ESTIMATING AND PROJECTING THE ECONOMIC IMPACT OF ANTIRETROVIRAL THERAPY ON THE US ECONOMY THROUGH AN UPDATED HIV MICROSIMULATION MODEL

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ABSTRACT

This paper proposes a comprehensively calibrated HIV simulation model, validated against HIV prevalence, related mortality, and viral load suppression rates. The model is designed for epidemiological forecasting and policy analysis. Using this model, we estimated the economic impact of antiretroviral therapy (ART) in the U.S. The model tracks the progression of the HIV epidemic on an individual basis, considering factors such as sex, age, transmission risk, and treatment adherence to project HIV prevalence and treatment statistics through 2040. It predicts an increase in the U.S. HIV population from 1.20 million in 2022 to 1.24 million by 2030, with a subsequent decrease to 1.21 million by 2040, reflecting demographic shifts and enhancements in ART access and effectiveness. Economically, the model predicts a significant rise in financial burden, with costs increasing from 38 billion US dollars in 2023 to 60 billion US dollars by 2040.

1 INTRODUCTION

The Human Immunodeficiency Virus (HIV) spreads mainly through sexual contact and/or infected blood/fluids. HIV weakens the immune system by attacking CD4 cells, leaving individuals vulnerable to infections and illnesses including cancer. Untreated HIV progresses to Acquired Immunodeficiency Syndrome (AIDS), a critical stage with severe immune system compromise. Antiretroviral therapy (ART) is the prescribed treatment for HIV, aiming to decrease the HIV viral load in the bloodstream. While ART does not eliminate HIV completely, it significantly extends the life expectancy of HIV-positive individuals close to that of people without HIV. Adhering to ART maintains the viral load undetectable for people with HIV (PWHIV), which is crucial in preventing the spread of HIV.

In the U.S., over 1.2 million people were estimated to be living with HIV by the end of 2021, with around 35,000 new HIV diagnoses each year (CDC 2023). Surveillance data indicate that of those diagnosed with HIV by the end of 2020 and still living at the end of 2021, only 59% achieved viral suppression, meaning they had an undetectable viral load (CDC 2023).

1.1 Literature Review

HIV is a well-studied disease. There are plenty of studies and clinical trials conducted for the effectiveness of ART, ART initiation, natural history of HIV infection, etc. Whereas these studies can be used to assess the effect of expanded eligibility criteria for individuals, mathematical models can be used to project the long-term effects of policy decisions. In the past decade, mathematical models have been useful for understanding the potential epidemiological effects, public health benefits, and costs of interventions for HIV in many populations. In literature, generally, three different types of models are used (i) compartmental, (ii) individual-level simulations (microsimulations), and (iii) agent-based simulations.

Agent-based models are widely used to simulate the spread of HIV among specific populations, emphasizing individual behaviors and interactions at a micro-level. These models are particularly effective in examining how personal behaviors and social networks impact HIV transmission dynamics. Bershteyn

et al. (2013) developed an agent-based simulation model using EMOD software, called EMOD-HIV. EMOD HIV models setting-specific demographics, individual and partnership characteristics, sexual activity frequency, disease progression, and transmission rates. It notably predicts the substantial impact and high costs of early antiretroviral therapy (ART) initiation. The model emphasizes the importance of targeting interventions at younger, highly active populations to effectively reduce future HIV infections, highlighting the complex dynamics of epidemic spread and the benefits of early treatment. Anderson et al. (2014), utilized mathematical modeling to explore the benefits of targeted HIV intervention strategies in Kenya, considering geographical and population-specific variations in HIV risk. It modeled interventions such as male circumcision, behavior change communication, early antiretroviral therapy, and pre-exposure prophylaxis, tailoring them to different population groups based on their risk behaviors or geographical locations. Smith et al. (2015) employed an agent-based modeling framework that utilized demographic, behavioral, and treatment data from rural KwaZulu-Natal to simulate the HIV dynamics within a community. The model, which mirrored real-world characteristics such as sexual behavior and partnership dynamics, aimed to assess the risks of HIV transmission and the impacts of various ART initiation thresholds and to evaluate the effectiveness and cost-effectiveness of HIV counseling and testing. Recently, Bingham et al. (2021) utilized an updated agent-based model, PATH 3.0, to estimate the lifetime economic burden of HIV in the U.S., incorporating current antiretroviral therapy regimens and costs. It simulated a cohort infected in 2015, tracking lifetime treatment costs across various health services until the cohort's lifetime.

Deterministic Compartmental Models (DCM) have been extensively utilized to analyze the population-level dynamics of HIV transmission and evaluate the impact of public health strategies. These models categorize the population into different compartments according to disease status and simulate the transitions between compartments to forecast epidemic trends. DCMs are crucial for evaluating outcomes such as shifts in HIV incidence, prevalence, mortality, and the cost-effectiveness of interventions. Khurana et al. (2018) developed the HIV Optimization and Prevention Economics (HOPE) model to simulate the sexually active US population aged 13 to 64 from 2010. The model stratifies this population into 195 groups by various demographic and risk factors to analyze the impact of achieving national HIV goals and implementing pre-exposure prophylaxis (PrEP). HOPE model evaluated the number of HIV infections averted from 2016 to 2020 by implementing different PrEP scenarios.

Individual-based (Micro) simulation models provide detailed simulations of individual life courses within a population, capturing the complexities and random nature of life events and disease progression. These models have been extensively used in HIV research to examine a variety of outcomes including life expectancy, development of drug resistance, viral load suppression, and the economic impact of treatment and prevention strategies. Several studies used microsimulations to assess the effectiveness and cost-efficiency of various interventions, including ART strategies, improved access to care, universal testing with immediate ART initiation, and PrEP (Walensky et al. 2016; Paltiel et al. 2005; Maheswaran et al. 2018; Kazemian et al. 2020).

1.2 Motivation

This paper introduces an updated version of our prior HIV Microsimulation Model (version 1.0.2), with revised calibration including data from the years 2017 and 2018 (Deshmukh et al. 2024). The model has undergone comprehensive calibration across various outcomes such as HIV prevalence, HIV-related mortality, HIV diagnoses, and rates of viral load suppression. This thorough calibration ensures the model accurately reflects current HIV dynamics and can be effectively utilized in epidemiological forecasting and policy analysis.

As a practical application of this updated model, we have conducted an estimation of the economic impact of antiretroviral therapy (ART) on the US economy. This analysis not only provides insights into the direct costs associated with ART but also explores the broader economic implications, including healthcare savings from averted HIV transmissions and improved productivity among individuals receiving treatment. This detailed examination helps in understanding the fiscal dimensions of ART interventions,

thereby aiding policymakers in making informed decisions about resource allocation in HIV management programs.

2 METHODS

We developed a detailed individual-level (micro) simulation model to project the progression of the HIV epidemic in the US. The model simulates each person living with HIV (PLWH), from infection through to disease progression, diagnosis, treatment initiation, adherence, and both HIV-specific and other-cause mortality. The model characterizes the PLWH by several factors such as sex/sexual orientation (Men who have Sex with Men [MSM], men who have sex with women [MSW], and women [W]), age, diagnosis status of HIV, both current and lowest CD4 count ranges, history of AIDS, number of opportunistic infections, treatment status, adherence levels, and viral suppression status. Data for the model parameters were obtained from CDC surveillance reports via the CDC's HIV surveillance tool (NCHHSTP AtlasPlus), and relevant literature, while unobservable parameters were estimated through calibration by aligning model outcomes with real-world data. The model was validated by comparing its predictions with actual data on HIV/AIDS diagnoses, deaths, and the virally suppressed HIV population. The model is capable of examining trends over time and across different groups by projecting future prevalence of HIV and treatment statistics by age, sex, and transmission risk up to 2040. The cycle length of the model was annual. The model was coded in R version 4.3.1 and RStudio version 2023.06.1.

2.1 Population Characteristics

Starting from 2010, the model simulates the prevalent population of PLWH. The newly infected PLWH is added to the model for each year. Table 1 shows the population characteristics and the potential values that can be assigned throughout the simulation. Based on the CDC's definition (as per the surveillance report), AIDS is identified by a nadir CD4 count of fewer than 200 cells per cubic millimeter of blood or by the diagnosis of an opportunistic infection (OI). The model is capable of providing the number of HIV prevalent cases and their trends over time for each characteristic.

Table 1: Population characteristics.

Characteristics	Potential Values
Age	Numeric value (years) {13, 14,, 99}
	MSM (Men who have Sex with Men) [MSM]
Sex/Sexual orientation	MSW (Men who have Sex with Women) [MSW]
	Women [W]
HIV diagnostic status	Diagnosed
The diagnostic status	Undiagnosed
Nadir CD4 count	Numeric value (cells/μL) [0-640]
Current CD4 count	Numeric value (cells/μL) [0-640]
History of opportunistic infection	No
History of opportunistic infection	Yes
Prior AIDS diagnosis	No
Filor AIDS diagnosis	Yes
Treatment status	Not currently under treatment
Treatment status	Under treatment
Current treatment adherence	Adherent
	Non-adherent
Vinal land assumance in	Suppressed
Viral load suppression	Not suppressed

The simulation began in 2010 with a cohort of PLWH, both diagnosed and undiagnosed. The CDC's HIV surveillance tool, CDC AtlasPlus, provides national data for the number of diagnosed and estimates for undiagnosed HIV patients, categorized by gender, transmission group, and age. The age distribution of the HIV population by sex/sexual orientation is derived from CDC HIV/AIDS surveillance reports. Information on HIV diagnosis status, by sex/sexual orientation, is sourced from CDC HIV/AIDS surveillance reports. Table 2 outlines the HIV population at the end of 2010 in the US, detailing age, sex/sexual orientation, and diagnosis status. For assigning the exact age of each HIV patient, a uniform distribution was utilized.

Age Group Diagnosed		Undiagnosed				
Age Group	MSM	MSW	Female	MSM	MSW	Female
13 - 14	107	713	1072	428	18	28
15 - 19	2138	1833	2680	10261	430	535
20 - 24	19132	2547	6967	32066	1343	1313
25 - 29	32055	3749	13296	13004	2406	3030
30 - 34	39178	6963	19945	15894	4468	4544
35 - 39	63363	15185	30274	10176	3666	4043
40 - 44	63363	15185	30274	10176	3666	4043
45 - 49	96959	28464	36621	8539	3906	4305
50 - 54	70211	28464	29963	5692	2604	2870
55 - 59	42775	21981	18437	2584	1725	1947
60 - 64	22945	12226	9538	1386	959	1007
65 - 69	9833	5203	4219	594	408	446
70 - 74	4097	2385	1950	248	187	206
75 - 79	1639	997	851	99	78	90
80 - 84	492	390	319	30	31	34
85 - 99	164	173	142	10	14	15

Table 2: Age distribution of the initial population.

Next, we assigned nadir CD4 counts (the lowest CD4 count during entire follow-up) to each patient based on age, sex/sexual orientation, and diagnosis status. The history of opportunistic infections (OIs) and nadir CD4 counts were modeled together for AIDS modeling. It was assumed that an individual diagnosed with an OI but previously unaware of their HIV status would become aware of their HIV status. Here, the history of OIs was modeled for only diagnosed HIV patients in the baseline population. Additionally, due to the distinct characteristics between diagnosed and undiagnosed patients, we calibrated the model separately for those unaware of their HIV status. This calibration utilized OI probabilities and nadir CD4 count distributions from the previous version of our model for the prevalent population living with HIV (PLWH). We utilized CDC Atlas receipt-of-care data to identify patients currently under treatment. Subsequently, we assigned their viral suppression status.

For the assignment of current CD4 levels, we used the assigned nadir CD4 levels and viral load suppression status using the following formula. For individuals who have achieved viral suppression, we adjusted CD4 count levels based on the study by Bishop et al. (2016).

$$CD4 = \begin{cases} Nadir CD4 & if VLS = 0\\ Nadir CD4 + U(195, 470) & if VLS = 1 \end{cases}$$
 (1)

2.2 HIV Surveillance, Progression, and Treatment

After assigning the characteristics of the prevalent HIV population in 2010, the model incorporated new infections each year. Data for these new cases up to 2021 were obtained from CDC's AtlasPlus. After 2021, projections of new infections were estimated using a Joinpoint regression model based on age and sexual orientation, using the Joinpoint Regression Program v5.0.2 from the National Cancer Institute. Joinpoint regression is a statistical method used to identify points where a significant change, or "joinpoint," occurs in a trend over time. The method estimates the number and location of these joinpoints and provides insights into how trends vary across different segments of data. The estimation of new HIV infections was based on the most recent trend segment from the regression model. The number of new HIV cases used in the model was presented in Figure 3.

Newly infected individuals enter the model as undiagnosed and not receiving treatment. Their CD4 count is assigned based on a uniform distribution: i) $\sim U(600-640)$ for those aged 34 and younger, and ii) $\sim U(550-600)$ for those aged 35 and older (Lodi et al. 2010; Touloumi et al. 2013). Undiagnosed PLWH may be diagnosed either through testing or due to symptoms (such as opportunistic infections). The model simulates HIV diagnosis based on transition probabilities that vary by sex/sexual orientation and CD4 count. These transition probabilities and the initial CD4 counts of undiagnosed individuals were obtained through calibration. These probabilities are given in Table 4. The model follows a square root CD4 depletion model (Lodi et al. 2010; Touloumi et al. 2013), where the depletion of CD4 cells over a year is calculated using the following equation.

$$\sqrt{CD4_{t+1}} - \sqrt{CD4_t} = b_1 \tag{2}$$

In the model, the *b* values for each individual were determined using a triangular distribution, whose parameters were shown in Table 3. We also incorporated the modeling of opportunistic illnesses, which are the second condition of the AIDS definition, using transition probabilities derived from both literature and calibration. We assumed that opportunistic infections (OIs) occur in individuals who do not achieve viral load suppression.

Table 3: CD4 count depletion model parameters.

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-		Peak	Lower	Upper
MSM	13-24	-1	-0.9	-1.14
	25-44	-1.15	-1.02	-1.3
	45-54	-1.35	-1.21	-1.53
	55+	-1.55	-1.4	-1.78
MSW	13-24	-1.25	-0.75	-1.79
	25-44	-1.4	-0.87	-1.91
	45-54	-1.6	-1.06	-2.1
	55+	-1.8	-1.25	-2.29
Women	13-24	-1.7	-1.15	-2.23
	25-44	-1.85	-1.27	-2.35
	45-54	-2.05	-1.46	-2.54
	55+	-2.25	-1.65	-2.73

In the model, treatment uptake and adherence vary based on sex/sexual orientation and AIDS history. Using the data from Bishop et al. (2016) Improvement in CD4 count with ART was modeled as a function of treatment duration (t_d) as shown in Equation (3).

$$CD4 = \begin{cases} CD4 + 195 & if \ t_d = 1\\ CD4 + 119 * (\ln(t_d) - \ln(t_d - 1)) & if \ t_d > 1 \end{cases}$$
 (3)

Typically, the individuals start their treatment at the time of diagnosis, and we estimated this probability using the linkage to care measure found in the CDC's HIV Surveillance reports. Considering the recent trends in linkage-to-care rates in recent years, we employed a linear trend model for different age groups (13-24, 25-34, 34-44, ≥45) to determine future linkage-to-care rates for newly diagnosed individuals. Here, we set an upper limit of 90% for the linkage-to-care probability. The model assumes an initial treatment effectiveness of 80% for the first regimen and 60% for the subsequent ones. For those initially untreated, the probability of eventually starting treatment is set through calibration. Treatment dropout probabilities are established using data from CDC reports, and calibration. Table 4 presents the annual probabilities of treatment uptake, dropout, treatment return, and treatment adherence, with specific values for different age groups.

Table 4: The annual probabilities of treatment uptake, treatment dropout, and treatment adherence.

Description	Value
Treatment uptake	
13-24	0.03
25-34	0.036
35-44	0.04
45-54	0.044
≥55	0.05
Treatment dropout	0.01
Treatment return	0.05
Treatment adherence	
13-24	0.85
25-34	0.9
35-44	0.92
45-54	0.94
≥55	0.95

The annual death probabilities are modeled as a function of age, sex/sexual orientation, AIDS history, and virally suppression status. The maximum age was set to 100 in the model. Mortality probabilities were obtained through calibration (Table 5). We also used a 0.5% improvement in mortality rates in order to capture the improvement in life expectancy among PLWH.

Table 5: The mortality probabilities used in the model.

	With AID	With AIDS History		IDS History
	Virally	Not Virally	Virally	Not Virally
	Suppressed	Suppressed	Suppressed	Suppressed
MSM				
13-24	0.0018	0.0225	0.0008	0.0016
25-34	0.0057	0.0261	0.0011	0.0026
35-44	0.0078	0.0270	0.0013	0.0050
45-54	0.0089	0.0347	0.0023	0.0086
55-64	0.0189	0.0472	0.0084	0.0168
65-74	0.0439	0.0715	0.0246	0.0307
75-84	0.1143	0.1860	0.0640	0.0800
85-99	0.3237	0.5267	0.1812	0.2265

MSW				_
13-24	0.0019	0.0242	0.0008	0.0017
25-34	0.0069	0.0313	0.0014	0.0032
35-44	0.0094	0.0324	0.0016	0.0060
45-54	0.0129	0.0503	0.0034	0.0125
55-64	0.0226	0.0566	0.0101	0.0201
65-74	0.0527	0.0858	0.0295	0.0369
75-84	0.1372	0.2233	0.0768	0.0960
85-99	0.3884	0.6320	0.2175	0.2718
Female				_
13-24	0.0019	0.0242	0.0009	0.0017
25-34	0.0069	0.0302	0.0015	0.0034
35-44	0.0091	0.0315	0.0015	0.0059
45-54	0.0119	0.0465	0.0031	0.0116
55-64	0.0198	0.0496	0.0089	0.0176
65-74	0.0461	0.0751	0.0258	0.0323
75-84	0.1200	0.1953	0.0672	0.0840
85-99	0.3398	0.5530	0.1903	0.2379

Age and health state-specific utility weights were obtained from published studies (Hanmer et al. (2006) and expert opinions. The utility values for patients in different health states are shown in Table 6.

Table 6: The mortality probabilities used in the model.

Parameter	Value
Age-specific utilities	
20-29	0.928
30-39	0.918
40-49	0.887
50-59	0.861
60-69	0.84
70-79	0.802
80-89	0.782
Health-state specific utilities	
HIV	0.9
AIDS	0.8

Lastly, the cost parameters for ART were obtained from McCann et al. (2020). We assumed that the inflation of ART costs would continue until 2040 at an approximate rate of 5% per year. We also applied a 3% discount rate. All cost values are presented in 2023 US Dollars.

2.3 Model Calibration

We performed parameter calibration to identify both unobservable and unknown parameters in the model. Particularly, we calibrated variables including the distribution of CD4 counts among undiagnosed individuals, probabilities of HIV diagnosis, rates of treatment uptake, dropout, and adherence. In the calibration process, we matched the model outcomes with the CDC Atlas data, specifically focusing on observed data from 2011 to 2018. Given that some parameters are age-specific and show significant trends,

we conducted a two-step approach in our calibration process. We used two goodness-of-fit functions Absolute Percent Error (APE) measure and Euclidean Distance (ED) measures.

$$APE_{i} = \left| \frac{\sum_{t=2011}^{2018} A_{t} - \sum_{t=2011}^{2018} M_{i,t}}{\sum_{t=2011}^{2018} A_{t}} \right|$$
(4)

$$ED_i^{Time} = \sqrt{\sum_{t=2011}^{2018} (A_t - M_{i,t})^2}$$
 (5)

$$APE_{i} = \left| \frac{\sum_{t=2011}^{2018} A_{t} - \sum_{t=2011}^{2018} M_{i,t}}{\sum_{t=2011}^{2018} A_{t}} \right|$$

$$ED_{i}^{Time} = \sqrt{\sum_{t=2011}^{2018} (A_{t} - M_{i,t})^{2}}$$

$$ED_{i}^{Age} = \sqrt{\sum_{a \in \{Age\ groups\}} \left(\sum_{t=2011}^{2018} A_{a,t} - \sum_{t=2011}^{2018} M_{a,i,t} \right)^{2}}$$

$$(6)$$

In Equation (4), APE_i shows the APE score of the parameter set i, A_t denotes the observed values for an indicator for year t, M_{i,t} represents the values estimated by the model using parameter set i for year t. Equation (5, 6) shows two Euclidean measures used in the calibration, ED₁^{Time} for the parameters where annual trends are important and ED_i^{Age} for age-specific parameters. We calculated the Euclidean distance by comparing age-specific observed (A_{a,t}) and model estimated (M_{a,t}) values.

To improve computational efficiency, we adopted a two-step calibration process. First, we calibrated the distribution of CD4 counts and diagnosis probabilities among undiagnosed People Living with HIV (PLWH), stratifying by sex/sexual orientation and CD4 count levels, using a grid-based approach. This approach resulted in a total of 615 unique CD4 count distribution sets. We then generated a random number (γ) between 0.15 and 0.25, representing the range of AIDS diagnoses at initial HIV diagnosis. Using γ and the observed HIV diagnosis data from 2011 (A_{2011}), we calculated the diagnosis probability for PLWH with a CD4 count under 200 ($p_{<200}^{dx}$). We assumed a descending order of diagnosis probability based on CD4 count levels ($p_{<200}^{dx} \ge p_{200-349}^{dx} \ge p_{2500-499}^{dx} \ge p_{\ge 500}^{dx}$). We selected parameter sets with APE scores under 10%, ranked them based on ED_i^{Time} , and identified the top 50 sets. We followed this process separately for MSM, MSW, and women.

In the second phase of calibration, we focused on parameters associated with HIV progression. Using a similar method to the first phase, we computed the APE and identified the top 50 solutions based on the ED_i^{Age} metric, matching model-generated AIDS prevalence with observed AIDS prevalence rates. We generated 5000 different parameter sets. As in the initial step, we refined each parameter set across 50 iterations, comparing APE values. In this step, we calibrated the variables including opportunistic infection (OI) probabilities, Nadir CD4 distribution among diagnosed PLWH, and the uptake of HIV medications. In the final stage, we calibrated mortality probabilities by comparing the annual HIV-related deaths generated by the model with reported deaths in the CDC Atlas.

3 **RESULTS**

We calibrated the model using data from the CDC Atlas from 2011 to 2018, matching model outcomes with observed values for HIV diagnosis, HIV deaths, AIDS prevalence, and HIV prevalence. Here, we identified the values for the unknown and unobservable parameters detailed in Section 2. For validation, we compared our model outcomes with observed data from 2019 to 2021. Figure 2 displays the results of our model and comparison with observed values (Figure 2.A for HIV diagnosis, Figure 2.B for HIV deaths, Figure 2.C for AIDS prevalence, and Figure 2.D for HIV prevalence).

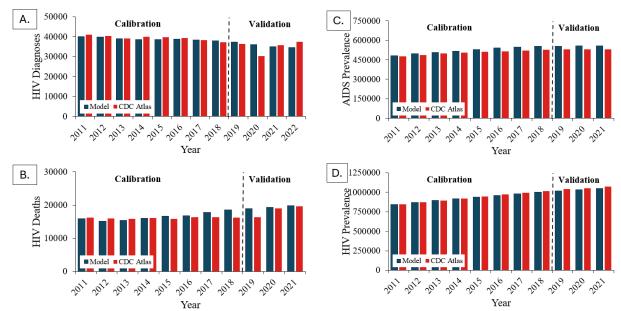
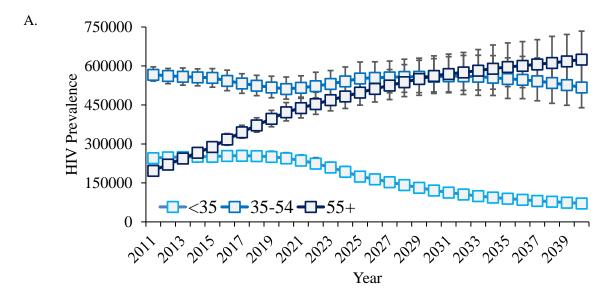


Figure 2: Results of our model and comparison with observed values. (A) for HIV diagnosis, (B) for HIV deaths, (C) for AIDS prevalence, and (D) for HIV prevalence.

Overall, the model offers promising validation results. It is important to note that the year 2020, marked by the COVID-19 pandemic, may significantly affect HIV diagnosis rates. Additionally, our model overestimated deaths for the years 2017-2019. Despite this, the Absolute Percentage Errors (APE) for both calibration and validation phases remain below 10%.



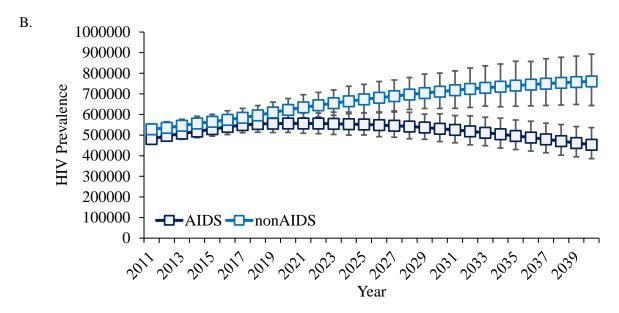


Figure 3: HIV prevalence projections by (A) Age, and (B) AIDS Status.

The projected number of people living with HIV (PLWH) in the United States is expected to increase from 1.20 million in 2022 to 1.24 million by 2030, as shown in Figure 3. After 2030, the prevalence of HIV is estimated to start declining, with the number of PLWH decreasing to 1.21 million by 2040. Figure 3.A shows a shift in age distribution, with individuals over 55 years increasing from 38% in 2022 to 51% in 2040, while those under 35 years decreased from 19% to 6%. Figure 3.B displays the distribution and burden of AIDS prevalence, projecting a continuous decline post-2022 as the proportion of PLWH with AIDS drops from 46% in 2022 to 37% in 2040, due to increased antiretroviral therapy (ART) usage and improved linkage to care.

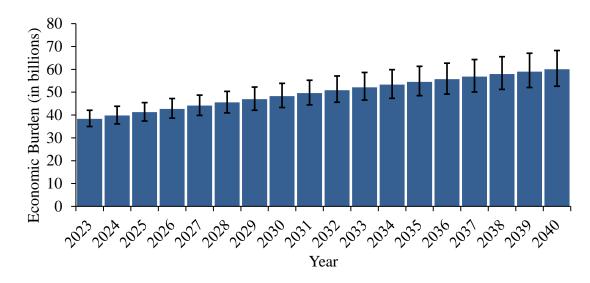


Figure 4: Economic burden projections of antiretroviral therapy.

Regarding the financial projections for HIV ART treatment from 2020 to 2040, it's assumed the annual cost of ART will rise by 5%, increasing the economic burden from \$38.33 billion in 2023 to \$60 billion in 2040 (Figure 4).

4 DISCUSSION

This study is the first to estimate and project the economic burden of antiretroviral therapy (ART) for people living with HIV (PLWH) in the United States. We updated and recalibrated our previous model by defining more granular age groups and re-calibrating input parameters to more accurately represent the US PLWH population. The inclusion of ART cost parameters was crucial to estimate the economic burden. These cost estimates and economic burden projections are crucial in decision-making for HIV prevention interventions (Freedberg et al. 2015). Our model estimated a similar burden of \$25.5 billion (in 2018 US dollars) as reported by The IQVIA Institute in 2019, which estimated \$22.5 billion. This estimated increasing economic burden underscores the necessity of curbing the trend of rapidly escalating ART costs.

Antiretroviral drug prices in the United States continue to rise annually at a rate of 4 to 6 times faster than inflation (McCann et al. 2020). Martin and Shackman (2018) demonstrated that switching from brandname to available generic formulations of ART regimens could yield a 25% reduction. Additionally, our projections suggest that an increasing number of PLWH will significantly impact the overall economic burden of ART on the US economy.

From a modeling perspective, our microsimulation model has several strengths that contribute to its robustness and applicability. As a microsimulation, it is capable of analyzing specific subpopulations among PLWH. This capability enables the model to flexibly simulate the dynamics of other diseases that may affect PLWH, providing a comprehensive overview of comorbid health scenarios.

Furthermore, the model's architecture allows for detailed evaluations of the effectiveness and costeffectiveness of various treatment regimens and behavioral interventions. By integrating these elements, our model can adapt to assess a wide range of health interventions, making it a valuable tool for health policymakers and researchers. It provides insights into how different strategies may perform in real-world settings, thereby supporting informed decision-making in public health and clinical practice. This flexibility highlights the model's potential to influence the optimization of healthcare resources and strategies aimed at improving the lives of PLWH.

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