

An Internally Consistent Model of HIV Burden for Countries with Vital Registration and Case
Notification Data

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Abstract

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This thesis aims to provide a novel, internally consistent approach to estimating HIV morbidity and mortality in countries with both vital registration and case notification data. In most high-income countries, case notifications and deaths recorded in vital registration serve as the primary data sources for monitoring the course of the HIV epidemic. However, past modelling efforts have encountered difficulty reconciling these two sources; achieving a good fit to diagnosis data has resulted in underestimating mortality, and vice versa. These incongruities have led to disconnected approaches to modelling HIV burden, producing morbidity and mortality estimates that are not internally consistent. This study extended an existing modelling framework, the Estimation and Projection Package Age/Sex Model (EPP-ASM), to develop internally consistent estimates of HIV burden in countries with case notification and high-quality

vital registration data. EPP-ASM was modified to carry out Bayesian inference on both HIV transmission dynamics and an adjustment to off-antiretroviral therapy (ART) HIV mortality rate. Three structural assumptions on the relationship between off-ART HIV mortality rate and ART coverage were considered. Vital registration data stratified by age and sex and case notifications were incorporated into the likelihood calculation within the model. EPP-ASM was fit for the Netherlands and Australia, and in-sample predictive validity was assessed using coverage of posterior predictive intervals and mean absolute error. EPP-ASM with no adjustment to off-ART mortality rate demonstrated the best model performance, and out-performed the Cohort Incidence Bias Adjustment method used by the Global Burden of Disease study. Future investigation of adjustments to HIV mortality rate and extension to additional locations could provide further insight into reconciliation of diagnosis and mortality data.

Introduction

Since the identification of HIV as a critical global threat to human health, modelling of the HIV epidemic has provided key insight on trends in disease burden and allowed for planning of prevention and treatment measures.¹⁻³ In many high-income countries, reported diagnoses and cause-specific deaths recorded in vital registration are available for monitoring the course of the epidemic. In contrast, in most countries with generalized epidemics, reliable registration systems do not exist and instead, sentinel surveillance and population-based seroprevalence surveys are used as the primary sources to monitor HIV burden. Groups that create global estimates of HIV morbidity and mortality have developed different models to estimate HIV burden in these two sets of countries. The UNAIDS Reference Group on Estimation, Modelling, and Projections has utilized the Case Surveillance and Vital Registration (CSAVR) model within the Spectrum software to create estimates of HIV burden for countries with such data.^{4,5} The Global Burden of Disease (GBD) Study has used a process called Cohort Incidence Bias Adjustment (CIBA) to generate estimates of HIV burden using deaths recorded in vital registration in countries with available data.^{6,7} For countries with generalized epidemics, both groups have used the Estimation and Projection Package (EPP) to develop estimates of HIV incidence and prevalence.^{8,9}

Both UNAIDS and GBD modelling strategies have employed a cohort component model from the Spectrum software to generate age- and sex-specific estimates of HIV deaths for all countries.⁵ Spectrum works by aging a population over time while applying disease incidence, progression, and mortality.⁹ Spectrum relies on on- and off-antiretroviral therapy (ART) mortality rates to generate HIV death estimates from projected people living with HIV (PLHIV) at each time step. GBD has modelled on-ART mortality with data from the Antiretroviral Therapy Cohort Collaboration (ART-CC) and off-ART mortality by fitting to survival data from

a group of 13 cohorts.^{9, 11, 12} Using these mortality rates along with annual incidence rate derived from case notifications data in CSAVR overshoots the number of HIV/AIDS deaths observed in vital registration data, especially after rollout of ART in the 1990s.¹¹ Likewise, incidence estimates created through back-calculating from vital registration data in CIBA using survival patterns derived from these mortality rates typically undershoot case notification data. These discrepancies indicate that mortality and disease progression rates estimated from cohort studies in conjunction with modelled treatment coverage do not align with observed mortality and incidence. This implies that model assumptions on HIV survival may not accurately reflect the entire population of people living with HIV in high-income countries.

This difficulty in reconciling incidence and mortality data has resulted in fragmented approaches to estimating HIV burden. The GBD study has used CIBA to generate incidence estimates to input to Spectrum. Spectrum provides final HIV prevalence results, but Spectrum-estimated incidence is then scaled up to case notification data, treating the notifications as a minimum bound.^{9, 12} Spectrum mortality results are not used; rather, smoothed vital registration data provide final HIV/AIDS mortality results. These discrepancies mean that, though final incidence and mortality results typically align well with data, estimated prevalence is not internally consistent with these measures.

The disconnects in modelling for high-income countries underscore the value of developing an internally consistent method for estimating HIV burden in these countries. The Estimation and Projection Package Age/Sex Model (EPP-ASM) provides a framework that can be used to create internally consistent estimates of HIV incidence, prevalence, and mortality.¹³ EPP-ASM is a natural history model that combines the population projection of Spectrum with the Bayesian inference of transmission dynamics of the EPP model. Similar to Spectrum, EPP-

ASM simulates a population over time while applying HIV infection, progression, and mortality, so EPP-ASM outputs include HIV incidence, prevalence, and deaths. In countries with generalized epidemics, EPP-ASM has proved to be effective at fitting to surveillance data.¹³ With this project, I propose to develop functionality in EPP-ASM for simultaneously fitting to deaths recorded in vital registration stratified by five-year age group and case notification data. This will allow EPP-ASM to be used to produce internally consistent estimates of HIV burden in high-income countries and to provide a harmonized modelling strategy across countries. A component of this analysis will involve testing adjustments to input mortality rates in order to reach a closer fit to input data. Though this model is intended for use across a large group of countries, I will limit this analysis to the Netherlands and Australia, since each country has 20 or more years of case notification data and high-quality vital registration data to allow for model validation. To achieve these goals, this study includes the following aims:

1. Incorporate vital registration and case notification data into the likelihood calculation in EPP-ASM
2. Parameterize adjustments to off-ART mortality rates
3. Incorporate a parametric model for HIV incidence rate into EPP-ASM
4. Fit the EPP-ASM model in the Netherlands and Australia and evaluate model fit

Methods

HIV mortality rate estimation

EPP-ASM requires HIV mortality rates stratified by age, sex, CD4 count, and treatment status. For this thesis, I used HIV mortality rates estimated for the Global Burden of Disease study. On-ART mortality rates were estimated using cohort data from high-income countries provided by ART-CC.¹⁴ These rates were adjusted for loss to follow-up using the methods developed by Verguet and colleagues.¹⁵ Off-ART mortality rates were estimated along with disease progression by optimizing a fit to cohort survival data.¹²

EPP-ASM Model

The EPP-ASM model extends the existing functionality of the EPP model, allowing for inference of transmission parameters while representing the changing demographics of the HIV epidemic over time. For each iteration of EPP-ASM, a set of parameters on force of infection, defined as the expected number of new infections for each prevalent case, and age distribution of incidence are sampled from prior distributions. A population ages 15+ stratified by age, sex, and HIV status is projected over time using input fertility, survival, and migration while applying HIV incidence, disease progression, and mortality. New infections are allocated using female-to-male and age-specific incidence rate ratios, which are calculated using previous GBD HIV estimates and are held constant over time.⁷ The likelihood of observed diagnoses and AIDS deaths given the simulated estimates is calculated and combined with the prior probability of the parameters to determine the posterior probability of a given set of parameters. All inputs to EPP-ASM are described in detail in Table 1.

Input	Description	Source
Population	Annual population stratified by single year of age and sex, ages 15-80+	Global Burden of Disease ¹⁶
Fertility rate	Annual fertility rate stratified by 5-year age group, ages 15-49	Global Burden of Disease ¹⁶
HIV-free survival rate	Survival rate excluding HIV-specific mortality stratified by single year of age and sex, ages 15-80+	Global Burden of Disease ¹⁷
Migration	Annual net migrants stratified by single year of age and sex, ages 15-80+	Global Burden of Disease (unpublished estimates)
Sex ratio at birth	Annual male-to-female ratio at birth	Global Burden of Disease ¹⁶
CD4 progression	Annual probability of progressing to the next lower CD4 group among untreated PLHIV, stratified by 10-year age group and 6 CD4 groups, estimated by optimizing a fit to cohort survival in conjunction with off-ART mortality	Global Burden of Disease ¹⁸
Off-ART mortality	Annual probability of death due to HIV among untreated PLHIV, stratified by 10-year age group and 7 CD4 groups, estimated by optimizing a fit to cohort survival in conjunction with CD4 progression	Global Burden of Disease ¹⁸
On-ART mortality	Annual probability of death due to HIV among treated PLHIV, stratified by 10-year age group, sex, and 7 CD4 groups, estimated using a model fit to cohort data from ART-CC	Global Burden of Disease ¹⁸
ART coverage	Either a number of individuals or proportion of PLHIV receiving ART in a given year, stratified by sex	UNAIDS ¹⁹
Vital registration data	Government records of annual HIV-specific deaths,	Global Burden of Disease ¹⁸

	stratified by 5-year age group and sex. These data are adjusted for misclassification of AIDS deaths and redistribution of uninformative coding.	
Case notification data	Reports of new HIV/AIDS diagnoses recorded in government registries	Netherlands – Stitching HIV Monitoring Report ²⁰ Australia – University of New South Wales Annual Surveillance Report ²¹

Table 1. Summary of EPP-ASM Inputs

Parameterization of HIV mortality rates

Allowing for flexibility in input HIV mortality parameters can aid in reconciling incongruities in case notification and vital registration data. In order to adjust on- and off-ART mortality parameters, reasonable structural assumptions on the parameters must be determined. It is theorized that off-ART mortality has an inverse relationship with ART coverage, because as treatment becomes more widely available those who are at highest risk of dying become more likely to reach treatment. Therefore, adjustments to off-ART mortality rates are parameterized so that they decrease with increasing ART coverage. Three models are considered, one in which off-ART mortality has a linear relationship with ART coverage, one with an exponentially decaying relationship, and one without an adjustment:

$$(1) \quad m_{s,a,t}^* = m_{s,a} \alpha \left[1 - \left(\frac{A_{s,a,t}}{I_{s,a,t}} \right) \right]$$

$$(2) \quad m_{s,a,t}^* = m_{s,a} e^{-\alpha \frac{A_{s,a,t}}{I_{s,a,t}}}$$

$$(3) \quad m_{s,a}^* = m_{s,a}$$

Where $A_{s,a,t}$ is the HIV-positive population on treatment for a given age a and sex s in year t , $I_{s,a,t}$ is the entire HIV-positive population, $m_{s,a}$ is the input off-ART mortality rate derived from cohort studies, $m_{s,a}^*$ is the adjusted off-ART mortality rate used in EPP-ASM, and α is a scalar drawn from a prior distribution.

I chose a prior distribution for α based on previous testing and model vetting. The GBD study previously multiplied off-ART mortality rates derived from cohort studies by half in order to better align Spectrum results with prevalence data from the NHANES survey in the United States.^{9,12} I used a prior based on past GBD modelling with a mean of two, defined as

$$\alpha \sim \text{Exp}(2)$$

The exponential distribution is used to limit scalar values to be greater than zero, and a rate of 2 (analogous to a mean of 0.5) is used to align with the previous adjustment used for GBD.

Incorporation of vital registration data in EPPASM

In order to create morbidity results that are consistent with mortality data, the likelihood of vital registration data given estimated deaths is calculated in each iteration of EPP-ASM. For each model simulation, expected deaths D are generated by applying mortality rates to the simulated population

$$D_{s,a,t} = m_{s,a,t}^* [I_{s,a,t} - A_{s,a,t}] + n_{s,a} A_{s,a,t}$$

Where $n_{s,a}$ is the on-ART mortality rate. A Poisson distribution is used as the likelihood for vital registration data $VR_{s,a,t}$ given the expected number of deaths

$$VR_{s,a,t} \sim \text{Poisson}(D_{s,a,t})$$

Incorporation of case notification data in EPP-ASM

CSAVR functionality has previously been incorporated into EPPASM.²² Three parametric models have been defined for generating HIV incidence rate: a single logistic model and a double logistic model for directly modelling incidence rate and a logistic model for modelling force of infection.²³ I have utilized the model parameterizing force of infection in order to more closely align with HIV modelling in countries with generalized epidemics.

A Poisson likelihood will be used with the case notification data C given expected diagnoses G in each simulation of EPP-ASM

$$C_t \sim \text{Poisson}(G_t)$$

In order to calculate G_t it is necessary to add a lag to estimated incidence to approximate year of diagnosis. Previous studies have used a number of methods to estimate the gap between incidence and diagnosis in high-income countries, most relying on data on CD4 count at diagnosis and assumptions on disease progression.^{24,25} Diagnoses for an incidence cohort in year k in EPP-ASM are distributed across the following years based on estimates of the mean lag to diagnosis lag_k developed by van Sighem and colleagues.²⁵ This model used data on new HIV diagnoses by CD4 count stratum from the Netherlands to infer annual diagnosis rate with a piecewise linear function over time based on the increasing availability of HIV testing over time. A gamma function with shape lag_k is used to model the distribution of diagnoses across the years following infection, aligning with the CSAVR methodology of estimating diagnosis rate as a function of the cumulative distribution function of gamma.^{11,22} The incident cases in year k reported in year t is defined as

$$G_{k,t} = G_k * f(t - k)$$

Where $f(x)$ is the density function for a Gamma distribution with shape lag_k and rate = 1.

Diagnoses will then be calculated as the summation of the proportion of new infections from all previous incidence cohorts $k = 1970 \dots t$ that were diagnosed in year t

$$G_t = \sum_{k=1970}^t G_{k,t}$$

Model validation and analysis

EPP-ASM was fit for the Netherlands and Australia. Uncertainty estimates were generated by running 1,000 draws of the model while varying the input HIV-free survival, fertility, CD4 progression, and HIV mortality parameters. For each draw of EPP-ASM, the Incremental Mixture Importance Sampling (IMIS) algorithm was used to approximate the posterior distribution, and one sample was taken from the posterior distribution.²⁶ IMIS was run with 10,000 initial samples and 1,000 at each following iteration.

In-sample predictive validity was assessed by calculating coverage of 95% posterior predictive intervals. For each mortality data point, the posterior predictive distribution was constructed by sampling a value for each draw from a Poisson distribution with lambda given by modeled deaths. Mean absolute error (MAE) was also calculated and compared across models. Measures of predictive validity were only calculated using observed and predicted mortality by age and sex; case notifications were not used to validate incidence results due to uncertainty in actual lag between infection and diagnosis.

Results

Model Comparison

Figures 1 and 2 show the fit to vital registration data across all ages for the three EPP-ASM models and Spectrum deaths adjusted using CIBA (labelled CIBA/Spectrum) in Australia and the Netherlands, respectively. A great degree of variation is apparent across the versions of EPP-ASM in the two countries. The EPP-ASM model with no mortality rate adjustment closely aligned with the peak of vital registration data for men in Australia, but underestimated the peak years of mortality for men in the Netherlands. This model slightly overestimated deaths in women in Australia prior to the rollout of ART and underestimated them thereafter, but provided a close fit to the data for women in the Netherlands. The model with a linear mortality rate adjustment produced a reasonable fit to peak mortality in the Netherlands, though it overestimated deaths in the 2000s, especially for women. However, it generated results that lacked face validity in Australia, estimating nearly zero deaths for both sexes until after the introduction of ART. The EPP-ASM model with an exponentially decaying mortality rate adjustment produced a close fit to the data in the Netherlands. Conversely, in Australia it overshot deaths in the pre-ART era and subsequently underestimated deaths following the introduction of ART. In both countries, the models followed male death data more closely than female.

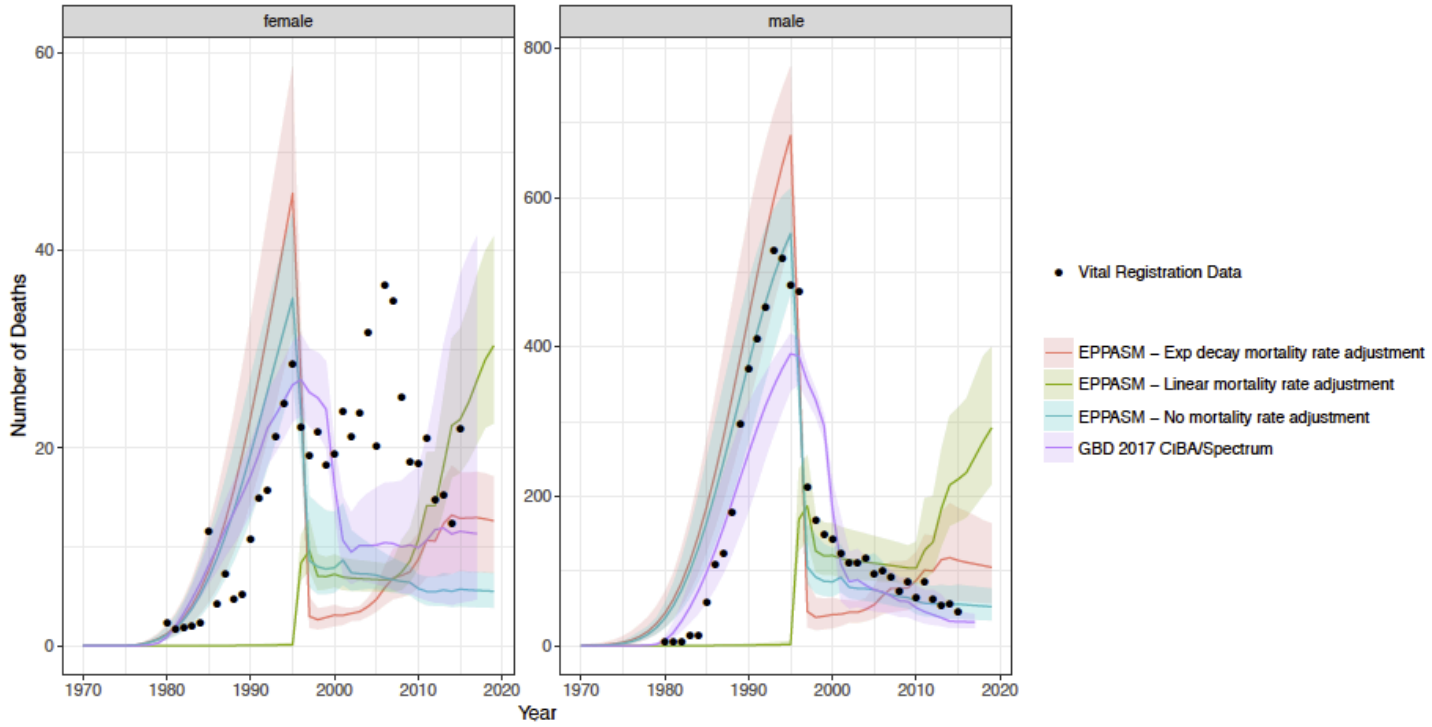


Fig. 1: Ages 15+ HIV Death Estimates for Australia

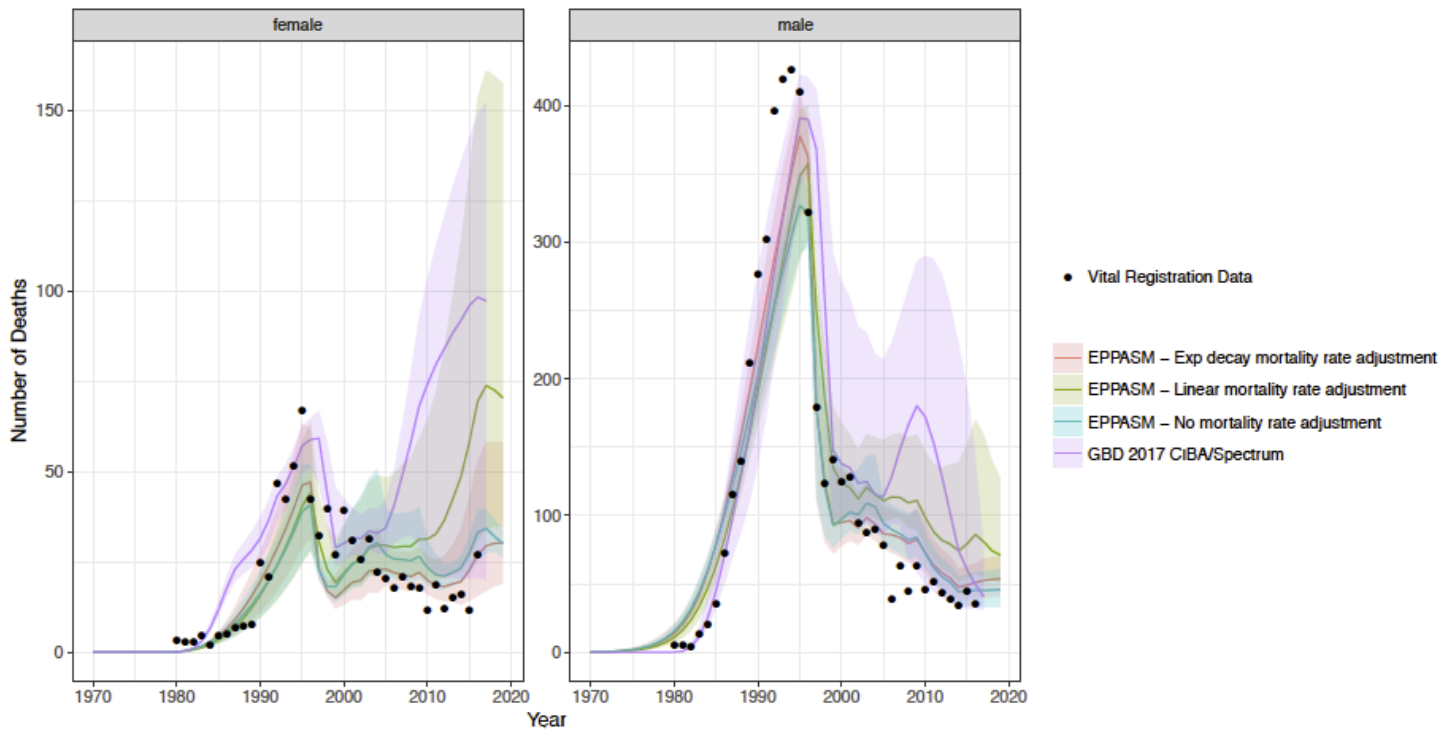


Fig. 2: Ages 15+ HIV Death Estimates for Netherlands

Table 2 provides the posterior means for the parameter α for each model, and Figure 3 illustrates the resulting adjustment to off-ART mortality as a function of the proportion of PLHIV on ART. For the EPP-ASM model with a linear mortality rate adjustment, the mean of the posterior distribution for the Netherlands was somewhat higher than the prior of 0.5, whereas the mean of the posterior in Australia fell to extremely low numbers, resulting in nearly zero estimated deaths before the introduction of ART. The posterior mean of the EPP-ASM model with an exponentially decaying mortality rate adjustment was substantially higher than the prior in both countries, representing a sharper decline in mortality rate with increasing ART coverage.

Location	Model	Posterior Mean
Australia	Linear mortality rate adjustment	0.000118
	Exp decay mortality rate adjustment	3.13
Netherlands	Linear mortality rate adjustment	0.690
	Exp decay mortality rate adjustment	2.88

Table 2. Posterior Mean for the Off-ART Mortality Adjustment Parameter α

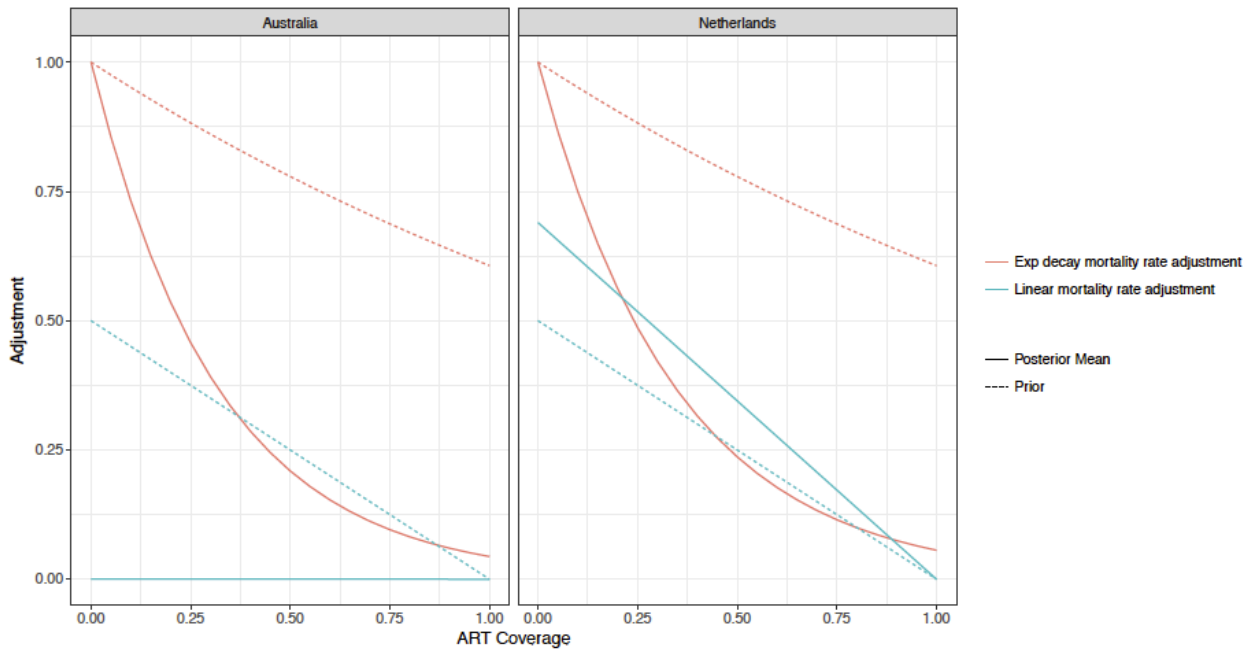


Fig. 3: Prior and Posterior Off-ART Mortality Adjustment

Measures of model fit are provided in Table 3. In Australia, GBD 2017 CIBA/Spectrum results had the lowest MAE and the best posterior predictive interval coverage, with 95% predictive intervals including observed mortality in 66.1% of cases. The EPP-ASM model with no mortality rate adjustment also had predictive interval coverage greater than 60% and similar MAE. In the Netherlands, the EPP-ASM model with an exponentially decaying mortality rate adjustment had the lowest MAE, though the EPP-ASM model with no mortality rate adjustment was only slightly higher. However, the EPP-ASM model with a linear mortality rate adjustment had the highest posterior predictive interval coverage, though all EPP-ASM models had similar coverage metrics. The model with the best performance across both countries was EPP-ASM with no mortality rate adjustment. Further analysis and comparisons are performed using that model.

Location	Model	Coverage	MAE (Deaths)
Australia	EPPASM - No mortality rate adjustment	61.6%	3.20
	EPPASM - Linear mortality rate adjustment	27.4%	5.91
	EPPASM - Exp decay mortality rate adjustment	53.7%	4.04
	GBD 2017 CIBA/Spectrum	66.1%	2.98
Netherlands	EPPASM - No mortality rate adjustment	74.2%	2.23
	EPPASM - Linear mortality rate adjustment	74.6%	2.65
	EPPASM - Exp decay mortality rate adjustment	73.5%	2.06
	GBD 2017 CIBA/Spectrum	71.3%	3.40

Table 3. Model Comparison Using In-Sample Measures of Predictive Validity

HIV Mortality Estimates

Both EPP-ASM and CIBA/Spectrum were fit to vital registration data stratified by 5-year age group. Figure 4 shows both-sexes, age-specific comparisons of EPP-ASM with no mortality

rate adjustment, CIBA/Spectrum, and vital registration data for Australia. In the age groups where the majority of HIV deaths occurred, between ages 30-50, EPP-ASM outperformed CIBA/Spectrum, aligning more closely with the peak of deaths recorded in vital registration and declining more sharply following rollout of ART. The peak in deaths estimated by CIBA/Spectrum appeared wider, extending beyond the introduction of ART in the mid-1990s. Both models estimated an early peak in deaths in ages 15-24, with EPP-ASM overshooting the data farther than CIBA/Spectrum. Both models showed a poor fit to data in older ages; EPP-ASM estimated a peak and decline in older ages where it does not exist in the data.

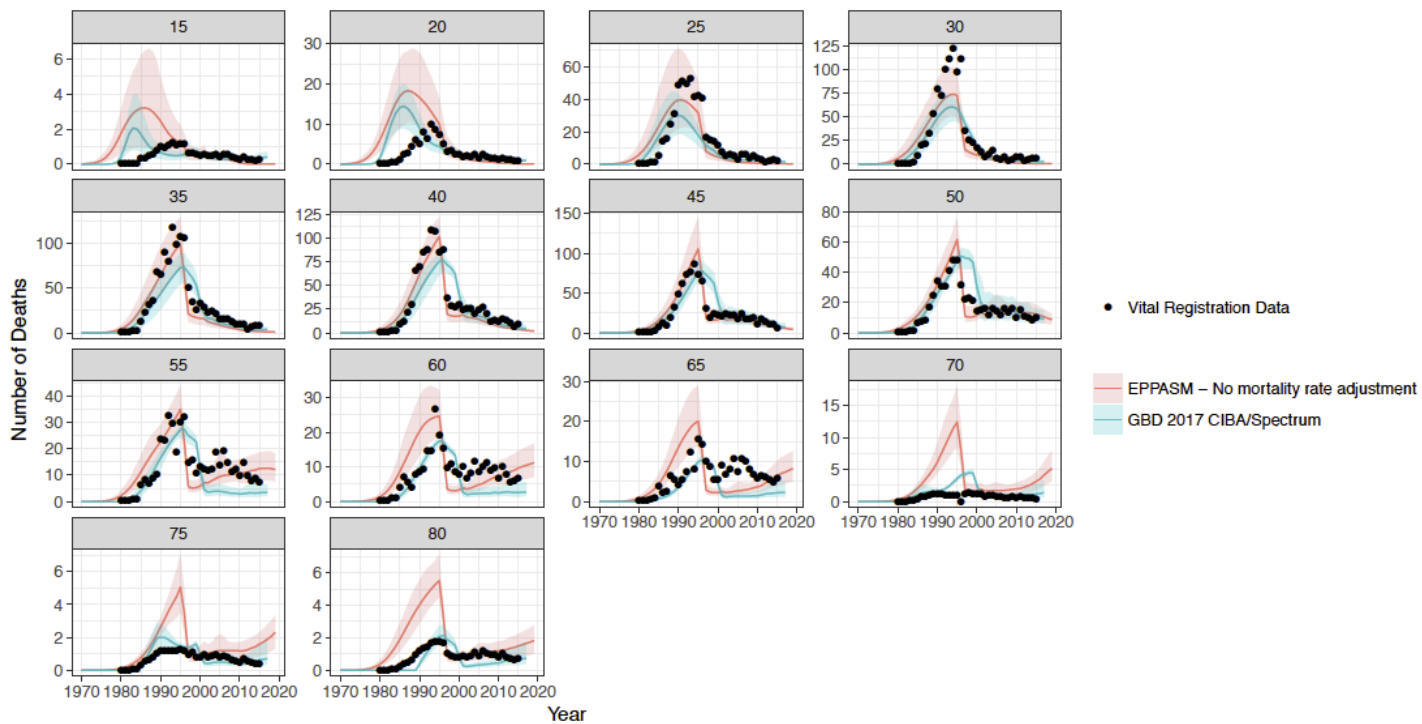


Fig. 4: Estimated HIV Deaths Stratified by 5-Year Age Group for Australia (Both Sexes Combined)

Estimated HIV deaths stratified by 5-year age group for the Netherlands are provided in Figure 5. EPP-ASM again aligned closely with the peak in data in the age groups with highest

burden of HIV, though it underestimated the peak in deaths in ages 25-40. Similar to Australia, EPP-ASM estimated an earlier peak in deaths than the data in ages 15-24. Nonetheless, EPP-ASM performed better than CIBA across almost all age groups in the era of ART. CIBA appeared to create a second peak in deaths around 2010, while EPP-ASM followed the data closely.

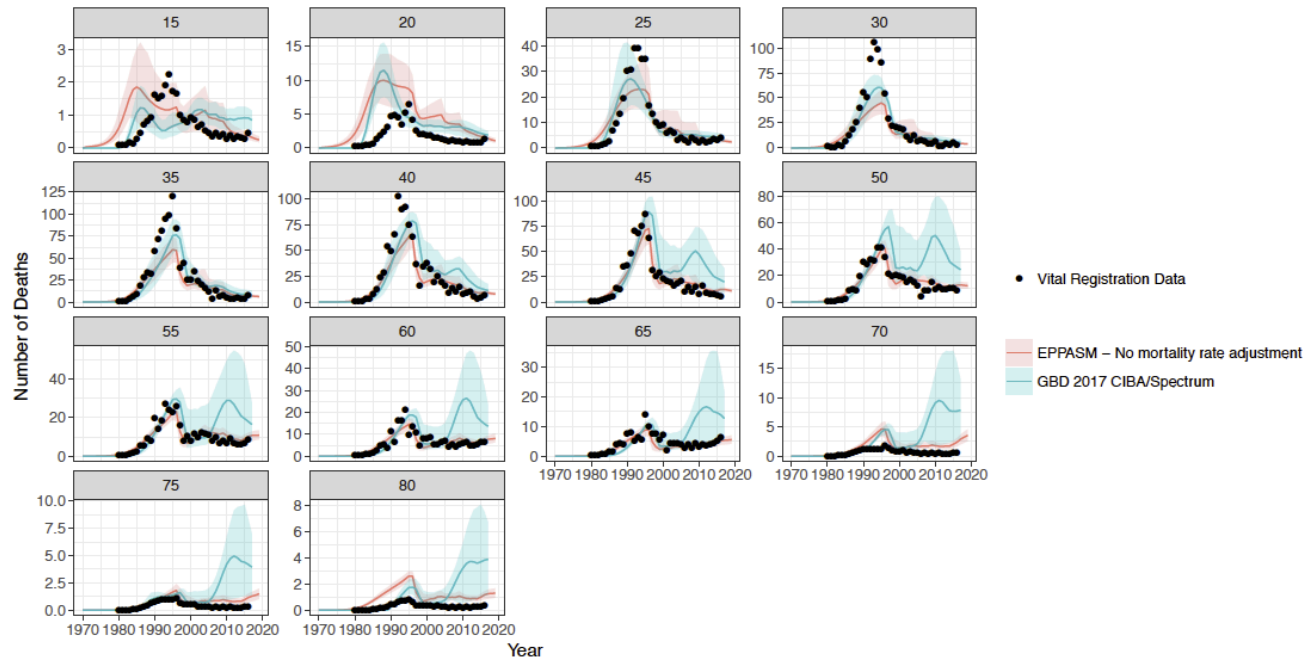


Fig. 5: Estimated HIV Deaths Stratified by 5-year Age Group for the Netherlands (Both Sexes Combined)

HIV Morbidity Estimates

EPP-ASM estimated relatively stable numbers of PLHIV in Australia over time, shown in Figure 6 along with CIBA/Spectrum and UNAIDS 2018 estimates.²⁷ CIBA/Spectrum projected increasing numbers of PLHIV, with a mean estimate of 17,096 in 2017 compared to the mean estimate of 12,020 in EPP-ASM. CIBA/Spectrum and EPP-ASM both had considerable uncertainty around their mean prevalence estimates. Estimated incident cases and corresponding diagnosed cases (dashed line) were substantially less than the number recorded in the case notification data. The logistic curve produced by EPP-ASM had a consistently decreasing trend

following the epidemic peak, reaching implausibly low numbers in recent years. UNAIDS estimated higher numbers of PLHIV and new infections than either model and aligned more closely with case notification data.

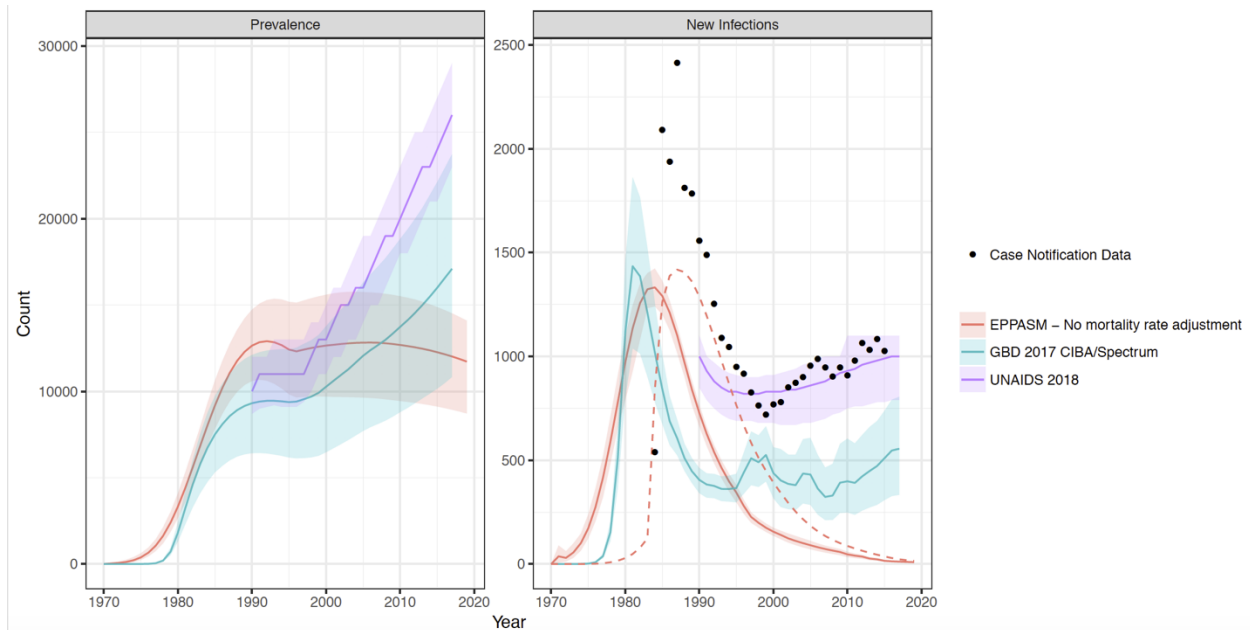


Fig. 6: Estimated People Living with HIV and New HIV Infections Ages 15+ for Australia (Estimated Diagnoses Shown with Dashed Line)

EPP-ASM produced a qualitatively more reasonable fit to case notification data in the Netherlands, illustrated in Figure 7. EPP-ASM estimated a much lower initial peak in new infections than CIBA, followed by a second, broader peak and declines in recent years. CIBA projected three distinct peaks that appear unsubstantiated by case notification data. EPP-ASM, UNAIDS, and CIBA/Spectrum estimated broadly similar trends and levels in prevalence, though CIBA/Spectrum results had considerably broader uncertainty intervals.

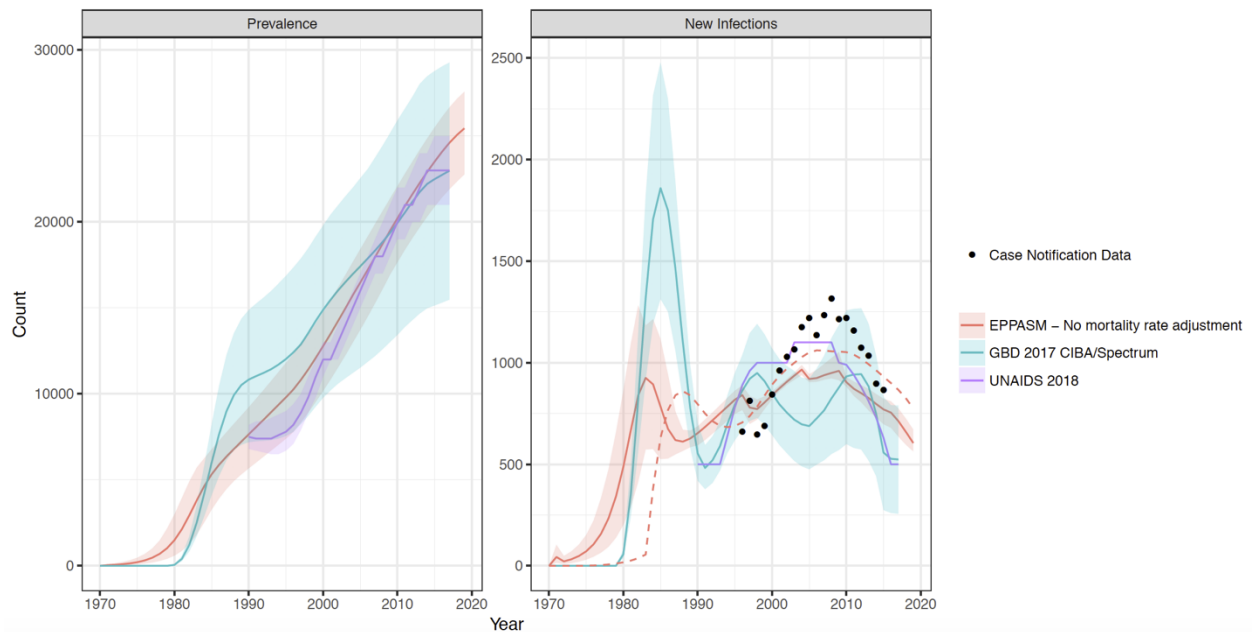


Fig. 7: Estimated People Living with HIV and New HIV Infections for the Netherlands (Estimated Diagnoses Shown with Dashed Line)

Discussion

The EPP-ASM model offers a flexible, internally consistent estimation framework for countries with high quality vital registration and case notification data as well as countries with surveillance data. It was speculated that imposing an inverse relationship between off-ART mortality rates and ART coverage could improve fits to vital registration and case notification data. However, the EPP-ASM model with no adjustment to off-ART mortality showed the best model performance overall. Nonetheless, the EPP-ASM model with an exponentially decaying adjustment to off-ART mortality rates produced promising results in the Netherlands and may be effective in other countries. Additional exploration could provide insight into whether different specification of the prior or other structural assumptions on mortality rate adjustments could generate better model fits.

Incorporating case notification and vital registration data into the EPP-ASM model offers a number of methodological improvements over the CIBA approach. Similar to CIBA, EPP-

ASM uses age-specific HIV mortality data to inform the age pattern of HIV incidence. However, unlike CIBA, a functional form is imposed on incidence through the use of a parametric model for force of infection. This avoids implausible year-to-year changes in incidence that have been observed in CIBA results.¹¹ Furthermore, EPP-ASM uses a statistical approach to find a best-fitting incidence curve to case notification and mortality data, whereas CIBA utilizes an algebraic approach to back-calculate incidence from mortality data and involves post-hoc adjustments to improve alignment with case notification data. Finally, EPP-ASM incorporates case notification data utilizing a changing lag to diagnosis based on increasing availability of HIV testing over time. This offers a much more plausible time trend in lag to diagnosis than the CIBA approach, which assumes a constant 5-year lag to diagnosis.

A number of limitations remain in using the EPP-ASM model for high-income countries. This model assumes that case notifications represent the true number of diagnoses each year; however, there is uncertainty in the quality of case notification data across countries and over time. Duplicated and missing diagnoses may bias the data in important and difficult-to-quantify ways.²⁸ Furthermore, in the modeling for this project, the distribution of incidence across ages and sexes was not allowed any flexibility over time. This resulted in poor fits to age-specific mortality data when there was a differential age pattern of mortality over time, which was apparent in younger ages in both countries. It also led to poor fits when epidemic trends differed by sex, as seen in the poor model performance for women in Australia. Additionally, incidence estimates produced by EPP-ASM were sometimes unrealistic, such as the near-zero incidence results in Australia in recent years. Modeled new infections from UNAIDS aligned much more closely with case notification data; however, this model was only fit to diagnosis data rather than trying to reconcile diagnosis and mortality data in one model. Finally, though EPP-ASM

achieved a closer fit to mortality data than CIBA, the model did not follow mortality data precisely, resulting in fairly poor coverage of 95% posterior predictive intervals. In countries where vital registration data is deemed reliable, separate models that are intended to provide a near-exact fit to mortality data, such as spatiotemporal gaussian process (ST-GPR) regression used by GBD, may still be desirable. Nonetheless, if ST-GPR results were to be substituted for mortality results, EPP-ASM would still offer more internal consistency between HIV morbidity and mortality results than CIBA/Spectrum, as evidenced by its improved error statistics.

Future model development could further improve fit to mortality and diagnosis data. The significant difference between the prior and posterior on α indicates that revised priors may help the model converge on proper adjustments to off-ART mortality rates. Additionally, better fit to varying time trends in age- and sex-specific mortality could be achieved through incorporating flexibility in the age and sex incidence rate ratios over time. Lastly, allowing additional flexibility in force of infection parameters may lead to an improved fit to case notification data in locations like Australia. These potential directions could build upon the methodological foundation provided by EPP-ASM to continue refining prediction of HIV burden in high-income locations.

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