)	ln (-5.64, 0.14)	ln (-5.3, 0.107)	ln (-5.93, 0.129)	ln (-5.63, 0.166)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Black MWID						
PE	0.00802	0.00428	0.00569	0.00802	0.00428	0.00569
Distribution	ln (-4.83, 0.146)	ln (-5.45, 0.162)	ln (-5.17, 0.167)	ln (-4.83, 0.146)	ln (-5.45, 0.162)	ln (-5.17, 0.198)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Black HET						
PE	0.00449	0.00239	0.00318	0.00449	0.00239	0.00318
Distribution	ln (-5.41, 0.102)	ln (-6.04, 0.122)	ln (-5.75, 0.156)	ln (-5.41, 0.102)	ln (-6.04, 0.122)	ln (-5.75, 0.168)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Hispanic PWID						
PE	0.00616	0.00328	0.00437	0.00616	0.00328	0.00430
Distribution	ln (-5.09, 0.149)	ln (-5.72, 0.16)	ln (-5.43, 0.178)	ln (-5.09, 0.149)	ln (-5.72, 0.16)	ln (-5.45, 0.192)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Hispanic MSM						
PE	0.00429	0.00228	0.00303	0.00429	0.00228	0.00306
Distribution	ln (-5.45, 0.125)	ln (-6.09, 0.145)	ln (-5.8, 0.164)	ln (-5.45, 0.125)	ln (-6.09, 0.145)	ln (-5.79, 0.174)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Hispanic MWID						
PE	0.00688	0.00366	0.00487	0.00688	0.00366	0.00486
Distribution	ln (-4.98, 0.163)	ln (-5.61, 0.172)	ln (-5.32, 0.193)	ln (-4.98, 0.163)	ln (-5.61, 0.172)	ln (-5.33, 0.204)
Monthly mortality rate for PLHIV on ART (CD4<200), Male Hispanic HET						
PE	0.00384	0.00204	0.00272	0.00384	0.00204	0.00271
Distribution	ln (-5.56, 0.135)	ln (-6.19, 0.149)	ln (-5.91, 0.166)	ln (-5.56, 0.135)	ln (-6.19, 0.149)	ln (-5.91, 0.177)
Monthly mortality rate for PLHIV on ART (CD4<200), Female White PWID						
PE	0.00856	0.00457	0.00608	0.00856	0.00457	0.00612
Distribution	ln (-4.76, 0.166)	ln (-5.39, 0.169)	ln (-5.1, 0.181)	ln (-4.76, 0.166)	ln (-5.39, 0.169)	ln (-5.1, 0.208)
Monthly mortality rate for PLHIV on ART (CD4<200), Female White HET						
PE	0.00534	0.00284	0.00378	0.00534	0.00284	0.00386
Distribution	ln (-5.23, 0.142)	ln (-5.86, 0.167)	ln (-5.58, 0.172)	ln (-5.23, 0.142)	ln (-5.86, 0.167)	ln (-5.56, 0.189)

Monthly mortality rate for PLHIV on ART (CD4<200), Female Black PWID						
PE	0.00770	0.00412	0.00547	0.00770	0.00412	0.00537
Distribution	ln (-4.87, 0.132)	ln (-5.49, 0.149)	ln (-5.21, 0.178)	ln (-4.87, 0.132)	ln (-5.49, 0.149)	ln (-5.23, 0.196)
Monthly mortality rate for PLHIV on ART (CD4<200), Female Black HET						
PE	0.00481	0.00256	0.00341	0.00481	0.00256	0.00339
Distribution	ln (-5.34, 0.112)	ln (-5.97, 0.138)	ln (-5.68, 0.161)	ln (-5.34, 0.112)	ln (-5.97, 0.138)	ln (-5.69, 0.179)
Monthly mortality rate for PLHIV on ART (CD4<200), Female Hispanic PWID						
PE	0.00661	0.00352	0.00468	0.00661	0.00352	0.00458
Distribution	ln (-5.02, 0.173)	ln (-5.65, 0.177)	ln (-5.36, 0.199)	ln (-5.02, 0.173)	ln (-5.65, 0.177)	ln (-5.39, 0.204)
Monthly mortality rate for PLHIV on ART (CD4<200), Female Hispanic HET						
PE	0.00412	0.00219	0.00292	0.00412	0.00219	0.00289
Distribution	ln (-5.49, 0.15)	ln (-6.12, 0.159)	ln (-5.84, 0.177)	ln (-5.49, 0.15)	ln (-6.12, 0.159)	ln (-5.85, 0.196)
IMMEDIATE ART ENGAGEMENT						
Probability of direct ART engagement following diagnosis (CD4>500), PWID						
PE	0.226	0.226	0.226	0.226	0.226	0.226
Distribution	Beta (12, 41)	Beta (12, 41)	Beta (12, 41)	Beta (12, 41)	Beta (12, 41)	Beta (12, 41)
Probability of direct ART engagement following diagnosis (CD4>500), MWID						
PE	0.200	0.200	0.200	0.200	0.200	0.200
Distribution	Beta (8, 32)	Beta (8, 32)	Beta (8, 32)	Beta (8, 32)	Beta (8, 32)	Beta (8, 32)
Probability of direct ART engagement following diagnosis (CD4>500), MSM						
PE	0.146	0.349	0.251	0.146	0.349	0.349
Distribution	Beta (66, 387)	Beta (176, 329)	Beta (44, 131)	Beta (66, 387)	Beta (176, 329)	Beta (176, 329)
Probability of direct ART engagement following diagnosis (CD4>500), Male, HET						
PE	0.0893	0.421	0.105	0.0893	0.421	0.421
Distribution	Beta (10, 102)	Beta (40, 55)	Beta (2, 17)	Beta (10, 102)	Beta (40, 55)	Beta (40, 55)
Probability of direct ART engagement following diagnosis (CD4>500), Female, HET						
PE	0.165	0.281	0.269	0.165	0.281	0.281
Distribution	Beta (36, 182)	Beta (27, 69)	Beta (7, 19)	Beta (36, 182)	Beta (27, 69)	Beta (27, 69)
Probability of direct ART engagement following diagnosis (CD4: 200-499), PWID						
PE	0.294	0.294	0.294	0.294	0.294	0.294
Distribution	Beta (15, 36)	Beta (15, 36)	Beta (15, 36)	Beta (15, 36)	Beta (15, 36)	Beta (15, 36)
Probability of direct ART engagement following diagnosis (CD4: 200-499), MWID						
PE	0.333	0.333	0.333	0.333	0.333	0.333
Distribution	Beta (10, 20)	Beta (10, 20)	Beta (10, 20)	Beta (10, 20)	Beta (10, 20)	Beta (10, 20)
Probability of direct ART engagement following diagnosis (CD4: 200-499), MSM						
PE	0.265	0.435	0.321	0.265	0.435	0.435
Distribution	Beta (198, 550)	Beta (237, 308)	Beta (69, 146)	Beta (198, 550)	Beta (237, 308)	Beta (237, 308)
Probability of direct ART engagement following diagnosis (CD4: 200-499), Male, HET						
PE	0.349	0.297	0.246	0.349	0.297	0.297
Distribution	Beta (84, 157)	Beta (35, 83)	Beta (15, 46)	Beta (84, 157)	Beta (35, 83)	Beta (35, 83)
Probability of direct ART engagement following diagnosis (CD4: 200-499), Female, HET						
PE	0.295	0.424	0.425	0.295	0.424	0.424

Distribution	Beta (80, 191)	Beta (39, 53)	Beta (17, 23)	Beta (80, 191)	Beta (39, 53)	Beta (39, 53)
Probability of direct ART engagement following diagnosis (CD4<200), PWID						
PE	0.515	0.515	0.515	0.515	0.515	0.515
Distribution	Beta (34, 32)	Beta (34, 32)	Beta (34, 32)	Beta (34, 32)	Beta (34, 32)	Beta (34, 32)
Probability of direct ART engagement following diagnosis (CD4<200), MWID						
PE	0.545	0.545	0.545	0.545	0.545	0.545
Distribution	Beta (12, 10)	Beta (12, 10)	Beta (12, 10)	Beta (12, 10)	Beta (12, 10)	Beta (12, 10)
Probability of direct ART engagement following diagnosis (CD4<200), MSM						
PE	0.526	0.596	0.644	0.526	0.596	0.596
Distribution	Beta (242, 218)	Beta (115, 78)	Beta (87, 48)	Beta (242, 218)	Beta (115, 78)	Beta (115, 78)
Probability of direct ART engagement following diagnosis (CD4<200), Male, HET						
PE	0.460	0.577	0.701	0.460	0.577	0.577
Distribution	Beta (159, 187)	Beta (45, 33)	Beta (47, 20)	Beta (159, 187)	Beta (45, 33)	Beta (45, 33)
Probability of direct ART engagement following diagnosis (CD4<200), Female, HET						
PE	0.457	0.475	0.486	0.457	0.475	0.475
Distribution	Beta (100, 119)	Beta (28, 31)	Beta (18, 19)	Beta (100, 119)	Beta (28, 31)	Beta (28, 31)
ART ENGAGEMENT: INITIATION						
Monthly ART initiation rate (CD4>500), PWID						
PE	0.0292	0.0292	0.0292	0.0292	0.0292	0.0292
Distribution	Poisson (23) / 789.01	Poisson (23) / 789.01	Poisson (23) / 789.01	Poisson (23) / 789.01	Poisson (23) / 789.01	Poisson (23) / 789.01
Monthly ART initiation rate (CD4>500), MSM						
PE	0.0556	0.0662	0.0853	0.0556	0.0662	0.0662
Distribution	Poisson (280) / 5039.22	Poisson (259) / 3914.6	Poisson (107) / 1254.01	Poisson (280) / 5039.22	Poisson (259) / 3914.6	Poisson (259) / 3914.6
Monthly ART initiation rate (CD4>500), MWID						
PE	0.0690	0.0690	0.0690	0.0690	0.0690	0.0690
Distribution	Poisson (23) / 333.49	Poisson (23) / 333.49	Poisson (23) / 333.49	Poisson (23) / 333.49	Poisson (23) / 333.49	Poisson (23) / 333.49
Monthly ART initiation rate (CD4>500), Male, HET						
PE	0.0425	0.0782	0.0800	0.0425	0.0782	0.0782
Distribution	Poisson (65) / 1529.89	Poisson (38) / 486.15	Poisson (14) / 174.99	Poisson (65) / 1529.89	Poisson (38) / 486.15	Poisson (38) / 486.15
Monthly ART initiation rate (CD4>500), Female, HET						
PE	0.0398	0.0551	0.0866	0.0398	0.0551	0.0551
Distribution	Poisson (120) / 3011.48	Poisson (46) / 834.31	Poisson (17) / 196.37	Poisson (120) / 3011.48	Poisson (46) / 834.31	Poisson (46) / 834.31
Monthly ART initiation rate (CD4: 200-499), PWID						
PE	0.108	0.108	0.108	0.108	0.108	0.108
Distribution	Poisson (30) / 277.24	Poisson (30) / 277.24	Poisson (30) / 277.24	Poisson (30) / 277.24	Poisson (30) / 277.24	Poisson (30) / 277.24
Monthly ART initiation rate (CD4: 200-499), MSM						
PE	0.145	0.149	0.184	0.145	0.149	0.149
Distribution	Poisson (490) / 3375.28	Poisson (271) / 1823.46	Poisson (131) / 710.62	Poisson (490) / 3375.28	Poisson (271) / 1823.46	Poisson (271) / 1823.46
Monthly ART initiation rate (CD4: 200-499), MWID						
PE	0.0573	0.0573	0.0573	0.0573	0.0573	0.0573
Distribution	Poisson (14) / 244.44	Poisson (14) / 244.44	Poisson (14) / 244.44	Poisson (14) / 244.44	Poisson (14) / 244.44	Poisson (14) / 244.44

Monthly ART initiation rate (CD4: 200-499), Male, HET						
PE	0.118	0.189	0.134	0.118	0.189	0.189
Distribution	Poisson (134) / 1135.85	Poisson (74) / 390.83	Poisson (42) / 312.92	Poisson (134) / 1135.85	Poisson (74) / 390.83	Poisson (74) / 390.83
Monthly ART initiation rate (CD4: 200-499), Female, HET						
PE	0.142	0.125	0.149	0.142	0.125	0.125
Distribution	Poisson (175) / 1231.67	Poisson (46) / 368.53	Poisson (21) / 141.34	Poisson (175) / 1231.67	Poisson (46) / 368.53	Poisson (46) / 368.53
Monthly ART initiation rate (CD4<200), PWID						
PE	0.314	0.314	0.314	0.314	0.314	0.314
Distribution	Poisson (31) / 98.84	Poisson (31) / 98.84	Poisson (31) / 98.84	Poisson (31) / 98.84	Poisson (31) / 98.84	Poisson (31) / 98.84
Monthly ART initiation rate (CD4<200), MSM						
PE	0.282	0.257	0.190	0.282	0.257	0.257
Distribution	Poisson (206) / 730.76	Poisson (74) / 287.61	Poisson (43) / 226.7	Poisson (206) / 730.76	Poisson (74) / 287.61	Poisson (74) / 287.61
Monthly ART initiation rate (CD4<200), MWID						
PE	0.240	0.240	0.240	0.240	0.240	0.240
Distribution	Poisson (9) / 37.45	Poisson (9) / 37.45	Poisson (9) / 37.45	Poisson (9) / 37.45	Poisson (9) / 37.45	Poisson (9) / 37.45
Monthly ART initiation rate (CD4<200), Male, HET						
PE	0.262	0.230	0.182	0.262	0.230	0.230
Distribution	Poisson (180) / 686.23	Poisson (28) / 121.9	Poisson (18) / 98.92	Poisson (180) / 686.23	Poisson (28) / 121.9	Poisson (28) / 121.9
Monthly ART initiation rate (CD4<200), Female, HET						
PE	0.296	0.113	0.294	0.296	0.113	0.113
Distribution	Poisson (112) / 378.97	Poisson (24) / 212.4	Poisson (19) / 64.72	Poisson (112) / 378.97	Poisson (24) / 212.4	Poisson (24) / 212.4
ART ENGAGEMENT: RETENTION						
Monthly ART dropout rate (CD4>500), Male White PWID						
PE	0.0191	0.00725	0.00970	0.0191	0.00725	0.00427
Distribution	ln (-3.96, 0.0689)	ln (-4.93, 0.098)	ln (-4.64, 0.1369)	ln (-3.96, 0.0689)	ln (-4.93, 0.098)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4>500), Male White MSM						
PE	0.0132	0.00398	0.00920	0.0132	0.00398	0.00340
Distribution	ln (-4.33, 0.0428)	ln (-5.53, 0.0551)	ln (-4.69, 0.0503)	ln (-4.33, 0.0428)	ln (-5.53, 0.0551)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Male White MWID						
PE	0.0189	0.00442	0.0114	0.0189	0.00442	0.00340
Distribution	ln (-3.97, 0.0644)	ln (-5.42, 0.0995)	ln (-4.48, 0.1018)	ln (-3.97, 0.0644)	ln (-5.42, 0.0995)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Male White HET						
PE	0.0133	0.00654	0.00784	0.0133	0.00654	0.00516
Distribution	ln (-4.32, 0.0587)	ln (-5.03, 0.0905)	ln (-4.85, 0.1122)	ln (-4.32, 0.0587)	ln (-5.03, 0.0905)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4>500), Male Black PWID						
PE	0.0182	0.00725	0.00919	0.0182	0.00725	0.00427
Distribution	ln (-4, 0.0607)	ln (-4.93, 0.0901)	ln (-4.69, 0.1454)	ln (-4, 0.0607)	ln (-4.93, 0.0901)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4>500), Male Black MSM						
PE	0.0125	0.00398	0.00871	0.0125	0.00398	0.00703
Distribution	ln (-4.38, 0.0404)	ln (-5.53, 0.061)	ln (-4.74, 0.0942)	ln (-4.38, 0.0404)	ln (-5.53, 0.061)	Unif (0.0056, 0.0084)
Monthly ART dropout rate (CD4>500), Male Black MWID						

PE	0.0180	0.00442	0.0108	0.0180	0.00442	0.00571
Distribution	ln (-4.02, 0.0622)	ln (-5.42, 0.1008)	ln (-4.53, 0.1372)	ln (-4.02, 0.0622)	ln (-5.42, 0.1008)	Unif (0.0046, 0.0069)
Monthly ART dropout rate (CD4>500), Male Black HET						
PE	0.0127	0.00654	0.00743	0.0127	0.00654	0.00516
Distribution	ln (-4.37, 0.0453)	ln (-5.03, 0.0689)	ln (-4.9, 0.1276)	ln (-4.37, 0.0453)	ln (-5.03, 0.0689)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4>500), Male Hispanic PWID						
PE	0.0109	0.00744	0.00595	0.0109	0.00744	0.00475
Distribution	ln (-4.52, 0.0802)	ln (-4.9, 0.0928)	ln (-5.12, 0.1507)	ln (-4.52, 0.0802)	ln (-4.9, 0.0928)	Unif (0.0038, 0.0057)
Monthly ART dropout rate (CD4>500), Male Hispanic MSM						
PE	0.0075	0.00408	0.00564	0.0075	0.00408	0.00340
Distribution	ln (-4.9, 0.0625)	ln (-5.5, 0.0624)	ln (-5.18, 0.0912)	ln (-4.9, 0.0625)	ln (-5.5, 0.0624)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Male Hispanic MWID						
PE	0.0107	0.00453	0.00698	0.0107	0.00453	0.00340
Distribution	ln (-4.53, 0.0832)	ln (-5.4, 0.1066)	ln (-4.96, 0.1318)	ln (-4.53, 0.0832)	ln (-5.4, 0.1066)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Male Hispanic HET						
PE	0.0076	0.00670	0.00481	0.0076	0.00670	0.00516
Distribution	ln (-4.89, 0.0696)	ln (-5.01, 0.0727)	ln (-5.34, 0.1294)	ln (-4.89, 0.0696)	ln (-5.01, 0.0727)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4>500), Female White PWID						
PE	0.0191	0.00725	0.00970	0.0191	0.00725	0.00427
Distribution	ln (-3.96, 0.0695)	ln (-4.93, 0.0993)	ln (-4.64, 0.1272)	ln (-3.96, 0.0695)	ln (-4.93, 0.0993)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4>500), Female White HET						
PE	0.0133	0.00654	0.00784	0.0133	0.00654	0.00340
Distribution	ln (-4.32, 0.0601)	ln (-5.03, 0.0889)	ln (-4.85, 0.1169)	ln (-4.32, 0.0601)	ln (-5.03, 0.0889)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Female Black PWID						
PE	0.0182	0.00725	0.00919	0.0182	0.00725	0.00427
Distribution	ln (-4, 0.055)	ln (-4.93, 0.0924)	ln (-4.69, 0.1437)	ln (-4, 0.055)	ln (-4.93, 0.0924)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4>500), Female Black HET						
PE	0.0127	0.00654	0.00743	0.0127	0.00654	0.00340
Distribution	ln (-4.37, 0.0444)	ln (-5.03, 0.0713)	ln (-4.9, 0.1333)	ln (-4.37, 0.0444)	ln (-5.03, 0.0713)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4>500), Female Hispanic PWID						
PE	0.0109	0.00744	0.00595	0.0109	0.00744	0.00427
Distribution	ln (-4.52, 0.0789)	ln (-4.9, 0.0933)	ln (-5.12, 0.1518)	ln (-4.52, 0.0789)	ln (-4.9, 0.0933)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4>500), Female Hispanic HET						
PE	0.0076	0.00670	0.00481	0.0076	0.00670	0.00340
Distribution	ln (-4.89, 0.0662)	ln (-5.01, 0.075)	ln (-5.34, 0.1309)	ln (-4.89, 0.0662)	ln (-5.01, 0.075)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Male White PWID						
PE	0.0262	0.00925	0.0128	0.0262	0.00925	0.00427
Distribution	ln (-3.64, 0.0669)	ln (-4.68, 0.1123)	ln (-4.36, 0.1218)	ln (-3.64, 0.0669)	ln (-4.68, 0.1123)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4: 200-499), Male White MSM						
PE	0.0141	0.00661	0.0110	0.0141	0.00661	0.00340
Distribution	ln (-4.26, 0.0449)	ln (-5.02, 0.063)	ln (-4.51, 0.0601)	ln (-4.26, 0.0449)	ln (-5.02, 0.063)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Male White MWID						

PE	0.0235	0.00703	0.0134	0.0235	0.00703	0.00340
Distribution	ln (-3.75, 0.0691)	ln (-4.96, 0.1073)	ln (-4.31, 0.1129)	ln (-3.75, 0.0691)	ln (-4.96, 0.1073)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Male White HET						
PE	0.0157	0.00871	0.0105	0.0157	0.00871	0.00516
Distribution	ln (-4.16, 0.0583)	ln (-4.74, 0.0937)	ln (-4.56, 0.1137)	ln (-4.16, 0.0583)	ln (-4.74, 0.0937)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4: 200-499), Male Black PWID						
PE	0.0296	0.00939	0.0143	0.0296	0.00939	0.00427
Distribution	ln (-3.52, 0.054)	ln (-4.67, 0.0893)	ln (-4.25, 0.1435)	ln (-3.52, 0.054)	ln (-4.67, 0.0893)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4: 200-499), Male Black MSM						
PE	0.0159	0.00671	0.0123	0.0159	0.00671	0.00703
Distribution	ln (-4.14, 0.0407)	ln (-5, 0.0679)	ln (-4.4, 0.0986)	ln (-4.14, 0.0407)	ln (-5, 0.0679)	Unif (0.0056, 0.0084)
Monthly ART dropout rate (CD4: 200-499), Male Black MWID						
PE	0.0266	0.00713	0.0150	0.0266	0.00713	0.00571
Distribution	ln (-3.63, 0.0605)	ln (-4.94, 0.1093)	ln (-4.2, 0.1381)	ln (-3.63, 0.0605)	ln (-4.94, 0.1093)	Unif (0.0046, 0.0069)
Monthly ART dropout rate (CD4: 200-499), Male Black HET						
PE	0.0177	0.00884	0.0117	0.0177	0.00884	0.00516
Distribution	ln (-4.03, 0.0401)	ln (-4.73, 0.0707)	ln (-4.45, 0.1183)	ln (-4.03, 0.0401)	ln (-4.73, 0.0707)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4: 200-499), Male Hispanic PWID						
PE	0.0208	0.01032	0.0107	0.0208	0.01032	0.00475
Distribution	ln (-3.87, 0.0685)	ln (-4.57, 0.0891)	ln (-4.54, 0.1428)	ln (-3.87, 0.0685)	ln (-4.57, 0.0891)	Unif (0.0038, 0.0057)
Monthly ART dropout rate (CD4: 200-499), Male Hispanic MSM						
PE	0.0111	0.00737	0.0092	0.0111	0.00737	0.00340
Distribution	ln (-4.5, 0.0544)	ln (-4.91, 0.0678)	ln (-4.69, 0.0816)	ln (-4.5, 0.0544)	ln (-4.91, 0.0678)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Male Hispanic MWID						
PE	0.0187	0.00784	0.0112	0.0187	0.00784	0.00340
Distribution	ln (-3.98, 0.0759)	ln (-4.85, 0.1083)	ln (-4.49, 0.1306)	ln (-3.98, 0.0759)	ln (-4.85, 0.1083)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Male Hispanic HET						
PE	0.0124	0.00971	0.00875	0.0124	0.00971	0.00516
Distribution	ln (-4.39, 0.0587)	ln (-4.63, 0.0718)	ln (-4.74, 0.1205)	ln (-4.39, 0.0587)	ln (-4.63, 0.0718)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4: 200-499), Female White PWID						
PE	0.0262	0.00925	0.0128	0.0262	0.00925	0.00427
Distribution	ln (-3.64, 0.0704)	ln (-4.68, 0.1067)	ln (-4.36, 0.1317)	ln (-3.64, 0.0704)	ln (-4.68, 0.1067)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4: 200-499), Female White HET						
PE	0.0157	0.00871	0.0105	0.0157	0.00871	0.00340
Distribution	ln (-4.16, 0.0577)	ln (-4.74, 0.0937)	ln (-4.56, 0.1042)	ln (-4.16, 0.0577)	ln (-4.74, 0.0937)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Female Black PWID						
PE	0.0296	0.00939	0.0143	0.0296	0.00939	0.00427
Distribution	ln (-3.52, 0.0501)	ln (-4.67, 0.0894)	ln (-4.25, 0.1317)	ln (-3.52, 0.0501)	ln (-4.67, 0.0894)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4: 200-499), Female Black HET						
PE	0.0177	0.00884	0.0117	0.0177	0.00884	0.00340
Distribution	ln (-4.03, 0.0404)	ln (-4.73, 0.072)	ln (-4.45, 0.1165)	ln (-4.03, 0.0404)	ln (-4.73, 0.072)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4: 200-499), Female Hispanic PWID						

PE	0.0208	0.0103	0.0107	0.0208	0.0103	0.00427
Distribution	ln (-3.87, 0.0698)	ln (-4.57, 0.0885)	ln (-4.54, 0.1485)	ln (-3.87, 0.0698)	ln (-4.57, 0.0885)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4: 200-499), Female Hispanic HET						
PE	0.0124	0.0097	0.00875	0.0124	0.0097	0.00340
Distribution	ln (-4.39, 0.0606)	ln (-4.63, 0.0712)	ln (-4.74, 0.1153)	ln (-4.39, 0.0606)	ln (-4.63, 0.0712)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Male White PWID						
PE	0.0314	0.0129	0.0241	0.0314	0.0129	0.00427
Distribution	ln (-3.46, 0.0993)	ln (-4.35, 0.1465)	ln (-3.73, 0.1711)	ln (-3.46, 0.0993)	ln (-4.35, 0.1465)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4<200), Male White MSM						
PE	0.0188	0.0113	0.0141	0.0188	0.0113	0.00340
Distribution	ln (-3.97, 0.0799)	ln (-4.49, 0.1252)	ln (-4.26, 0.1152)	ln (-3.97, 0.0799)	ln (-4.49, 0.1252)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Male White MWID						
PE	0.0281	0.0137	0.0208	0.0281	0.0137	0.00340
Distribution	ln (-3.57, 0.0987)	ln (-4.29, 0.1621)	ln (-3.88, 0.1642)	ln (-3.57, 0.0987)	ln (-4.29, 0.1621)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Male White HET						
PE	0.0210	0.0106	0.0164	0.0210	0.0106	0.00516
Distribution	ln (-3.86, 0.0894)	ln (-4.55, 0.1473)	ln (-4.11, 0.1571)	ln (-3.86, 0.0894)	ln (-4.55, 0.1473)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4<200), Male Black PWID						
PE	0.0405	0.0156	0.0259	0.0405	0.0156	0.00427
Distribution	ln (-3.21, 0.0774)	ln (-4.16, 0.1202)	ln (-3.65, 0.1763)	ln (-3.21, 0.0774)	ln (-4.16, 0.1202)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4<200), Male Black MSM						
PE	0.0243	0.0136	0.0152	0.0243	0.0136	0.00703
Distribution	ln (-3.72, 0.0645)	ln (-4.3, 0.1014)	ln (-4.18, 0.1406)	ln (-3.72, 0.0645)	ln (-4.3, 0.1014)	Unif (0.0056, 0.0084)
Monthly ART dropout rate (CD4<200), Male Black MWID						
PE	0.0363	0.0166	0.0224	0.0363	0.0166	0.00571
Distribution	ln (-3.32, 0.0958)	ln (-4.1, 0.1409)	ln (-3.8, 0.1828)	ln (-3.32, 0.0958)	ln (-4.1, 0.1409)	Unif (0.0046, 0.0069)
Monthly ART dropout rate (CD4<200), Male Black HET						
PE	0.0272	0.0128	0.0177	0.0272	0.0128	0.00516
Distribution	ln (-3.61, 0.0606)	ln (-4.36, 0.1077)	ln (-4.04, 0.1541)	ln (-3.61, 0.0606)	ln (-4.36, 0.1077)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4<200), Male Hispanic PWID						
PE	0.0240	0.0170	0.0176	0.0240	0.0170	0.00475
Distribution	ln (-3.73, 0.1086)	ln (-4.07, 0.1252)	ln (-4.04, 0.2068)	ln (-3.73, 0.1086)	ln (-4.07, 0.1252)	Unif (0.0038, 0.0057)
Monthly ART dropout rate (CD4<200), Male Hispanic MSM						
PE	0.0144	0.0148	0.0103	0.0144	0.0148	0.00340
Distribution	ln (-4.24, 0.0903)	ln (-4.21, 0.1143)	ln (-4.57, 0.1468)	ln (-4.24, 0.0903)	ln (-4.21, 0.1143)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Male Hispanic MWID						
PE	0.0215	0.0181	0.0152	0.0215	0.0181	0.00340
Distribution	ln (-3.84, 0.1193)	ln (-4.01, 0.1516)	ln (-4.19, 0.2084)	ln (-3.84, 0.1193)	ln (-4.01, 0.1516)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Male Hispanic HET						
PE	0.0161	0.0139	0.0120	0.0161	0.0139	0.00516
Distribution	ln (-4.13, 0.0931)	ln (-4.27, 0.1027)	ln (-4.43, 0.1747)	ln (-4.13, 0.0931)	ln (-4.27, 0.1027)	Unif (0.0041, 0.0062)
Monthly ART dropout rate (CD4<200), Female White PWID						

PE	0.0314	0.0129	0.0241	0.0314	0.0129	0.00427
Distribution	ln (-3.46, 0.0987)	ln (-4.35, 0.149)	ln (-3.73, 0.177)	ln (-3.46, 0.0987)	ln (-4.35, 0.149)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4<200), Female White HET						
PE	0.0210	0.0106	0.0164	0.0210	0.0106	0.00340
Distribution	ln (-3.86, 0.0895)	ln (-4.55, 0.1348)	ln (-4.11, 0.1504)	ln (-3.86, 0.0895)	ln (-4.55, 0.1348)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Female Black PWID						
PE	0.0405	0.0156	0.0259	0.0405	0.0156	0.00427
Distribution	ln (-3.21, 0.0761)	ln (-4.16, 0.1174)	ln (-3.65, 0.1839)	ln (-3.21, 0.0761)	ln (-4.16, 0.1174)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4<200), Female Black HET						
PE	0.0272	0.0128	0.0177	0.0272	0.0128	0.00340
Distribution	ln (-3.61, 0.0581)	ln (-4.36, 0.0961)	ln (-4.04, 0.1538)	ln (-3.61, 0.0581)	ln (-4.36, 0.0961)	Unif (0.0027, 0.0041)
Monthly ART dropout rate (CD4<200), Female Hispanic PWID						
PE	0.0240	0.0170	0.0176	0.0240	0.0170	0.00427
Distribution	ln (-3.73, 0.1041)	ln (-4.07, 0.1338)	ln (-4.04, 0.2026)	ln (-3.73, 0.1041)	ln (-4.07, 0.1338)	Unif (0.0034, 0.0051)
Monthly ART dropout rate (CD4<200), Female Hispanic HET						
PE	0.0161	0.0139	0.0120	0.0161	0.0139	0.00340
Distribution	ln (-4.13, 0.0953)	ln (-4.27, 0.1026)	ln (-4.43, 0.1754)	ln (-4.13, 0.0953)	ln (-4.27, 0.1026)	Unif (0.0027, 0.0041)
NUMBER OF SEXUAL PARTNERS						
Monthly number of homosexual partners: White, low-risk MSM						
PE	0.174	0.174	0.174	0.174	0.174	0.174
Distribution	Gamma (133, 0.00131)	Gamma (133, 0.00131)	Gamma (133, 0.00131)	Gamma (133, 0.00131)	Gamma (133, 0.00131)	Gamma (133, 0.00131)
Monthly number of homosexual partners: Black low-risk MSM						
PE	0.213	0.213	0.213	0.213	0.213	0.213
Distribution	Gamma (26.5, 0.00806)	Gamma (26.5, 0.00806)	Gamma (26.5, 0.00806)	Gamma (26.5, 0.00806)	Gamma (26.5, 0.00806)	Gamma (26.5, 0.00806)
Monthly number of homosexual partners: Hispanic low-risk MSM						
PE	0.158	0.158	0.158	0.158	0.158	0.158
Distribution	Gamma (39.2, 0.00404)	Gamma (39.2, 0.00404)	Gamma (39.2, 0.00404)	Gamma (39.2, 0.00404)	Gamma (39.2, 0.00404)	Gamma (39.2, 0.00404)
Monthly number of homosexual partners: White, high-risk MSM						
PE	0.802	0.904	0.857	1.30	0.907	0.669
Distribution	Pert (3.23, 4.52)	Pert (2.55, 4.67)	Pert (3.35, 4.47)	Pert (3.32, 4.48)	Pert (3.23, 4.52)	Pert (3.14, 4.55)
Monthly number of homosexual partners: Black, high-risk MSM						
PE	0.457	0.665	0.633	1.06	0.603	0.558
Distribution	Pert (1.51, 4.37)	Pert (3.48, 4.40)	Pert (2.52, 4.67)	Pert (3.27, 4.50)	Pert (2.38, 4.67)	Pert (1.91, 4.57)
Monthly number of homosexual partners: Hispanic, high-risk MSM						
PE	0.72	0.932	0.725	1.04	0.817	0.757
Distribution	Pert (3.06, 4.58)	Pert (3.11, 4.57)	Pert (3.50, 4.38)	Pert (3.19, 4.54)	Pert (3.51, 4.38)	Pert (2.98, 4.61)
Monthly number of heterosexual partners: Male, White, low-risk MSM and MWID						
PE	0.0219	0.0219	0.0219	0.0219	0.0219	0.0219
Distribution	Gamma (31, 0.00071)	Gamma (31, 0.00071)	Gamma (31, 0.00071)	Gamma (31, 0.00071)	Gamma (31, 0.00071)	Gamma (31, 0.00071)
Monthly number of heterosexual partners: Male, White, low-risk HET						
PE	0.0883	0.0883	0.0800	0.0883	0.0883	0.0800

Distribution	Gamma (1248, 0.00007)	Gamma (1248, 0.00007)	Gamma (490, 0.00016)	Gamma (1248, 0.00007)	Gamma (1248, 0.00007)	Gamma (490, 0.00016)
Monthly number of heterosexual partners: Male, Black, low-risk MSM and MWID						
PE	0.0220	0.0220	0.0220	0.0220	0.0220	0.0220
Distribution	Gamma (13, 0.00176)	Gamma (13, 0.00176)	Gamma (13, 0.00176)	Gamma (13, 0.00176)	Gamma (13, 0.00176)	Gamma (13, 0.00176)
Monthly number of heterosexual partners: Male, Black, low-risk HET						
PE	0.110	0.110	0.105	0.110	0.108	0.105
Distribution	Gamma (697, 0.00016)	Gamma (697, 0.00016)	Gamma (68, 0.00155)	Gamma (697, 0.00016)	Gamma (152, 0.00071)	Gamma (68, 0.00155)
Monthly number of heterosexual partners: Male, Hispanic, low-risk MSM and MWID						
PE	0.0181	0.0181	0.0181	0.0181	0.0181	0.0181
Distribution	Gamma (6, 0.00282)	Gamma (6, 0.00282)	Gamma (6, 0.00282)	Gamma (6, 0.00282)	Gamma (6, 0.00282)	Gamma (6, 0.00282)
Monthly number of heterosexual partners: Male, Hispanic, low-risk HET						
PE	0.0842	0.0842	0.0867	0.0842	0.0908	0.0867
Distribution	Gamma (638, 0.00013)	Gamma (638, 0.00013)	Gamma (513, 0.00017)	Gamma (638, 0.00013)	Gamma (317, 0.00029)	Gamma (513, 0.00017)
Monthly number of heterosexual partners: Female, White, low-risk HET						
PE	0.0825	0.0825	0.0825	0.0825	0.0925	0.0825
Distribution	Gamma (1089, 0.00008)	Gamma (1089, 0.00008)	Gamma (1046, 0.00008)	Gamma (1089, 0.00008)	Gamma (740, 0.00013)	Gamma (1046, 0.00008)
Monthly number of heterosexual partners: Female, Black, low-risk HET						
PE	0.0875	0.0875	0.0925	0.0875	0.0992	0.0925
Distribution	Gamma (689, 0.00013)	Gamma (689, 0.00013)	Gamma (174, 0.00053)	Gamma (689, 0.00013)	Gamma (44, 0.00223)	Gamma (174, 0.00053)
Monthly number of heterosexual partners: Female, Hispanic, low-risk HET						
PE	0.0850	0.0850	0.0808	0.0850	0.0858	0.0808
Distribution	Gamma (1156, 0.00007)	Gamma (1156, 0.00007)	Gamma (643, 0.00013)	Gamma (1156, 0.00007)	Gamma (261, 0.00033)	Gamma (643, 0.00013)
Monthly number of heterosexual partners: Male, White, high-risk MSM and MWID						
PE	0.0149	0.0191	0.0125	0.0264	0.0212	0.0419
Distribution	Pert (3.42, 4.43)	Pert (3.03, 4.59)	Pert (2.97, 4.61)	Pert (2.99, 4.6)	Pert (2.84, 4.64)	Pert (4.37, 3.53)
Monthly number of heterosexual partners: Male, White, high-risk HET						
PE	0.670	0.6700	0.623	0.6700	0.591	0.6225
Distribution	Gamma (121, 0.00552)	Gamma (121, 0.00552)	Gamma (253, 0.00246)	Gamma (121, 0.00552)	Gamma (66, 0.009)	Gamma (253, 0.00246)
Monthly number of heterosexual partners: Male, Black, high-risk MSM and MWID						
PE	0.0795	0.0631	0.0321	0.0595	0.0285	0.0357
Distribution	Pert (3.88, 4.11)	Pert (3.8, 4.18)	Pert (2.23, 4.65)	Pert (3.64, 4.3)	Pert (3.4, 4.44)	Pert (2.72, 4.66)
Monthly number of heterosexual partners: Male, Black, high-risk HET						
PE	0.633	0.633	0.814	0.633	0.990	0.814
Distribution	Gamma (327, 0.00193)	Gamma (327, 0.00193)	Gamma (24, 0.03447)	Gamma (327, 0.00193)	Gamma (43, 0.02282)	Gamma (24, 0.03447)
Monthly number of heterosexual partners: Male, Hispanic, high-risk MSM and MWID						
PE	0.0371	0.0535	0.0263	0.0719	0.0263	0.0471
Distribution	Pert (1.71, 4.49)	Pert (3.04, 4.59)	Pert (1.85, 4.55)	Pert (3.43, 4.43)	Pert (2.59, 4.67)	Pert (3.62, 4.31)
Monthly number of heterosexual partners: Male, Hispanic, high-risk HET						
PE	0.579	0.579	0.722	0.579	0.703	0.722
Distribution	Gamma (302, 0.00192)	Gamma (302, 0.00192)	Gamma (541, 0.00133)	Gamma (302, 0.00192)	Gamma (55, 0.01274)	Gamma (541, 0.00133)
Monthly number of heterosexual partners: Female, White, high-risk HET						

PE	0.657	0.657	0.666	0.657	0.581	0.666
Distribution	Gamma (213, 0.00308)	Gamma (213, 0.00308)	Gamma (460, 0.00145)	Gamma (213, 0.00308)	Gamma (40, 0.01439)	Gamma (460, 0.00145)
Monthly number of heterosexual partners: Female, Black, high-risk HET						
PE	0.545	0.545	0.533	0.545	0.672	0.533
Distribution	Gamma (85, 0.00642)	Gamma (85, 0.00642)	Gamma (201, 0.00265)	Gamma (85, 0.00642)	Gamma (305, 0.0022)	Gamma (201, 0.00265)
Monthly number of heterosexual partners: Female, Hispanic, high-risk HET						
PE	0.474	0.474	0.626	0.474	0.608	0.626
Distribution	Gamma (193, 0.00246)	Gamma (193, 0.00246)	Gamma (76, 0.00825)	Gamma (193, 0.00246)	Gamma (167, 0.00363)	Gamma (76, 0.00825)
Monthly number of heterosexual partner multiplier: PWID to HET						
PE	0.400	0.400	0.400	0.400	0.400	0.400
Distribution	Unif (0.1, 2)	Unif (0.1, 2)	Unif (0.1, 2)	Unif (0.1, 2)	Unif (0.1, 2)	Unif (0.1, 2)
TRANSMISSION PROBABILITY PER HETEROSEXUAL PARTNERSHIP						
Transmission probability (CD4>500): Female to Male						
PE	0.0150	0.0150	0.0150	0.0150	0.0150	0.0150
Distribution	Pert (1.638, 4.445)	Pert (1.638, 4.445)	Pert (1.638, 4.445)	Pert (1.638, 4.445)	Pert (1.638, 4.445)	Pert (1.638, 4.445)
Transmission probability (CD4: 200-499): Female to Male						
PE	0.0250	0.0250	0.0250	0.0250	0.0250	0.0250
Distribution	Pert (2.754, 4.654)	Pert (2.754, 4.654)	Pert (2.754, 4.654)	Pert (2.754, 4.654)	Pert (2.754, 4.654)	Pert (2.754, 4.654)
Transmission probability (CD4<200): Female to Male						
PE	0.0500	0.0500	0.0500	0.0500	0.0500	0.0500
Distribution	Pert (2.656, 4.666)	Pert (2.656, 4.666)	Pert (2.656, 4.666)	Pert (2.656, 4.666)	Pert (2.656, 4.666)	Pert (2.656, 4.666)
Transmission probability (CD4>500): Male to Female						
PE	0.0300	0.0300	0.0300	0.0300	0.0300	0.0300
Distribution	Pert (1.968, 4.592)	Pert (1.968, 4.592)	Pert (1.968, 4.592)	Pert (1.968, 4.592)	Pert (1.968, 4.592)	Pert (1.968, 4.592)
Transmission probability (CD4: 200-499): Male to Female						
PE	0.0500	0.0500	0.0500	0.0500	0.0500	0.0500
Distribution	Pert (4.443, 3.397)	Pert (4.443, 3.397)	Pert (4.443, 3.397)	Pert (4.443, 3.397)	Pert (4.443, 3.397)	Pert (4.443, 3.397)
Transmission probability (CD4<200): Male to Female						
PE	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Distribution	Pert (4.27, 3.681)	Pert (4.27, 3.681)	Pert (4.27, 3.681)	Pert (4.27, 3.681)	Pert (4.27, 3.681)	Pert (4.27, 3.681)
TRANSMISSION PROBABILITY PER HOMOSEXUAL PARTNERSHIP						
Transmission probability (CD4>500)						
PE	0.045	0.045	0.045	0.045	0.045	0.045
Distribution	Pert (2.456, 4.673)	Pert (2.456, 4.673)	Pert (2.456, 4.673)	Pert (2.456, 4.673)	Pert (2.456, 4.673)	Pert (2.456, 4.673)
Transmission probability (CD4: 200-499)						
PE	0.065	0.065	0.065	0.065	0.065	0.065
Distribution	Pert (4.168, 3.814)	Pert (4.168, 3.814)	Pert (4.168, 3.814)	Pert (4.168, 3.814)	Pert (4.168, 3.814)	Pert (4.168, 3.814)
Transmission probability (CD4<200)						
PE	0.125	0.125	0.125	0.125	0.125	0.125
Distribution	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)
TRANSMISSION PROBABILITY PER SHARED INJECTION						

Transmission probability (CD4>500)						
PE	0.0030	0.0030	0.0030	0.0030	0.0030	0.0030
Distribution	Pert (2.005, 4.604)	Pert (2.005, 4.604)	Pert (2.005, 4.604)	Pert (2.005, 4.604)	Pert (2.005, 4.604)	Pert (2.005, 4.604)
Transmission probability (CD4: 200-499)						
PE	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040
Distribution	Pert (2.938, 4.617)	Pert (2.938, 4.617)	Pert (2.938, 4.617)	Pert (2.938, 4.617)	Pert (2.938, 4.617)	Pert (2.938, 4.617)
Transmission probability (CD4<200)						
PE	0.0060	0.0060	0.0060	0.0060	0.0060	0.0060
Distribution	Pert (1.4, 4.283)	Pert (1.4, 4.283)	Pert (1.4, 4.283)	Pert (1.4, 4.283)	Pert (1.4, 4.283)	Pert (1.4, 4.283)
HIV TESTING						
Monthly rate of symptom-based case finding (CD4: 200-499)						
PE	0.00874	0.00874	0.00874	0.00874	0.00874	0.00874
Distribution	Pert (3.86, 4.13)	Pert (3.86, 4.13)	Pert (3.86, 4.13)	Pert (3.86, 4.13)	Pert (3.86, 4.13)	Pert (3.86, 4.13)
Monthly rate of symptom-based case finding (CD4<200)						
PE	0.0184	0.0184	0.0184	0.0184	0.0184	0.0184
Distribution	Pert (3.84, 4.15)	Pert (3.84, 4.15)	Pert (3.84, 4.15)	Pert (3.84, 4.15)	Pert (3.84, 4.15)	Pert (3.84, 4.15)
Monthly rate of HIV testing/screening: Male White PWID						
PE	0.0363	0.0984	0.0426	0.0544	0.0764	0.0595
Distribution	Beta (35.7, 65.4)	Beta (45, 20)	Beta (99.1, 148.6)	Beta (109, 118)	Beta (154, 103)	Beta (194, 187)
Monthly rate of HIV testing/screening: Male White low-risk MSM						
PE	0.0112	0.0066	0.0066	0.0061	0.0313	0.0058
Distribution	Beta (18.2, 127)	Beta (13.1, 158.7)	Beta (133.7, 1618.2)	Beta (68.3, 903)	Beta (102, 225)	Beta (93, 1292)
Monthly rate of HIV testing/screening: Male White high-risk MSM						
PE	0.0974	0.0955	0.1108	0.0787	0.1304	0.0860
Distribution	Beta (59.8, 26.9)	Beta (52.3, 24.4)	Beta (131, 47.2)	Beta (119, 75.6)	Beta (129, 34.2)	Beta (103, 57.1)
Monthly rate of HIV testing/screening: Male White MWID						
PE	0.0363	0.0984	0.0426	0.0544	0.0764	0.0595
Distribution	Beta (35.7, 65.4)	Beta (45, 20)	Beta (99.1, 149)	Beta (108.7, 118)	Beta (154, 103)	Beta (194, 187)
Monthly rate of HIV testing/screening: Male White low-risk HET						
PE	0.0112	0.0066	0.0066	0.0061	0.0313	0.0058
Distribution	Beta (18.2, 127)	Beta (13.1, 158.7)	Beta (134, 1618)	Beta (68.3, 903)	Beta (102, 225)	Beta (93, 1292)
Monthly rate of HIV testing/screening: Male White high-risk HET						
PE	0.116	0.0457	0.0143	0.2496	0.0916	0.0160
Distribution	Beta (53.7, 17.9)	Beta (13.2, 18)	Beta (19.3, 103.1)	Beta (348, 18.3)	Beta (125, 62.4)	Beta (24.4, 115)
Monthly rate of HIV testing/screening: Male Black PWID						
PE	0.0642	0.0984	0.0647	0.0892	0.0946	0.0440
Distribution	Beta (17.8, 15.3)	Beta (12.5, 5.5)	Beta (3.9, 3.4)	Beta (13.6, 7.1)	Beta (12.6, 5.99)	Beta (1.8, 2.7)
Monthly rate of HIV testing/screening: Male Black low-risk MSM						
PE	0.0236	0.0206	0.0170	0.0101	0.0336	0.0218
Distribution	Beta (19.1, 58.4)	Beta (27.8, 99)	Beta (22.1, 97.7)	Beta (17.7, 137)	Beta (113, 228)	Beta (12.2, 40.8)
Monthly rate of HIV testing/screening: Male Black high-risk MSM						
PE	0.113	0.0955	0.1651	0.0971	0.101	0.0578

Distribution	Beta (17.1, 5.9)	Beta (14.5, 6.8)	Beta (6.1, 0.97)	Beta (12.1, 5.5)	Beta (11.5, 4.9)	Beta (1.6, 1.6)
Monthly rate of HIV testing/screening: Male Black MWID						
PE	0.0642	0.0984	0.0647	0.0892	0.0946	0.0440
Distribution	Beta (17.8, 15.3)	Beta (12.5, 5.5)	Beta (3.9, 3.4)	Beta (13.6, 7.1)	Beta (12.6, 5.99)	Beta (1.8, 2.7)
Monthly rate of HIV testing/screening: Male Black low-risk HET						
PE	0.0236	0.0206	0.0170	0.0101	0.0336	0.0218
Distribution	Beta (19.1, 58.4)	Beta (27.8, 99)	Beta (22.1, 97.7)	Beta (17.7, 137)	Beta (113, 228)	Beta (12.2, 40.8)
Monthly rate of HIV testing/screening: Male Black high-risk HET						
PE	0.0473	0.0457	0.0338	0.0470	0.0561	0.0207
Distribution	Beta (12.2, 16)	Beta (3.5, 4.8)	Beta (2.2, 4.4)	Beta (9.8, 12.9)	Beta (8.2, 8.5)	Beta (0.84, 2.98)
Monthly rate of HIV testing/screening: Male Hispanic PWID						
PE	0.0578	0.0984	0.0595	0.0719	0.116	0.0501
Distribution	Beta (1.6, 1.6)	Beta (4, 1.8)	Beta (58.1, 55.8)	Beta (5.3, 3.9)	Beta (9.1, 3.03)	Beta (22.1, 26.8)
Monthly rate of HIV testing/screening: Male Hispanic low-risk MSM						
PE	0.0441	0.0150	0.0075	0.0157	0.0366	0.0039
Distribution	Beta (5.3, 7.6)	Beta (4, 20)	Beta (73.4, 785)	Beta (16.5, 79.6)	Beta (123, 223)	Beta (4.98, 104)
Monthly rate of HIV testing/screening: Male Hispanic high-risk MSM						
PE	0.0512	0.0955	0.106	0.0799	0.132	0.0897
Distribution	Beta (1.4, 1.7)	Beta (4.2, 2)	Beta (58.7, 23)	Beta (4.9, 3)	Beta (9.9, 2.5)	Beta (13, 6.7)
Monthly rate of HIV testing/screening: Male Hispanic MWID						
PE	0.0578	0.0984	0.0595	0.0719	0.116	0.0501
Distribution	Beta (1.6, 1.6)	Beta (4, 1.8)	Beta (58.1, 55.8)	Beta (5.3, 3.9)	Beta (9.1, 3.03)	Beta (22.1, 26.8)
Monthly rate of HIV testing/screening: Male Hispanic low-risk HET						
PE	0.0441	0.0150	0.0075	0.0157	0.0366	0.0039
Distribution	Beta (5.3, 7.6)	Beta (4, 20)	Beta (73.4, 785)	Beta (16.5, 79.6)	Beta (123, 223)	Beta (4.98, 104)
Monthly rate of HIV testing/screening: Male Hispanic high-risk HET						
PE	0.0186	0.0457	0.0144	0.0338	0.0547	0.0219
Distribution	Beta (0.8, 3)	Beta (1.3, 1.8)	Beta (8.5, 45.4)	Beta (2.8, 5.6)	Beta (5.9, 6.4)	Beta (5.03, 16.8)
Monthly rate of HIV testing/screening: Female White PWID						
PE	0.0530	0.0911	0.0381	0.104	0.142	0.0485
Distribution	Beta (191, 214)	Beta (60, 30)	Beta (122, 210)	Beta (241, 96)	Beta (184, 41)	Beta (263, 333)
Monthly rate of HIV testing/screening: Female White low-risk HET						
PE	0.0060	0.0071	0.0055	0.0052	0.0257	0.0050
Distribution	Beta (21.7, 289)	Beta (42.6, 479)	Beta (130, 1916)	Beta (91.7, 1434)	Beta (133.9, 370)	Beta (112.3, 1814)
Monthly rate of HIV testing/screening: Female White high-risk HET						
PE	0.0426	0.0627	0.0969	0.0916	0.0916	0.0459
Distribution	Beta (135, 203)	Beta (58, 52)	Beta (189, 86)	Beta (247, 123)	Beta (176, 88)	Beta (160, 217)
Monthly rate of HIV testing/screening: Female Black PWID						
PE	0.0659	0.0911	0.0880	0.1083	0.116	0.0657
Distribution	Beta (53.2, 44.1)	Beta (8.5, 4.3)	Beta (6, 3.2)	Beta (8.1, 3.03)	Beta (20.8, 6.9)	Beta (2.96, 2.5)
Monthly rate of HIV testing/screening: Female Black low-risk HET						
PE	0.0191	0.0278	0.0185	0.0223	0.0356	0.0135

Distribution	Beta (40, 156)	Beta (61.4, 155)	Beta (34.2, 137)	Beta (43.1, 140)	Beta (190, 358)	Beta (6.7, 38)
Monthly rate of HIV testing/screening: Female Black high-risk HET						
PE	0.0446	0.0627	0.0402	0.0486	0.0508	0.0343
Distribution	Beta (34.2, 48.2)	Beta (8.2, 7.3)	Beta (3.2, 5.2)	Beta (6.4, 8.1)	Beta (13.2, 15.8)	Beta (1.5, 2.9)
Monthly rate of HIV testing/screening: Female Hispanic PWID						
PE	0.0034	0.0911	0.0609	0.0706	0.123	0.0372
Distribution	Beta (8, 192.7)	Beta (2.8, 1.4)	Beta (60.1, 55.8)	Beta (23, 17.2)	Beta (16.4, 4.9)	Beta (11.6, 20.6)
Monthly rate of HIV testing/screening: Female Hispanic low-risk HET						
PE	0.0024	0.0161	0.0112	0.0076	0.0407	0.0091
Distribution	Beta (1.2, 40)	Beta (6.5, 30.5)	Beta (154.5, 1078.8)	Beta (18.6, 194)	Beta (225, 357)	Beta (19.4, 168)
Monthly rate of HIV testing/screening: Female Hispanic high-risk HET						
PE	0.0764	0.0627	0.0251	0.0392	0.0603	0.0338
Distribution	Beta (86.7, 57.8)	Beta (1.8, 1.6)	Beta (20.7, 59)	Beta (14.6, 24.3)	Beta (12.2, 11.5)	Beta (6.5, 12.9)
Annual change in HIV testing rate						
PE	0.05	0.05	0.05	0.05	0.05	0.05
Distribution	Unif (0, 0.1)	Unif (0, 0.1)	Unif (0, 0.1)	Unif (0, 0.1)	Unif (0, 0.1)	Unif (0, 0.1)
QUALITY-ADJUSTED LIFE-YEAR WEIGHTS						
QALY weight for infected PLHIV (CD4>500)						
PE	0.91	0.91	0.91	0.91	0.91	0.91
Distribution	Pert (4.44, 3.4)	Pert (4.44, 3.4)	Pert (4.44, 3.4)	Pert (4.44, 3.4)	Pert (4.44, 3.4)	Pert (4.44, 3.4)
QALY weight for infected PLHIV (CD4: 200-499)						
PE	0.79	0.79	0.79	0.79	0.79	0.79
Distribution	Pert (4.17, 1.27)	Pert (4.17, 1.27)	Pert (4.17, 1.27)	Pert (4.17, 1.27)	Pert (4.17, 1.27)	Pert (4.17, 1.27)
QALY weight for infected PLHIV (CD4<200)						
PE	0.72	0.72	0.72	0.72	0.72	0.72
Distribution	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)
QALY weight for diagnosed PLHIV (CD4>500)						
PE	0.865	0.865	0.865	0.865	0.865	0.865
Distribution	Pert (1.61, 4.43)	Pert (1.61, 4.43)	Pert (1.61, 4.43)	Pert (1.61, 4.43)	Pert (1.61, 4.43)	Pert (1.61, 4.43)
QALY weight for diagnosed PLHIV (CD4: 200-499)						
PE	0.72	0.72	0.72	0.72	0.72	0.72
Distribution	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)
QALY weight for diagnosed PLHIV (CD4<200)						
PE	0.72	0.72	0.72	0.72	0.72	0.72
Distribution	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)	Pert (4.59, 1.97)
QALY weight for treated PLHIV (CD4>500)						
PE	0.865	0.865	0.865	0.865	0.865	0.865
Distribution	Pert (1.611, 4.429)	Pert (1.611, 4.429)	Pert (1.611, 4.429)	Pert (1.611, 4.429)	Pert (1.611, 4.429)	Pert (1.611, 4.429)
QALY weight for treated PLHIV (CD4: 200-499)						
PE	0.83	0.83	0.83	0.83	0.83	0.83
Distribution	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)	Pert (1.97, 4.59)
QALY weight for treated PLHIV (CD4<200)						

PE	0.82	0.82	0.82	0.82	0.82	0.82
Distribution	Pert (0.667, 3.33)	Pert (0.667, 3.33)	Pert (0.667, 3.33)	Pert (0.667, 3.33)	Pert (0.667, 3.33)	Pert (0.667, 3.33)
QALY weight adjusted for PWID						
PE	0.174	0.174	0.174	0.174	0.174	0.174
Distribution	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)	Pert (4, 4)
QALY weight adjusted for opioid agonist therapy recipients						
PE	0.213	0.213	0.213	0.213	0.213	0.213
Distribution	Pert (3.7, 4.25)	Pert (3.7, 4.25)	Pert (3.7, 4.25)	Pert (3.7, 4.25)	Pert (3.7, 4.25)	Pert (3.7, 4.25)
HEALTH CARE COSTS FOR PLHIV RECEIVING ART						
Health care cost (CD4>500): Male PWID						
PE	4559	4219	4604	4559	4219	4604
Distribution	Gamma (6301, 2.17)	Gamma (6511, 1.94)	Gamma (5048, 2.74)	Gamma (6301, 2.17)	Gamma (6511, 1.94)	Gamma (5048, 2.74)
Health care cost (CD4>500): Male MSM						
PE	3784	3503	3821	3784	3503	3821
Distribution	Gamma (24395, 0.47)	Gamma (28851, 0.36)	Gamma (15423, 0.74)	Gamma (24395, 0.47)	Gamma (28851, 0.36)	Gamma (15423, 0.74)
Health care cost (CD4>500): Male MWID						
PE	4173	3862	4214	4173	3862	4214
Distribution	Gamma (3013, 4.15)	Gamma (3027, 3.83)	Gamma (2989, 4.23)	Gamma (3013, 4.15)	Gamma (3027, 3.83)	Gamma (2989, 4.23)
Health care cost (CD4>500): Male HET						
PE	3951	3657	3990	3951	3657	3990
Distribution	Gamma (14940, 0.79)	Gamma (14297, 0.77)	Gamma (9092, 1.32)	Gamma (14940, 0.79)	Gamma (14297, 0.77)	Gamma (9092, 1.32)
Health care cost (CD4>500): Female PWID						
PE	4781	4425	4828	4781	4425	4828
Distribution	Gamma (3594, 3.99)	Gamma (3615, 3.67)	Gamma (3142, 4.61)	Gamma (3594, 3.99)	Gamma (3615, 3.67)	Gamma (3142, 4.61)
Health care cost (CD4>500): Female HET						
PE	4090	3786	4130	4090	3786	4130
Distribution	Gamma (17345, 0.71)	Gamma (16692, 0.68)	Gamma (9559, 1.3)	Gamma (17345, 0.71)	Gamma (16692, 0.68)	Gamma (9559, 1.3)
Health care cost (CD4: 200-499): Male PWID						
PE	4620	4277	4666	4620	4277	4666
Distribution	Gamma (6362, 2.18)	Gamma (6526, 1.97)	Gamma (5072, 2.76)	Gamma (6362, 2.18)	Gamma (6526, 1.97)	Gamma (5072, 2.76)
Health care cost (CD4: 200-499): Male MSM						
PE	3835	3550	3873	3835	3550	3873
Distribution	Gamma (24477, 0.47)	Gamma (28010, 0.38)	Gamma (15325, 0.76)	Gamma (24477, 0.47)	Gamma (28010, 0.38)	Gamma (15325, 0.76)
Health care cost (CD4: 200-499): Male MWID						
PE	4229	3914	4271	4229	3914	4271
Distribution	Gamma (3020, 4.2)	Gamma (3024, 3.88)	Gamma (2991, 4.28)	Gamma (3020, 4.2)	Gamma (3024, 3.88)	Gamma (2991, 4.28)
Health care cost (CD4: 200-499): Male HET						
PE	4004	3706	4044	4004	3706	4044
Distribution	Gamma (15199, 0.79)	Gamma (14288, 0.78)	Gamma (9140, 1.33)	Gamma (15199, 0.79)	Gamma (14288, 0.78)	Gamma (9140, 1.33)
Health care cost (CD4: 200-499): Female PWID						
PE	4845	4485	4893	4845	4485	4893

Distribution	Gamma (3595, 4.04)	Gamma (3602, 3.74)	Gamma (3137, 4.68)	Gamma (3595, 4.04)	Gamma (3602, 3.74)	Gamma (3137, 4.68)
Health care cost (CD4: 200-499): Female HET						
PE	4145	3837	4186	4145	3837	4186
Distribution	Gamma (17205, 0.72)	Gamma (16243, 0.71)	Gamma (9466, 1.33)	Gamma (17205, 0.72)	Gamma (16243, 0.71)	Gamma (9466, 1.33)
Health care cost (CD4<200): Male PWID						
PE	4928	4561	4977	4928	4561	4977
Distribution	Gamma (5983, 2.47)	Gamma (6089, 2.25)	Gamma (4815, 3.1)	Gamma (5983, 2.47)	Gamma (6089, 2.25)	Gamma (4815, 3.1)
Health care cost (CD4<200): Male MSM						
PE	4091	3786	4131	4091	3786	4131
Distribution	Gamma (18905, 0.65)	Gamma (20517, 0.55)	Gamma (12845, 0.96)	Gamma (18905, 0.65)	Gamma (20517, 0.55)	Gamma (12845, 0.96)
Health care cost (CD4<200): Male MWID						
PE	4511	4175	4555	4511	4175	4555
Distribution	Gamma (2921, 4.63)	Gamma (2916, 4.3)	Gamma (2889, 4.73)	Gamma (2921, 4.63)	Gamma (2916, 4.3)	Gamma (2889, 4.73)
Health care cost (CD4<200): Male HET						
PE	4271	3953	4313	4271	3953	4313
Distribution	Gamma (13136, 0.98)	Gamma (12299, 0.96)	Gamma (8314, 1.56)	Gamma (13136, 0.98)	Gamma (12299, 0.96)	Gamma (8314, 1.56)
Health care cost (CD4<200): Female PWID						
PE	5168	4783	5219	5168	4783	5219
Distribution	Gamma (3455, 4.49)	Gamma (3449, 4.16)	Gamma (3025, 5.18)	Gamma (3455, 4.49)	Gamma (3449, 4.16)	Gamma (3025, 5.18)
Health care cost (CD4<200): Female HET						
PE	4421	4092	4465	4421	4092	4465
Distribution	Gamma (14313, 0.93)	Gamma (13461, 0.91)	Gamma (8481, 1.58)	Gamma (14313, 0.93)	Gamma (13461, 0.91)	Gamma (8481, 1.58)

PE: point estimate; PLHIV: people living with HIV; PWID: people who inject drugs; MSM: men who have sex with men; MWID: men who are both MSM and PWID; HET: heterosexual; ln: lognormal; Unif: uniform; QALY: quality-adjusted life year.