



A Growing Number of Men Who Have Sex With Men Aging With HIV (2021–2031): A Comparison of Two Microsimulation Models

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Background. Men who have sex with men (MSM) on antiretroviral therapy (ART) are at risk for multimorbidity as life expectancy increases. Simulation models can project population sizes and age distributions to assist with health policy planning.

Methods. We populated the CEPAC-US model with CDC data to project the HIV epidemic among MSM in the United States. The PEARL model was predominantly informed by NA-ACCORD data (2009–2017). We compared projected population sizes and age distributions of MSM receiving ART (2021–2031) and investigated how parameters and assumptions affected results.

Results. We projected an aging and increasing population of MSM on ART: CEPAC-US, mean age 48.6 (SD 13.7) years in 2021 versus 53.9 (SD 15.0) years in 2031; PEARL, 46.7 (SD 13.2) years versus 49.2 (SD 14.6) years. We projected 548 800 MSM on ART (147 020 ≥ 65 years) in 2031 (CEPAC-US) and 599 410 (113 400 ≥ 65 years) (PEARL). Compared with PEARL, CEPAC-US projected a smaller population of MSM on ART by 2031 and a slower increase in population size, driven by higher estimates of disengagement in care and mortality.

Conclusions. Findings from two structurally distinct microsimulation models suggest that the MSM population receiving ART in the United States will increase and age over the next decade. Subgroup-specific data regarding engagement in care and mortality can improve projections and inform health care policy planning.

Keywords. ART; HIV; MSM; United States; age distribution; aging; microsimulation model.

INTRODUCTION

Ending the human immunodeficiency virus (HIV) epidemic is a national priority and will require not only reducing new HIV infections, but also creating a comprehensive response to improve the health of people with HIV (PWH), which includes healthy aging. Clinical programs and health policy initiatives would benefit from clear projections of people aging with HIV. With increasing life expectancy and declines in new HIV infections, the number of PWH in the United States is increasing and the age distribution of PWH on antiretroviral therapy (ART) in the United States is shifting toward older ages with a greater burden of multimorbidity, even though

the highest HIV incidence continues to occur among younger adults [1–6]. Men who have sex with men (MSM) are a group of particular interest because they account for >66% of all new diagnoses of HIV infection in the United States since 2015 and comprise almost 55% of PWH in care, even though MSM are estimated to represent at least 3.9% of the adult male US population [7, 8].

Simulation models are effective tools to project long-term outcomes based on observational data and inform priorities in clinical care and public health policy by emphasizing the likelihood of future outcomes [9, 10]. A range of simulation models have been used to examine the HIV epidemic in the United States and globally to project life expectancy, anticipate costs of care, and investigate the clinical benefits and cost-effectiveness of specific public health strategies [11–15]. Although evidence from model-based analyses has been cited in both national and international HIV clinical guidelines [16, 17], direct comparisons of independent modeling approaches are rare [18], and projections from various models may not always agree, given the complex interplay between new HIV transmissions, HIV diagnosis and linkage rates, dynamic rates of engagement and disengagement in care, and

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mortality. It is unknown whether independently developed models will provide corroborative evidence that suggests consistent, reliable conclusions or highlight important differences in assumptions, which creates greater uncertainty.

To highlight priorities for future clinical focus and policy planning, we used two independent HIV simulation models that are conceptually, structurally, and operationally different to estimate and compare projections of the numbers and age distribution of MSM receiving ART in the United States from 2021 to 2031.

METHODS

Analytic Plan

We compared projections of the HIV epidemic among MSM in the United States using the Cost-Effectiveness of Preventing

AIDS Complications (CEPAC-US) and the ProjEcting Age, multimorbidity, and polypharmacy (PEARL) models (Figure 1) [15, 19]. The primary outcomes of interest were (1) the projected population size of MSM receiving ART in the United States from 2021 to 2031, and (2) the age distribution of MSM on ART in the same period. We further examined specific secondary outcomes to identify influential characteristics, similarities, and differences of the models. Finally, we performed sensitivity analyses to examine uncertainties in parameter estimates; we examined the change in primary outcomes given changes in the value of selected parameters in each model.

CEPAC-US Model Structure and Input Parameters

The CEPAC-US model is a validated microsimulation model of HIV disease, treatment, and transmission [20–22].

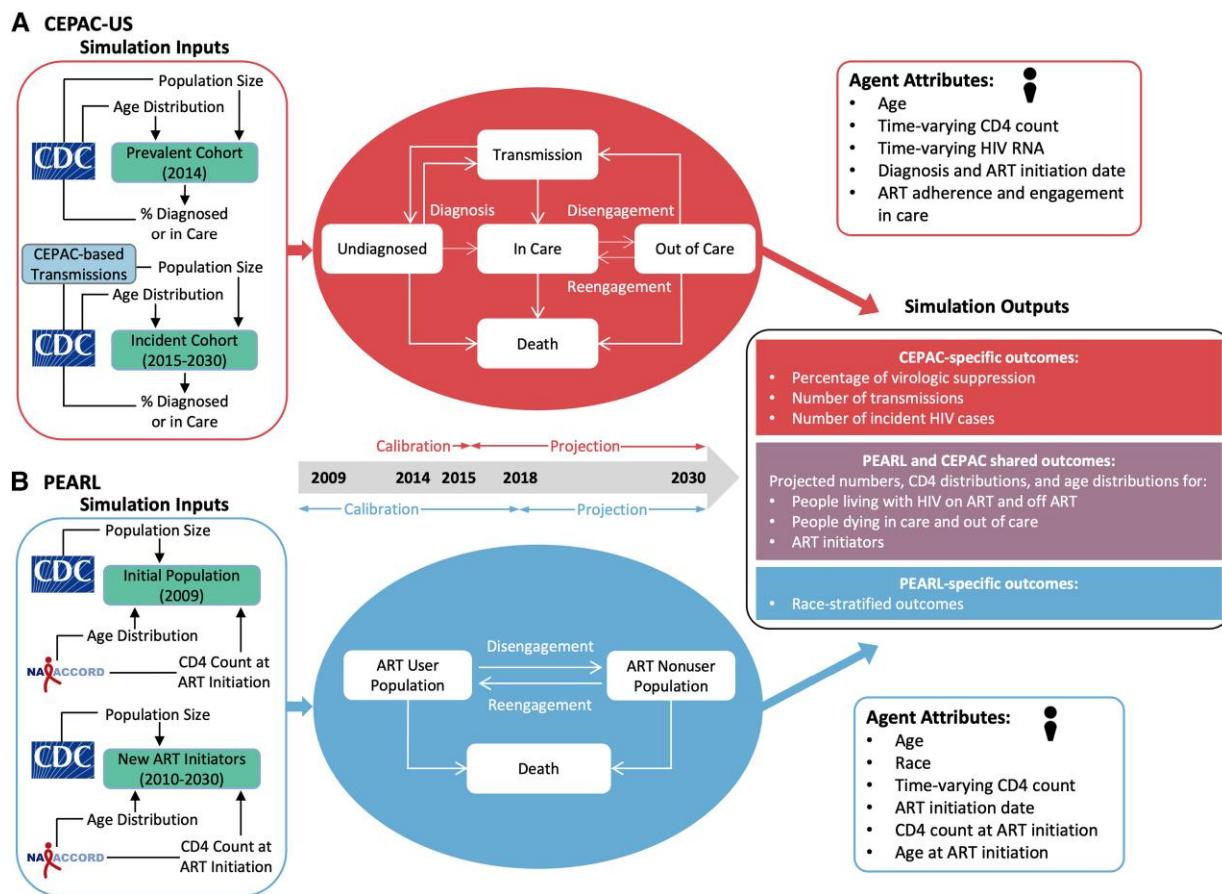


Figure 1. Comparison of CEPAC-US and PEARL model structures specific to estimates of the projected age distribution of MSM. This schematic displays a summary of simulation inputs (left), model structure (center), and agent attributes and model outputs (right) for the CEPAC-US and PEARL models. Each model can project the CD4, age distribution, mortality, and total number of MSM at different stages of the HIV care continuum. *A*, In the CEPAC-US model, MSM link to care when diagnosed with HIV, initiate ART, and can disengage from care and then reengage with care. Transmissions are estimated given the monthly estimates of viremic MSM. *B*, In the PEARL model, MSM who initiate ART will experience a rate of disengagement from care and future reengagement in care. In both models, MSM with HIV are at risk for death due to HIV-related or non-HIV-related causes. Abbreviations: ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; HIV, human immunodeficiency virus; MSM, men who have sex with men; NA-ACCORD, North American AIDS Cohort Collaboration on Research and Design; PEARL, ProjEcting Age, multimorbidity, and polypharmacy model.

Simulated MSM with HIV can be diagnosed, linked, and initiated on ART, and disengaged from or reengaged in clinical care. Time-varying covariates, including age, CD4 count, and HIV RNA levels, govern monthly transitions between health states and risk of death. Rates of engagement in care and adherence to ART are related to age; older MSM are more likely than younger MSM to remain engaged in care [23, 24]. Mortality is stratified by HIV-related causes (eg, opportunistic infections) and non-HIV-related causes (ie, age-stratified and sex-specific mortality) that are adjusted for risk behaviors more common among people with HIV [25–28]. Because MSM are more likely to use tobacco than the general population, mortality rates among simulated MSM older than 40 years are increased compared with nonsmokers without HIV [27–29]. Transmissions occur based on the population viral load each month [19]. Given the use of preexposure prophylaxis (PrEP) among MSM in the United States, we incorporated a reduction in annual transmissions attributable to PrEP use [30].

The model was populated with data regarding cohort characteristics, disease progression, ART outcomes, and engagement in care from published trials and cohort studies ([Supplementary Table 1](#)). All simulated MSM draw patient-level characteristics at model start based on the HIV care continuum: undiagnosed HIV, engaged in care on ART, and off ART after disengaging from care [7, 31]. Assuming that all MSM who disengage from care will remain out of care for 12 months unless they develop an opportunistic infection, rates of disengagement from care were age- and adherence-stratified (range, 0.01%–7.5%/month) and calibrated so that 78% of MSM remain in care at one year [32, 33]. MSM engaged in care are treated with guideline-concordant care and ART [16]. Full specification of the model is provided at <https://www.massgeneral.org/medicine/mpec/research/cpac-model> [34].

PEARL Model Structure and Input Parameters

PEARL is an agent-based simulation model of people with HIV who have initiated ART in the United States [15]. The simulated population comprises 15 race/ethnicity-sex-and-HIV acquisition risk subgroups. For this analysis, the focus is on the MSM subgroup, representing the population of Black/African American, White, and Hispanic MSM who have initiated ART in the United States. The PEARL model was initialized with a simulated population of ART users in 2009, informed by the reported number of people with diagnosed HIV from the Centers for Disease Control and Prevention (CDC) and estimates of age and CD4 count distributions among ART users in 2009 from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) [35]. New individuals enter the model every calendar year at ART initiation. The number of individuals and distribution of age and CD4 count at ART initiation were further informed by CDC and

NA-ACCORD data from 2010 to 2018 and projected forward to year 2031.

Simulated individuals can disengage from ART, reengage with ART, or die while in or out of care. Disengagement was defined as two or more years with no CD4 or HIV RNA laboratory results. The rate of reengagement in care and ART reinitiation is modeled via the number of years spent out of care, estimated between 1 to 7 years in NA-ACCORD [15]. Using data from NA-ACCORD, the probabilities of disengagement, reengagement, and death were estimated via mathematical functions that include calendar year, time-varying age, ART initiation date, CD4 count at ART initiation, and other individual-level characteristics; the PEARL model, therefore, incorporates assumptions regarding a gradual reduction in HIV mortality over time. All parameters and mathematical functions in PEARL were estimated separately for Black, White, and Hispanic MSM ever on ART in the United States with details available at <https://pearlhivmodel.org/> [15, 36].

Comparison Between the CEPAC-US and PEARL Models

Given differences in model structures and parameterizations, we identified a set of secondary outcomes closely linked to the primary outcome of interest and compared these outcomes at 2015 (representative of the calibration period in both models), 2021 (baseline year), and 2031 (end of projections). These secondary outcomes included (1) annual number of ART initiators, (2) proportion of MSM ever on ART currently engaged in care, and (3) mortality rates among MSM on and off ART. We also compared the age distributions, mean CD4 counts, and population sizes along the HIV care continuum in 2015, 2021, and 2031.

Sensitivity Analyses

We performed one-way sensitivity analyses in CEPAC-US and PEARL by varying key parameters individually by $\pm 20\%$ of the base case value while holding all other parameters at their baseline values ([Supplementary Table 2](#)). To this end, parameters were divided into two groups: those varied at model start (year 2014 in CEPAC-US and 2009 in PEARL), and those varied throughout the simulation (years 2015 to 2031 in CEPAC-US; years 2010 to 2031 in PEARL). To align certain parameters in both models, we varied selected parameters in tandem to achieve $\pm 20\%$ of the base case value ([Supplementary Tables 3–6](#)). We then assessed the impact of sensitivity analyses on primary outcomes separately, namely (1) the number of MSM on ART and (2) the proportion of MSM on ART who would be older than 65 years in 2031. We considered a parameter to have a substantial impact if the projected outcome varied by 5% or more when sensitivity analysis inputs were used compared with baseline values.

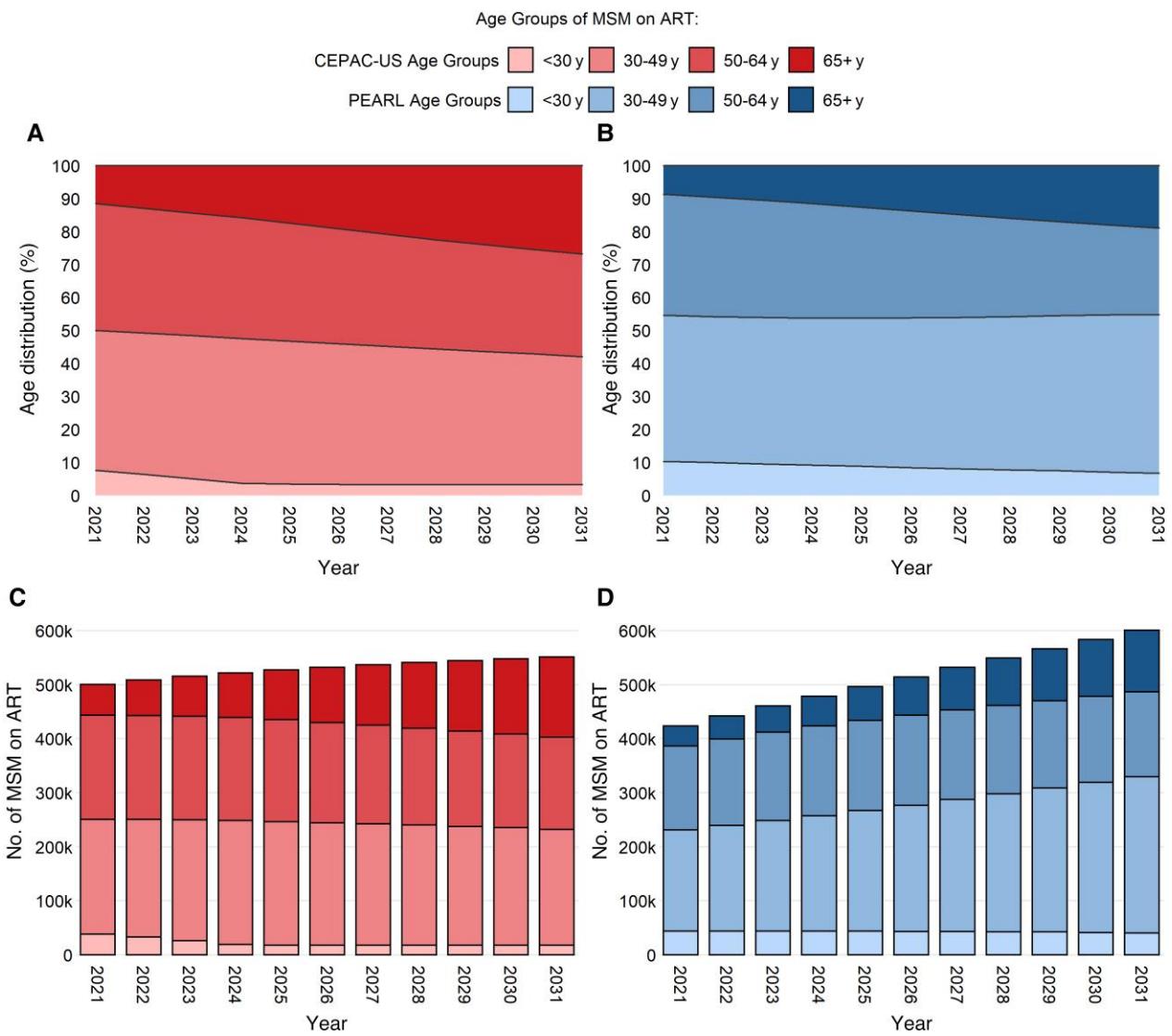


Figure 2. The projected age distribution, age, and numbers of MSM on ART from the CEPAC-US and PEARL models (2021–2031). The age distribution among MSM on ART over the next decade is projected by the (A) CEPAC-US and (B) PEARL models, as well as the numbers of MSM on ART projected by (C) CEPAC-US and (D) PEARL, stratified by age. MSM on ART who are 65 years or older are highlighted as the top portion of each graph in terms of the percent of the population (A and B) and absolute numbers (C and D). Abbreviations: ART, antiretroviral therapy; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; MSM, men who have sex with men; PEARL, ProjEcting Age, multimorbidity, and polypharmacy model.

RESULTS

With each model, we projected an increasing and aging population of MSM on ART over the next decade in the United States, as informed by recent patterns in new HIV diagnoses and mortality rates. With CEPAC-US, we projected the mean age of MSM on ART to be 48.6 (SD 13.7) years in 2021 and 53.9 (SD 15.0) years in 2031, with the proportion of MSM 65 years and older rising from 11.1% in 2021 to 25.6% in 2031 (Figure 2A). With PEARL, we projected a slightly younger population of MSM on ART: mean age, 46.7 (SD 3.2) years in 2021 and 49.2 (SD 14.6) years in 2031. Although both models' projections included a decline

in MSM younger than 30 years on ART over the next decade (mean populations, CEPAC-US, 38 380 [2021] and 17 920 [2031]; PEARL, 43 710 [2021] and 40 560 [2031]), PEARL's projections suggest a greater proportion of MSM younger than 30 years on ART compared with CEPAC-US (Figure 2B). A growing population of MSM on ART over the next decade was projected with both models, reaching a projected mean of 548 800 MSM in CEPAC-US and 599 410 MSM in PEARL by 2031, as well as a greater than 2.5-fold increase in the number of MSM aged ≥65 years on ART from 2021 to 2031 (CEPAC-US, 57 040 to 147 020 [Figure 2C] and PEARL, 36 730 to 113 400 [Figure 2D]). In comparison with CEPAC-US projections, PEARL projections showed a

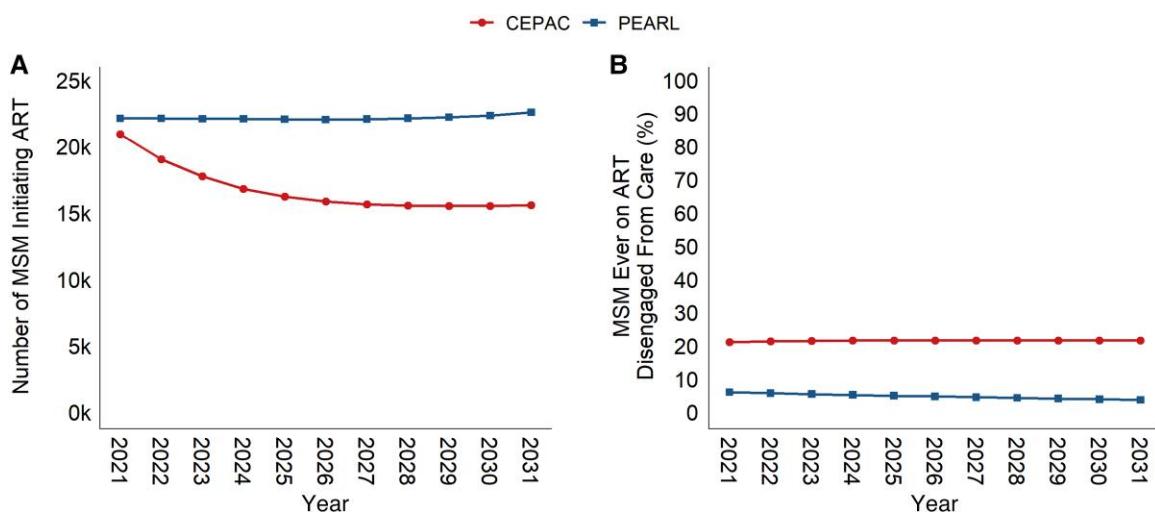


Figure 3. The number of MSM who initiate ART and percent of MSM who disengage from care projected by the CEPAC-US and PEARL models (2021–2031). *A*, The number of MSM who initiate ART over the next decade projected by the CEPAC-US (red circle) and PEARL (blue square) models. *B*, The percent of MSM on ART who disengaged from care was defined in CEPAC-US as one or more years with no CD4, HIV RNA, or clinical visits and in PEARL as two or more years with no CD4 or HIV RNA results. In both models, there is always at least a 4:1 ratio of MSM on ART compared with off ART. Abbreviations: ART, antiretroviral therapy; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; HIV, human immunodeficiency virus; MSM, men who have sex with men; PEARL, ProjEcting Age, multimorbidity, and polypharmacy model.

more rapid increase in the number of MSM on ART over the next decade (PEARL, 4.2% annual increase; CEPAC-US, 1.0%), as reflected in the steeper slope of the bars (Figure 2C and 2D); the most rapid increase occurred among MSM aged 30–49 years in PEARL projections.

We examined three secondary outcomes that varied substantially between CEPAC-US and PEARL projections (Figure 3 and Figure 4). With CEPAC-US, we projected a declining number of MSM initiating ART over the next decade (2021, 20 890; 2031, 15 530), given a stable number of new HIV infections among MSM (2021, 15 100; 2031, 15 790) and accompanied by an overall reduction in the number of MSM with undiagnosed HIV (2021, 50 720; 2031, 39 380) (Figure 3A and Table 1). In comparison, PEARL projections showed a stable trend in the number of MSM initiating ART over the next decade (2021, 22 120; 2031, 22 580), driven by the rising numbers of Hispanic MSM initiating ART (4.2% annual increase) and mitigated by the decreasing numbers of White MSM initiating ART (4.8% annual reduction) (Figure 3A and Table 1).

We projected a higher likelihood of disengagement from care among MSM using ART in 2031 with CEPAC-US compared with PEARL (CEPAC-US, 21.7% vs PEARL, 3.7%; Figure 3B and Supplementary Table 7). With CEPAC-US, we projected an increase in the overall population of MSM disengaged from care (2021, 134 270; 2031, 151 690), along with an increase in the proportion of MSM who have ever reengaged in care over time (2021, 41.0%; 2031, 52.9%). Using PEARL, we projected a decreasing population of MSM off ART over time (2021, 26 910; 2031, 22 900) with a declining rate of ART disengagement (2021, 3400 disengagements per 100 000

MSM on ART; 2031, 1980 disengagements per 100 000 MSM on ART) and stable rates of ART reengagement in care (ie, 53 010 to 53 170 reengagements per 100 000 MSM in 2021–2031).

Projected overall mortality among MSM ever on ART from CEPAC-US exceeded PEARL projections. In CEPAC-US, mortality rates rose from 2021 to 2031 among MSM on ART (910 deaths [2021] vs 1430 deaths [2031] per 100 000 person years [PYs]) and off ART (2030 deaths [2021] vs 2520 deaths [2031] per 100 000 PYs), whereas mortality among MSM on ART increased more slowly in PEARL (800 deaths [2021] vs 1070 deaths [2031] per 100 000 PYs), and mortality among MSM off ART remained stable over the decade (1150 deaths [2021] vs 1160 deaths [2031] per 100 000 PYs) (Figure 4A). Further comparison of age-stratified mortality rates suggested a close correspondence between projections of mortality at younger ages <30 years (Figure 4B) that diverged in the 30–64-year-old age group (Figure 4C). The greatest differences in mortality occurred among the 65 years and older age group: in CEPAC-US, projected mortality for MSM on ART (3150–3680 deaths per 100 000 PYs in 2021–2031) and off ART (4580–5320 deaths per 100 000 PYs in 2021–2031) were greater than projected mortalities via PEARL (MSM on ART, 2920–3360 deaths per 100 000 PYs in 2021–2031; MSM off ART, 3500–3560 deaths per 100 000 PYs in 2021–2031) (Figure 4D).

Sensitivity Analyses

Influential CEPAC-US parameters regarding the number of MSM on ART in 2031 were the number and ages of MSM on ART at model start (2014) and the percent of MSM who ever

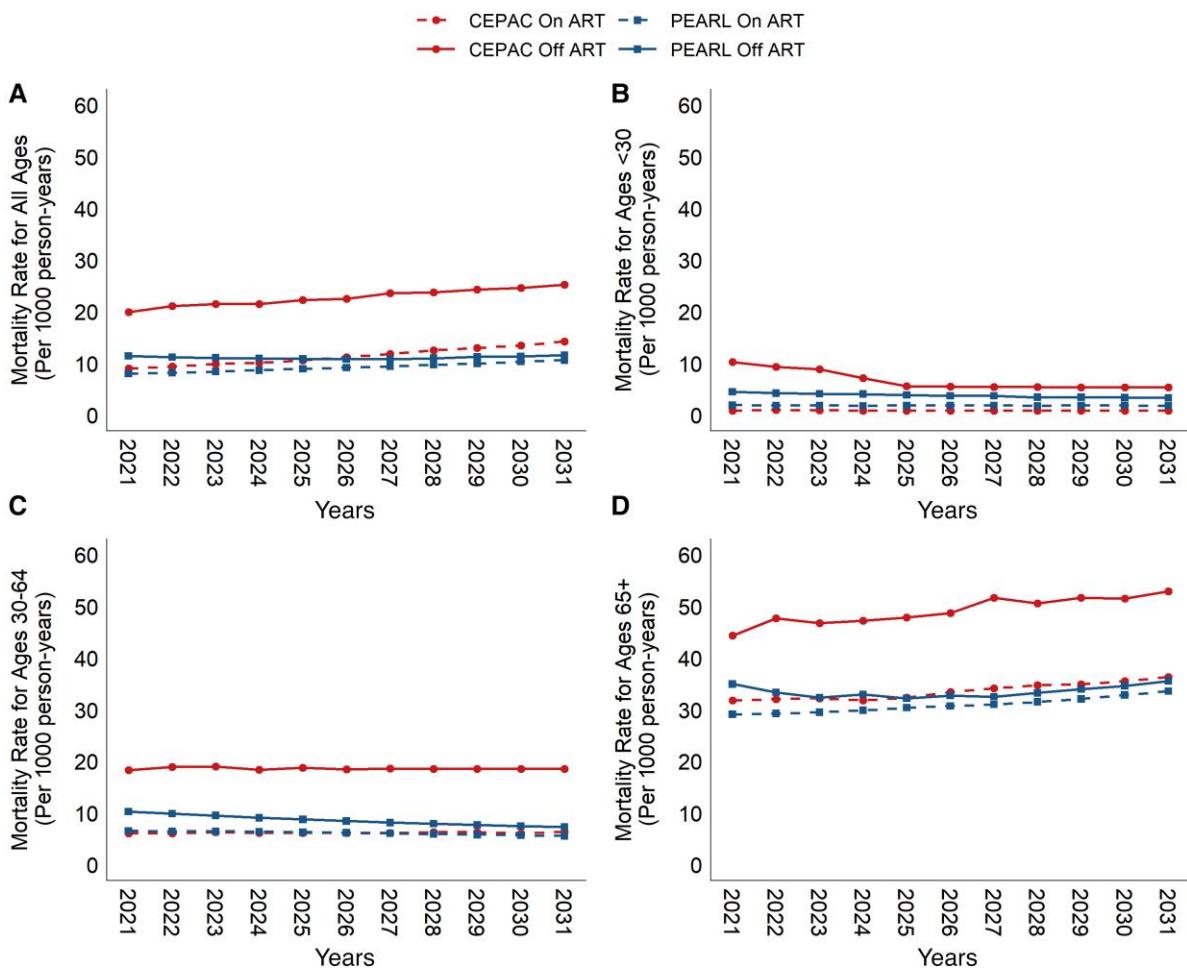


Figure 4. The projected mortality among MSM on and off ART from the CEPAC-US and PEARL models (2021–2031). *A*, The projected mortality rates for all MSM diagnosed with HIV from the CEPAC-US (red circle) and PEARL (blue square) models with mortality rates among MSM on ART (dashed line) and off ART (solid line); mortality rates increase over the decade given that a greater percentage of the populations are of older ages. Age-stratified mortality rates are displayed for MSM <30 years of age (*B*), 30–64 years of age (*C*), and 65+ years of age (*D*). In both models, there is always at least a 4:1 ratio of MSM on ART compared with off ART. Abbreviations: ART, antiretroviral therapy; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; HIV, human immunodeficiency virus; MSM, men who have sex with men; PEARL, ProjEcting Age, multimorbidity, and polypharmacy model.

disengage from care (Figure 5A). In a similar comparison, the most influential parameter in PEARL was the annual number of ART initiators (Figure 5A). The mean age of all ART users was most influential on the proportion of MSM on ART who are 65 years or older in 2031 in CEPAC-US, whereas the mean age of ART initiators was most influential in PEARL (Figure 5B). Varying other input parameters by $\pm 20\%$ resulted in less than a 5% change from base case outcomes in both directions (Supplementary Figures 1 and 2).

DISCUSSION

We used two independent simulation models and projected substantial growth in the population of aging MSM with HIV on ART in the United States over the next 15 years. Despite underlying differences in parameters, structure, and assumptions

of the CEPAC-US and PEARL models, we projected more than twice the number of MSM older than 65 years on ART by 2031 compared with 2021 with both models. Despite new HIV infections occurring most frequently among MSM at younger ages, these model-based estimates underscore the dramatic growth and aging that should be anticipated among MSM with HIV in the United States over the next decade (the largest subgroup of people living with HIV), which is likely to be accompanied by a rise in multimorbidity, polypharmacy, and complexity of medical decision making. Quantitative projections such as these are essential to assist in health systems planning and to underscore the unique needs and importance of this growing population for clinicians and public health professionals.

Although previously published modeling projections suggest that the number of people with HIV may decline over time [11, 37], our model-based findings indicate a further rise in

Table 1. Population Size Outcomes Projected With CEPAC-US and PEARL Models in Selected Years

Population	2015		2021		2031	
	CEPAC-US	PEARL	CEPAC-US	PEARL	CEPAC-US	PEARL
MSM with undiagnosed HIV	104 540	...	50 720	...	39 380	...
MSM with HIV initiating ART annually	24 390	22 210	20 890	22 120	15 530	22 580
MSM with HIV on ART	403 490	All MSM, 309 380 Black, 104 810 White, 131 850 Hispanic, 72 800	498 120	All MSM, 423 100 Black, 151 330 White, 160 390 Hispanic, 111 420	548 800	All MSM, 599 410 Black, 223 420 White, 180 540 Hispanic, 196 030
MSM with diagnosed HIV disengaged from care ^a	107 670	All MSM, 26 720 Black, 9060 White, 11 620 Hispanic, 6070	134 270	All MSM, 26 910 Black, 9220 White, 10 950 Hispanic, 6730	151 690	All MSM, 22 900 Black, 7340 White, 8490 Hispanic, 7070

Abbreviations: ART, antiretroviral therapy; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; MSM, men who have sex with men; PEARL, ProjEcting Age, multimoRbidity, and poLypharmacy model.

^aDisengaged from care was defined in CEPAC-US as 1 or more years with no CD4 or HIV RNA results, or clinical visits, and more conservatively in PEARL as 2 or more years with no CD4 or HIV RNA results.

the population over the next decade, accompanied by substantial aging. These findings are consistent with epidemiologic findings that people with HIV are likely to experience life expectancies similar to people without HIV, given significant reductions in HIV-related mortality over the past decade [38–40]. With increasing life expectancy, we can expect an overall increase in the numbers of people living with HIV despite declining HIV incidence in the United States and a greater proportion of MSM with HIV aged 65 years and older compared with the general population [41, 42].

While both models project an increasing population of MSM with HIV in the United States, we found a steeper rise projected with the PEARL model compared with CEPAC-US, in particular among MSM aged 40–59 years. In detailed comparisons of the models' parameters and assumptions, we determined influential factors, including estimated rates of disengagement/reengagement in care and mortality, and identified important features of how these parameters are defined and calibrated in each model.

The engagement/disengagement rates in CEPAC-US are modeled as a function of adherence to ART and calibrated to CDC data [23]. CEPAC-US assumes stable rates of disengagement from care so that approximately 20% of MSM ever on ART would experience at least a one year disengagement from care at some point over their lifetime. In contrast, the functions describing disengagement rates among Black, White, and Hispanic MSM in PEARL rely on available NA-ACCORD data, including a conservative estimate in identifying care disengagement (ie, two or more years with no CD4 or viral load results) [15]. Model projections reflect a lower rate of disengagement in care via the PEARL model compared with CEPAC-US, which leads to a steeper increase in the projected number of MSM receiving ART in the PEARL model. Each model follows a unique set of assumptions based on available data to define and parameterize engagement in HIV care,

which provides valuable insights regarding the potential future growth and aging of the MSM population on ART in the United States.

We also examined the influence of mortality rates on the model projections. In detailed comparisons, we found that both models projected similar mortality among MSM younger than 65 years and higher mortality among MSM off ART than on ART. However, CEPAC-US projected higher overall mortality rates for MSM with HIV older than 65 years compared with PEARL. If mortality rates among older MSM with HIV are closer to CEPAC-US projections, which account for an increased burden of tobacco-related illnesses and other noncommunicable diseases associated with aging [27, 43], then the total number of MSM with HIV on ART may grow more slowly due to competing risks of death from other causes. Alternatively, the PEARL projections, which are based on NA-ACCORD data, suggest gradual reductions in age-specific mortality rates among PWH over time that are in line with increased life expectancy in the “treat all” era [39]. These results are limited by the small sample size and high uncertainty in observed mortality among persons older than 65 years in NA-ACCORD. While projections from each model are not a precise representation of reality, they can inform an expected range for the population size of MSM on ART over the next decade. Such modeling projections can be revised and updated as additional data become available regarding changes in mortality risk in the setting of an increasing prevalence of metabolic syndrome and obesity, less toxic and more effective ART, changes in the racial/ethnic makeup of the epidemic, and differences in access to health care.

Although distinct model structures did not allow for traditional direct comparison, we performed sensitivity analyses to examine the implications of variation in estimates of key parameters in each model, representative of the heterogeneity in the HIV epidemic in the United States [9]. We found that

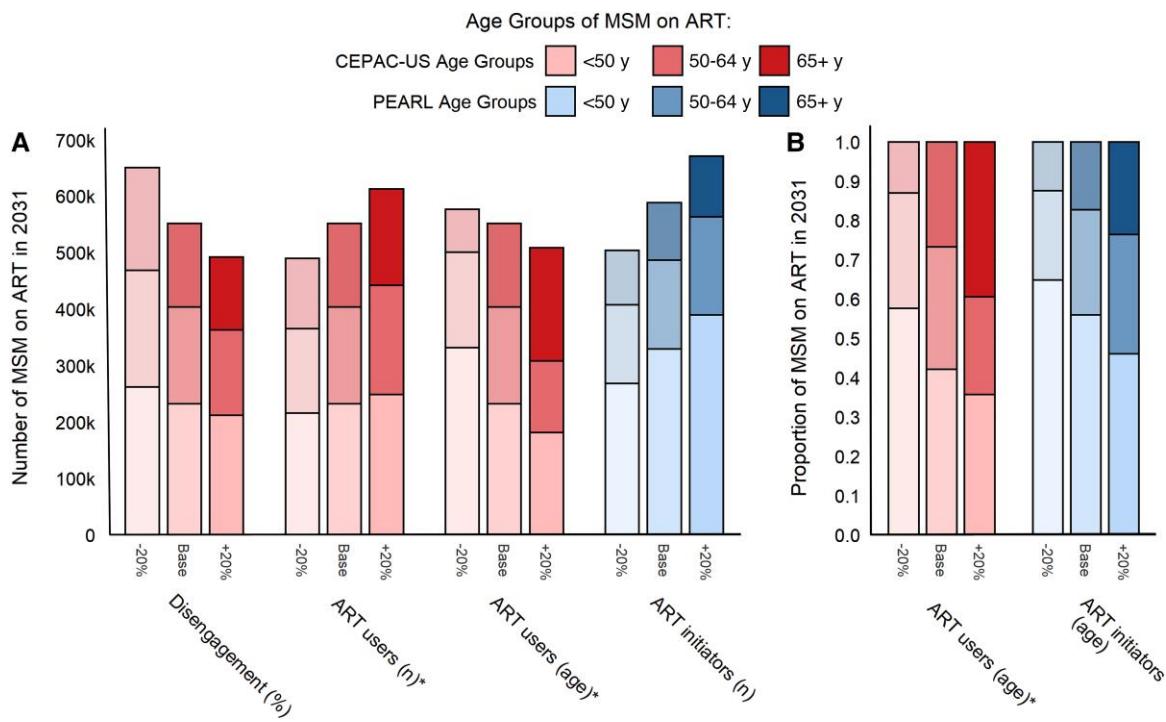


Figure 5. Selected one-way sensitivity analyses on (A) the projected number of MSM on ART in 2031 and (B) the proportion of MSM on ART older than 65 years in 2031. Results are shown for the CEPAC-US (red, left) and PEARL (blue, right) models. The most influential input parameters are displayed along the x-axis. Each parameter is represented with a cluster of three bars, showing the projected results at the base case value (middle), when the input value is -20% of the base case (left), and when the input value is +20% of the base case (right). Asterisks denote parameters that were varied only in the starting year for each model (eg, 2014 in CEPAC-US and 2009 in PEARL); parameters without an asterisk were varied annually (2021–2031). Additional details on one-way sensitivity analyses are reported in the *Supplementary Material*. Abbreviations: ART, antiretroviral therapy; CEPAC-US, Cost-Effectiveness of Preventing AIDS Complications model; MSM, men who have sex with men; PEARL, ProjEcting Age, multimorbidity, and polypharmacy model.

each model was most sensitive to assumptions at model start, including the number and ages of MSM on ART or disengaged from care. This highlights the importance of improving available data regarding age- and subgroup-specific estimates of care indicators from the HIV surveillance system. Calibrating models to capture the population under study is critical; our findings underscore the utility of locally tailored models to represent heterogeneities in HIV epidemiology.

This comparative analysis has several limitations. In this analysis, CEPAC-US outcomes are not stratified by race/ethnicity, which could result in less comprehensive estimates regarding trends in the HIV care continuum and mortality. Although PEARL is populated with data from NA-ACCORD, which represents outcomes from people receiving clinical care, it does not include individual patient-level details of HIV-focused clinical care (eg, frequency of CD4 cell counts). Neither model incorporates the future impact of changing prevention efforts (eg, time-updated PrEP coverage) on HIV transmission or the potential implications of different ART regimens, obesity, or metabolic parameters. CEPAC-US estimated incident HIV cases depending on model-projected viral load within the simulated population, whereas PEARL applied

CDC-estimated new HIV diagnoses to project new ART initiations. Neither model includes the specific impact of the COVID-19 pandemic on new transmissions, diagnoses, engagement in care, or mortality because the decade-long model-based projections are unlikely to be affected by the short-term implications of reduced HIV testing and health care access during the 2020 COVID-19-related lockdowns, as well as the data suggesting COVID-19-related mortality in PWH is low (particularly among the vaccinated) [44, 45].

In conclusion, two independent simulation models projected that the numbers of MSM on ART in the United States will continue to grow over the next decade, given recent trends in the HIV care continuum, with more than 100 000 MSM older than 65 years on ART by 2031. With multimorbidity already common and increasing, these results underscore the need to improve and expand the broad range of clinical care, management, and resources available to people aging with HIV.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not

copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Potential conflicts of interest. K. N. A. reports serving on the Scientific Advisory Board for Trio Health Inc; and as a consultant to the All of Us Study (National Institutes of Health). P. F. R. received consultancy payments from Gilead and Johnson and Johnson. K. A. G. receives consultancy payments from UpToDate, Teach for America, and the Aspen Institute. None of these have direct relation to, or impact on, the findings presented here. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Cahill S, Geffen S, Samantha M, Taylor SW. Strategies to improve the health of older adults living with HIV. Boston (MA): National Center for Innovation in HIV, 2016.
2. Joint United Nations Program on HIV and AIDS. HIV and aging: a special supplement to the UNAIDS report on the global AIDS epidemic 2013. https://www.unaids.org/sites/default/files/media_asset/20131101_JC2563_hiv-and-aging_en_0.pdf. Accessed 19 December 2022.
3. Mahy M, Autenrieth CS, Stanecki K, Wynd S. Increasing trends in HIV prevalence among people aged 50 years and older: evidence from estimates and survey data. *AIDS* 2014; 28(Suppl 4):S453–9.
4. Mitsch A, Singh S, Li J, Balaji A, Linley L, Selik R. Age-associated trends in diagnosis and prevalence of infection with HIV among men who have sex with men—United States, 2008–2016. *MMWR Morb Mortal Wkly Rep* 2018; 67:1025–31.
5. Singh S, Song R, Johnson AS, McCray E, Hall HI. HIV Incidence, prevalence, and undiagnosed infections in US men who have sex with men. *Ann Intern Med* 2018; 168: 685–94.
6. Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2019. HIV Surveillance Report 2019; Vol 32. cdc.gov/hiv/library/reports/hiv-surveillance/vol-32/index.html. Accessed 19 December 2022.
7. Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2016. HIV Surveillance Supplemental Report 2018; Vol 23, No. 4. <https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Accessed 19 December 2022.
8. Grey JA, Bernstein KT, Sullivan PS, et al. Estimating the population sizes of men who have sex with men in US states and counties using data from the American community survey. *JMIR Public Health Surveill* 2016; 2:e14.
9. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA* 2016; 316:1093–103.
10. Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling good research practices—overview: a report of the ISPOR-SMDM modeling good research practices task force-1. *Med Decis Making* 2012; 32:667–77.
11. Shiels MS, Islam JY, Rosenberg PS, Hall HI, Jacobson E, Engels EA. Projected cancer incidence rates and burden of incident cancer cases in HIV-infected adults in the United States through 2030. *Ann Intern Med* 2018; 168: 866–73.
12. Zang X, Krebs E, Min JE, et al. Development and calibration of a dynamic HIV transmission model for 6 US cities. *Med Decis Making* 2020; 40:3–16.
13. Nosyk B, Zang X, Krebs E, et al. Ending the epidemic in America will not happen if the status quo continues: modeled projections for human immunodeficiency virus incidence in 6 US cities. *Clin Infect Dis* 2019; 69:2195–8.
14. Walensky RP, Paltiel AD, Losina E, et al. The survival benefits of AIDS treatment in the United States. *J Infect Dis* 2006; 194:11–9.
15. Kasai P, Stewart C, Humes E, et al. Projecting the age-distribution of men who have sex with men receiving

- HIV treatment in the United States. *Ann Epidemiol* **2021**; 65:46–55.
16. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Department of Health and Human Services. <https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf>. Accessed 19 December 2022.
 17. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, 2nd ed. <https://www.who.int/hiv/pub/arv/arv-2016/en/>. Accessed 19 December 2022.
 18. Jewell BL, Mudimu E, Stover J, et al. Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: results from multiple mathematical models. *Lancet HIV* **2020**; 7:e629–40.
 19. Borre ED, Hyle EP, Paltiel AD, et al. The clinical and economic impact of attaining national HIV/AIDS strategy treatment targets in the United States. *J Infect Dis* **2017**; 216:798–807.
 20. Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med* **2001**; 344:824–31.
 21. Walensky RP, Paltiel AD, Losina E, et al. Test and treat DC: forecasting the impact of a comprehensive HIV strategy in Washington DC. *Clin Infect Dis* **2010**; 51:392–400.
 22. Walensky RP, Ross EL, Kumarasamy N, et al. Cost-effectiveness of HIV treatment as prevention in sero-discordant couples. *N Engl J Med* **2013**; 369:1715–25.
 23. Ross EL, Weinstein MC, Schackman BR, et al. The clinical role and cost-effectiveness of long-acting antiretroviral therapy. *Clin Infect Dis* **2015**; 60:1102–10.
 24. Sax PE, Meyers JL, Mugavero M, Davis KL. Adherence to antiretroviral treatment and correlation with risk of hospitalization among commercially insured HIV patients in the United States. *PLoS One* **2012**; 7:e31591.
 25. Johns Hopkins University, Center for Analysis and Management of Multicenter AIDS Cohort Study. Multicenter AIDS Cohort Study (MACS) public dataset. <https://statepi.jhsph.edu/mwccs/>. Accessed 19 December 2022.
 26. Jha P, Ramasundarahettige C, Landsman V, et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* **2013**; 368:341–50.
 27. Reddy KP, Parker RA, Losina E, et al. Impact of cigarette smoking and smoking cessation on life expectancy among people with HIV: a US-based modeling study. *J Infect Dis* **2016**; 214:1672–81.
 28. Thun MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med* **2013**; 368:351–64.
 29. Mdodo R, Frazier EL, Dube SR, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. *Ann Intern Med* **2015**; 162:335–44.
 30. Jenness SM, Goodreau SM, Rosenberg E, et al. Impact of the Centers for Disease Control's HIV preexposure prophylaxis guidelines for men who have sex with men in the United States. *J Infect Dis* **2016**; 214:1800–7.
 31. Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2014–2018. HIV Surveillance Supplemental Report 2020, Vol 25, No. 1. <https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Accessed 19 December 2022.
 32. Rebeiro PF, Gange SJ, Horberg MA, et al. Geographic variations in retention in care among HIV-infected adults in the United States. *PLoS One* **2016**; 11:e0146119.
 33. Zheng Y, Hughes MD, Lockman S, et al. Antiretroviral therapy and efficacy after virologic failure on first-line boosted protease inhibitor regimens. *Clin Infect Dis* **2014**; 59:888–96.
 34. Massachusetts General Hospital. CEPAC model. <https://www.massgeneral.org/medicine/mpec/research/cpac-model>. Accessed 19 December 2022.
 35. North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). <https://naaccord.org/>. Accessed 19 December 2022.
 36. Johns Hopkins University. The PEARL model. <https://pearlhivmodel.org/>. Accessed 19 December 2022.
 37. Shah M, Perry A, Risher K, et al. Quantifying the impact of the national HIV/AIDS strategy targets for improved HIV care engagement in the US: a modelling study. *Lancet HIV* **2016**; 3:e140–6.
 38. Marcus JL, Leyden WA, Alexeef SE, et al. Comparison of overall and comorbidity-free life expectancy between insured adults with and without HIV infection, 2000–2016. *JAMA Netw Open* **2020**; 3:e207954.
 39. Edwards JK, Cole SR, Breger TL, et al. Five-year mortality for adults entering human immunodeficiency virus care under universal early treatment compared with the general US population. *Clin Infect Dis* **2022**; 75:867–74.
 40. Bosh KA, Johnson AS, Hernandez AL, et al. Vital signs: deaths among persons with diagnosed HIV infection, United States, 2010–2018. *MMWR Morb Mortal Wkly Rep* **2020**; 69:1717–24.
 41. Bosh KA, Hall HI, Eastham L, Daskalakis DC, Mermin JH. Estimated annual number of HIV infections—United States, 1981–2019. *MMWR Morb Mortal Wkly Rep* **2021**; 70:801–6.

42. Vespa J, Medina L, Armstrong DM. Demographic turning points for the United States: population projections for 2020 to 2060. Current population reports, report No. P25-1144. Washington, DC: US Census Bureau, 2020.
43. Wong C, Gange SJ, Moore RD, et al. Multimorbidity among persons living with human immunodeficiency virus in the United States. *Clin Infect Dis* 2018; 66: 1230–8.
44. Dzinamarira T, Murewanhema G, Chitungo I, et al. Risk of mortality in HIV-infected COVID-19 patients: a systematic review and meta-analysis. *J Infect Public Health* 2022; 15:654–61.
45. Meyer D, Slone SE, Ogungbe O, Duroseau B, Farley JE. Impact of the COVID-19 pandemic on HIV healthcare service engagement, treatment adherence, and viral suppression in the United States: a systematic literature review. *AIDS Behav* 2023; 27:344–57.