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A Bayesian hierarchical model with novel prior specifications for estimating HIV testing rates

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Abstract

Human immunodeficiency virus (HIV) infection is a severe infectious disease actively spreading globally, and acquired immunodeficiency syndrome (AIDS) is an advanced stage of HIV infection. The HIV testing rate, that is, the probability that an AIDS-free HIV infected person seeks a test for HIV during a particular time interval, given no previous positive test has been obtained prior to the start of the time, is an important parameter for public health. In this paper, we propose a Bayesian hierarchical model with two levels of hierarchy to estimate the HIV testing rate using annual AIDS and AIDS-free HIV diagnoses data. At level one, we model the latent number of HIV infections for each year using a Poisson distribution with the intensity parameter representing the HIV incidence rate. At level two, the annual numbers of AIDS and AIDS-free HIV diagnosed cases and all undiagnosed cases stratified by the HIV infections at different years are modeled using a multinomial distribution with parameters including the HIV testing rate. We propose a new class of priors for the HIV incidence rate and HIV testing rate taking into account the temporal dependence of these parameters to improve the estimation accuracy. We develop an efficient posterior computation algorithm based on the adaptive rejection metropolis sampling technique. We demonstrate our model using simulation studies and the analysis of the national HIV surveillance data in the USA.

Keywords

HIV testing rate; Bayesian hierarchical model; temporal dependence; adaptive rejection metropolis sampling

1. Introduction

Human immunodeficiency virus (HIV) infection is a severe infectious disease actively spreading globally. Acquired immunodeficiency syndrome (AIDS) is an advanced stage of HIV infection with CD4 T-lymphocyte count less than 200/uL or opportunistic illnesses. The diagnosis of HIV infection by HIV testing is one of the most important tools for HIV prevention and treatment. It can foster early detection of HIV infection and is the first

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essential step for entry to clinical care to reduce morbidity and mortality. In addition, persons aware of their infections and on effective treatment are less likely to transmit the virus to others. Since HIV testing first became available in 1985, the importance of HIV testing was soon recognized, emphasized, and promoted [1]. However, a significant proportion of individuals infected with HIV still remain untested, undiagnosed, and unaware of their infection. As of December 2010, more than 1.1 million people were living with HIV infection in the USA and about 1 in 6 were unaware of their infections [2]. The HIV testing rate is defined as the probability that an AIDS-free HIV infected person seeks a test for HIV during a particular time interval, given no previous positive test has been obtained prior to the start of the time. In this study, we assume that the HIV test has perfect sensitivity and specificity, and an HIV positive person who gets tested is thereafter diagnosed. The accurate and timely estimation of the HIV testing rate is crucial for public health in that (1) it is a crucial component in the modeling framework that estimates the HIV incidence and reducing HIV incidence is the ultimate goal of HIV prevention; (2) it can be used to assess the effectiveness of HIV testing programs and provide guidance for future public health responses; and (3) it provides additional information on the average length of time between HIV infection and the first positive HIV test, informing how soon an HIV infection gets diagnosed.

It is challenging to obtain an accurate estimate of the HIV testing rate in that modeling the probability of HIV testing often involves the complex time lag from HIV infection to HIV diagnosis because the time of HIV infection is rarely observable [3, 4]. The HIV testing rate was initially introduced by Marschner [5] and Farewell [6], independently. In both of their work, HIV testing rate was simply assumed to be a constant, implying constant testing hazard for all individuals across calendar years. Following their work, various parametric models have been proposed to characterize individual's HIV testing behavior based on the time since HIV infection to diagnosis using the frequentist approach. Among them, one work models the HIV testing process using a two-parameter exponential distribution incorporating dependence between the time since infection and the calendar time [7]. Other methods include the heterogeneous mixed exponential model, leading to a Pareto distribution with a decreasing hazard function for the duration between HIV infection and HIV diagnosis [8–10], and the additive hazards model, which partitions the HIV testing process to the constant routine HIV testing and the symptoms-driven testing characterized by an exponential distribution [4, 11, 12]. Another framework of modeling the HIV disease and diagnosis process is through a multi-state formulation, describing the progression through various disease stages from infection to AIDS. Often various HIV disease stages are characterized by laboratory markers such as the CD4 T-cell count [13]. In recent years, Sweeting and Birrell proposed to use a Bayesian formulation of a similar multi-state model for estimation of HIV incidence, in which the natural disease progression probabilities and HIV testing probabilities collectively define the transition probabilities from one state to another. The HIV testing probabilities are estimated from external HIV diagnoses data [14, 15]. In addition, observed longitudinal CD4 data are used to model the date of HIV infection using joint linear mixed models [16]. However, the inclusion of additional information in the model increases the complexity of the model. This potentially introduces bias when the observed laboratory data are not representative of all the new diagnoses.

Although the HIV testing rate has been explored and modeled in various frameworks, it does not serve as a primary parameter of interest. It is an important parameter to the so-called back-calculation or back-projection model, which mainly focuses on reconstructing the past pattern of HIV infections in many countries using the annual numbers of diagnosed AIDS and AIDS-free HIV cases [9, 12, 17–19]. In those models, HIV testing rates are assumed to have certain parametric forms or to be a constant for a few years. These models are not flexible and do not adequately characterize changes over time. To the best of our knowledge, there is no existing statistical framework to systematically model and estimate the annual HIV testing rates over time. To fill this gap, this paper focuses on the Bayesian modeling of annual HIV testing rates over the calendar years using the annual observed numbers of persons diagnosed with HIV, with or without AIDS at HIV diagnosis. Numerous countries have established national HIV registries or surveillance systems to collect the numbers of AIDS and AIDS-free HIV diagnoses. For example, the dataset used for this work comes from the national HIV surveillance system in the USA that started collecting data on the number of persons diagnosed with AIDS since 1981 and the number of HIV diagnoses since 1994. Over time, additional states and local jurisdictions started reporting HIV diagnoses to national HIV surveillance system [19].

In this work, we assume that the HIV testing rate is only dependent on the calendar year, and these annual probabilities can be considered as the discrete-time analogue of the HIV testing intensity. To introduce the smoothness on the HIV testing rates and the HIV incidence rates over years, we resort to a Bayesian shrinkage approach by developing a new class of priors. In the past decade, the Bayesian shrinkage methods using various priors, such as Laplace priors, have been successful in many applications [20–24]. These methods are mainly developed for variable selection under a regression framework. In particular, the fused lasso priors [24, 25], that is, extended Laplace priors, are used to impose smoothness between the model parameters. In a similar fashion, for our problem, we develop a new class of priors that smooth the annual HIV testing rates and the HIV incidence rates.

Compared with existing models involving the HIV testing rate, our proposed approach has the following remarkable features: (1) our model is among the very first to propose a structured and systematic model to estimate the annual HIV testing rate in the USA; (2) unlike other back-calculation models [19], our model does not impose the constraints that HIV testing rates remain constant within certain years, nor does it make assumptions on the parametric form of the HIV testing rates; (3) our model has an ability to characterize the temporal dependence and smoothness between the annual HIV testing rates, which substantially improve the model fitting and parameter inference accuracy; and (4) our model is widely applicable in that it only needs the annual numbers of AIDS-free HIV and AIDS diagnoses as data in contrast to other approaches, such as the multi-state formulation that requires good representative laboratory data such as the CD4 data.

The paper is organized as follows: in Section 2, we present the detailed formation of our Bayesian hierarchical model for estimating annual HIV testing rates, where two new Laplace-type prior models are introduced. The corresponding properties are discussed in Section 2.3 and the posterior computation strategy are developed in Section 2.4. We demonstrate the superiority of our proposed method via simulation studies in Section 3 and

illustrate our method via analysis of the US national HIV surveillance data in Section 4. We conclude our paper with a discussion of future work in Section 5.

2. The model

2.1. Data and notation

First, we outline the problem and the observed data. We use January 1, 1977 as the time origin in this analysis because the earliest diagnosis dates of AIDS cases in the USA were in 1977. The time unit used in this analysis is calendar year.

We consider HIV infection from year 1 to year T in this paper. When an individual becomes infected with HIV in year i , he or she could be (1) diagnosed with AIDS-free HIV in year t , where $i \leq t \leq T$; or (2) diagnosed with AIDS in year t , where $i \leq t \leq T$; or (3) remain undiagnosed as of the most recent year T . The numbers of AIDS-free HIV and AIDS diagnoses in a calendar year include persons infected with HIV any time up to and including that year. Note that there does not exist a diagnosis test to determine when the individual became infected.

Denote by A_{it} the number of persons infected in year i and diagnosed with AIDS in year t , by H_{it} the number of persons infected in year i and diagnosed with AIDS-free HIV in year t and by U_{iT} as the number of persons infected in year i but remain undiagnosed at the end of year T . Let N_i be the total number of new HIV infections in year i . We have

$$N_i = \sum_{t=i}^T (A_{it} + H_{it}) + U_{iT}. \quad (1)$$

We observe the total number of cases diagnosed with AIDS and the total number of cases diagnosed with AIDS-free HIV in year t , denoted by A_t and H_t respectively. We have

$$A_t = \sum_{i=1}^t A_{it} \quad \text{and} \quad H_t = \sum_{i=1}^t H_{it}. \quad (2)$$

Table I illustrates the relationship between N_i , A_{it} , H_{it} , U_{iT} , A_t and H_t where columns characterize the number of persons diagnosed with AIDS and AIDS-free HIV, and those undiagnosed, and rows represent the number of infections at different years.

2.2. A hierarchical model

The primary interest of this study is to estimate the annual HIV testing rates and re-construct the trend in the HIV testing process over the years. We propose a Bayesian hierarchical model with two levels of hierarchy. To begin with the top level, we model the latent total numbers of HIV infections N_i for $i = 1, \dots, T$, which are assumed to be mutually independent and follow Poisson distributions with intensity λ_i that is,

$$[N_i | \lambda_i] \sim \text{Poisson}(\lambda_i), \quad (3)$$

where $\text{Poisson}(\mu)$ denotes a Poisson distribution with mean μ .

At level 2, given N_i , we model the annual numbers of AIDS, AIDS-free HIV cases, and all the undiagnosed cases stratified by the HIV infections at different years. Write

$\mathbf{N}_i^{AHU} = (A_{ii}, A_{i,i+1}, \dots, A_{iT}, H_{ii}, H_{i,i+1}, \dots, H_{iT}, U_{iT})$ for $i = 1, \dots, T$. It represents a collection of the numbers of persons diagnosed with AIDS, AIDS-free HIV, and undiagnosed persons, infected with HIV in year i and diagnosed in different years. Let $\text{multinomial}(\mathbf{p}, n)$ represent a multinomial distribution with event probability $\mathbf{p}$ and number of trials n , for $i = 1, \dots, T$, then we assume

$$[\mathbf{N}_i^{AHU} | \mathbf{q}_i^{AHU}, N_i] \sim \text{multinomial}(\mathbf{q}_i^{AHU}, N_i), \quad (4)$$

where $\mathbf{q}_i^{AHU} = (q_{ii}^A, q_{i,i+1}^A, \dots, q_{iT}^A, q_{ii}^H, q_{i,i+1}^H, \dots, q_{iT}^H, q_{iT}^U)$. Given that a person is infected with HIV in year i , q_{it}^A and q_{it}^H represent the probability of being diagnosed with AIDS and AIDS-free HIV in year t , respectively, for $1 \leq i \leq t \leq T$, and q_{iT}^U is the probability of remaining undiagnosed at the end of year T . Note that for all i , $\sum_{t=i}^T (q_{it}^A + q_{it}^H) + q_{iT}^U = 1$ and $q_{it}^A, q_{it}^H, q_{iT}^U \geq 0$.

To characterize $\mathbf{q}_i^{AHU}$, we introduce two types of conditional probabilities: the annual AIDS diagnosis rate denoted by p_{t-i}^A and the annual HIV testing rate denoted by p_t^H , which is the primary interest of this study. The annual AIDS diagnosis rate p_{t-i}^A is the probability that a person infected with HIV in year i gets diagnosed with AIDS in year t , $t \geq i$ given no previous positive test has been obtained prior to the start of year t . We assume that all persons newly diagnosed with AIDS did not receive HIV treatment before diagnosis. The treatment-free AIDS diagnosis rate p_{t-i}^A can be generated from the known AIDS incubation period, which has been studied and modeled by a gamma distribution with the shape parameter of 2 and the scale parameter of 4 [26, 27]. The AIDS incubation period is only determined by the time interval from HIV infection to AIDS diagnosis, that is, the value of $(t - i)$. This means that without treatment, the AIDS diagnosis rate p_{t-i}^A only depends on how long a person has been infected with HIV.

The annual HIV testing rate p_t^H is the probability that an AIDS-free HIV positive person seeks an HIV test in year t given no previous positive test has been obtained prior to the start of year t . We assume that persons diagnosed with HIV in the same year have the same HIV testing rate, regardless of when they became infected. That is, p_t^H is only dependent on the calendar year t and is independent of infection time i . In the first year of HIV infection, assuming HIV infection happens uniformly in the calendar year, HIV testing can only happen after HIV infection and before the calendar year-end. Therefore, the probability of being diagnosed with AIDS-free HIV in the year of HIV infection is proportional to the time interval from HIV infection to the calendar year-end. On average, the HIV testing rate in the year of HIV infection is half of the annual HIV testing rate. Thus, for $1 \leq i \leq t \leq T$, we can represent q_{it}^H using p_{t-i}^A and p_t^H , which is given by

$$q_{it}^H = \begin{cases} \frac{1}{2}p_i^H \times (1 - p_0^A) & t=i \\ p_i^H \left(1 - \frac{1}{2}p_i^H\right) \prod_{k=i+1}^{t-1} (1 - p_k^H) \times \prod_{k=i}^t (1 - p_{k-i}^A) & t \geq i+1 \end{cases} \quad (5)$$

where we define $\prod_{k=i+1}^i (1 - p_k^H) = 1$. The term $\frac{1}{2}p_i^H$ represents the conditional probability that a person gets HIV infected and tested in year i (the year of infection) given no AIDS

diagnosis in the same year. The term $(1 - p_0^A)$ represents the probability that a person is not diagnosed with AIDS in the same year of HIV infection. The term

$p_i^H \left(1 - \frac{1}{2}p_i^H\right) \prod_{k=i+1}^{t-1} (1 - p_k^H)$ represents the conditional probability that a person gets infected with HIV in year i but is not tested until year t given no AIDS diagnosis between year i and year t . The term $\prod_{k=i}^t (1 - p_{k-i}^A)$ represents the probability that a person is not diagnosed with AIDS from year i to year t . Similarly, we can represent q_{it}^A as

$$q_{it}^A = \begin{cases} p_0^A & t=i \\ p_{t-i}^A \prod_{k=i}^{t-1} (1 - p_{k-i}^A) \times \left(1 - \frac{1}{2}p_i^H\right) \prod_{k=i+1}^{t-1} (1 - p_k^H) & t \geq i+1. \end{cases} \quad (6)$$

This further implies that q_{iT}^U can be written as a function of p_{k-i}^A and p_i^H using

$$q_{iT}^U = 1 - \sum_{k=i}^T (q_{ik}^A + q_{ik}^H).$$

All the quantities in models (3)–(6) are latent. The only observed data are $\mathbf{A} = \{A_t\}_{t=1}^T$ and $\mathbf{H} = \{H_t\}_{t=1}^T$ in (2). The estimated values of parameter $\mathbf{P}^A = \{p_{t-i}^A\}_{t \geq i}$ can be obtained from published literatures [26, 27]. Our primary interest is in making inference on the HIV testing rates $\mathbf{P}^H = \{p_t^H\}_{t=1}^T$.

Another quantity of great interest in the public health community related to the HIV testing rates $\mathbf{P}^H$ is the expected time-since-infection. Let ξ_t denote the time from infection to AIDS-free HIV or AIDS diagnosis for individuals diagnosed during year t . According to the definition of q_{it}^A and q_{it}^H , we can represent the probability mass function for ξ_t as

$$Pr(\xi_t = t - i | q_{it}^A, q_{it}^H) \propto (q_{it}^A + q_{it}^H) \lambda_i, \text{ for } i=1, \dots, t.$$

This implies that the expected time-since-infection, denoted η_t , can be represented in terms of $\{q_i^{AHU}\}_{i=1}^t$, which are functions of $\mathbf{P}^H$ and $\boldsymbol{\lambda}$, that is,

$$\eta_t = E \left(\xi_t | \mathbf{p}^H, \boldsymbol{\lambda} \right) = \frac{\sum_{i=1}^t (t-i) (q_{it}^A + q_{it}^H) \lambda_i}{\sum_{i=1}^t (q_{it}^A + q_{it}^H) \lambda_i}, \text{ for } t=1, \dots, T.$$

This informs on average how long individuals diagnosed with AIDS-free HIV or AIDS in a certain year have been infected. Because η_t is a deterministic function of $\mathbf{p}^H$ and $\boldsymbol{\lambda}$, the posterior inference on η_t can be obtained straightforwardly through the posterior inference on $\mathbf{p}^H$, for which we introduce a class of new priors in Section 2.3.

2.3. Prior specifications

In this section, we discuss the prior specifications for our proposed hierarchical model. We start from the most important parameter in our analysis, that is, the HIV testing rates $\mathbf{p}^H$. It is believed that the HIV testing process usually does not change dramatically between two succeeding years. Thus, it is reasonable to assume that the HIV testing rate in the current year is associated with the rate in the previous year. To characterize such an association, we propose a new family of probability distributions defined on $[0, 1]$, based on which we construct a prior for $\mathbf{p}^H$ taking into account the temporal dependence between HIV testing rates over the years. Specifically, we introduce the following definition of the new distribution.

Definition 2.1 (Laplace-beta distribution)

Let $\mu \in [0, 1]$, $a, b, c \in \mathbb{R}^+$. For $x \in [0, 1]$, let

$$\pi(x; \mu, a, b, c) = \frac{1}{L(\mu, a, b, c)} x^{a-1} (1-x)^{b-1} \exp(-c|x-\mu|), \quad (7)$$

where $L(\mu, a, b, c) = \int_0^1 x^{a-1} (1-x)^{b-1} \exp(-c|x-\mu|) dx$. We refer to $\pi(x; \mu, a, b, c)$ as the probability density function of a Laplace-beta distribution with the location parameter μ , the rate parameter c and two shape parameters a and b . A random variable X following this distribution is denoted as $X \sim \text{Laplace-beta}(\mu, a, b, c)$.

Remark

1) when $c = 0$, the Laplace-beta distribution reduces to a beta distribution with shape parameters a and b . 2) When $a = b = 1$, the Laplace-beta distribution becomes a truncated Laplace distribution with location parameter $\mu \in [0, 1]$ and rate parameter c . Also, the properties of the Laplace-beta distribution are summarized in the following proposition.

Proposition 2.1

Let $X \sim \text{Laplace-beta}(\mu, a, b, c)$. Then

- (1) $1 - X \sim \text{Laplace-beta}(1 - \mu, b, a, c)$.
- (2) The n th moment of X is given by

$$E[X^n] = \frac{L(\mu, a+n, b, c)}{L(\mu, a, b, c)}, \quad \text{for } n=1, 2, \dots, \quad (8)$$

where $L(\mu, a, b, c)$ is defined in Definition 2.1.

(3) Given $a, b \in \mathbb{R}^+$ and $\mu \in [0, 1]$, we have

$$\lim_{c \uparrow +\infty} E[X] = \mu \quad \text{and} \quad \lim_{c \downarrow 0} E[X] = \frac{a}{a+b}. \quad (9)$$

See the proof in the Appendix. Proposition 2.1(3) implies that the parameters c and μ control how the mean of Laplace-beta(μ, a, b, c) deviates from the mean of beta(a, b). It approximately equals to μ when c is sufficiently large, and it gets close to the mean of beta(a, b) for a small c .

Now, we assign the priors for the annual HIV testing rates using Laplace-beta distributions. Specifically, we have

$$p_1^H \sim \text{beta}(a^H, b^H) \quad \text{and} \quad [p_{t+1}^H | p_t^H] \sim \text{Laplace-beta}(p_t^H, a^H, b^H, c^H), \quad (10)$$

for $t = 1, \dots, T-1$. This implies a priori, the distribution of p_{t+1}^H borrows information from p_t^H . According to the property of the Laplace-beta distribution, the parameter c^H controls the difference between $E(p_{t+1}^H | p_t^H)$ and p_t^H , which reflects the average change of the HIV testing rate from year t to $t+1$. The larger c^H is, the closer $E(p_{t+1}^H | p_t^H)$ gets to p_t^H . In other words, the choice of c^H controls the overall smoothness of the HIV testing rates over the years. A range of the c^H can be specified according to the coefficient of variation of p_{t+1}^H given p_t^H . Several values of c^H can be picked within this range and an optimal value can be chosen by maximizing the Bayes factor [28, 29]. We will discuss more details in Section 2.4. In light of the published literature, it is believed that the annual HIV testing rate in the past three decades should range from 0 to 0.4 with a mean of 0.2 and lower testing rates in the earlier years [30]. For hyperparameters a^H and b^H , we choose the values such that $E(p_1^H) = 0.05$.

Similar to the HIV testing rates, the annual HIV incidence rates that are reflected by parameters $\lambda = \{\lambda_i\}_{i=1}^T$ in (3) is also dependent on time measured in years. To characterize such temporal dependence, we introduce another new family of probability distributions to specify the priors for λ .

Definition 2.2 (Laplace-gamma distribution)

Let $a, b, c, \mu \in \mathbb{R}^+$. For $x \in \mathbb{R}^+$, let

$$\pi(x; \mu, a, b, c) = \frac{1}{K(\mu, a, b, c)} x^{a-1} \exp(-bx - c|x - \mu|),$$

where $K(\mu, a, b, c) = \int_0^\infty x^{a-1} \exp(-bx - c|x - \mu|) dx$. We refer to $\pi(x; \mu, a, b, c)$ as the probability density function of a Laplace-gamma distribution with the location parameter μ , the shape parameter a and two rate parameters b and c . A random variable X following this distribution is denoted as $X \sim \text{Laplace-gamma}(\mu, a, b, c)$.

Remark

1) when $c = 0$, the Laplace-gamma distribution reduces to a gamma distribution with shape a and rate b . 2) when $a = 1$ and $b = 0$, the Laplace-gamma distribution becomes a truncated Laplace distribution with location μ and rate c . The properties of the Laplace-gamma distribution are summarized in the following proposition.

Proposition 2.2

Let $X \sim \text{Laplace-gamma}(\mu, a, b, c)$. Then

- (1) For $\tau \in \mathbb{R}^+$, $X/\tau \sim \text{Laplace-gamma}(\mu/\tau, a, \tau b, \tau c)$.
- (2) The n th moment of X is given by

$$E[X^n] = \frac{K(\mu, a+n, b, c)}{K(\mu, a, b, c)}, \quad \text{for } n=1, 2, \dots, \quad (11)$$

where $K(\mu, a, b, c)$ is defined in Definition 2.2.

- (3) Given $a, b, \mu \in \mathbb{R}^+$, we have

$$\lim_{c \uparrow +\infty} E[X] = \mu \quad \text{and} \quad \lim_{c \downarrow 0} E[X] = \frac{a}{b}. \quad (12)$$

The proof is straightforward and similar to proposition 2.1. Proposition (2.2)(3) implies that the parameters c and μ reflect how different the mean of $\text{Laplace-gamma}(\mu, a, b, c)$ is from the mean of $\text{gamma}(a, b)$. It gets close to μ when c is sufficiently large and it approaches to the mean of $\text{gamma}(a, b)$ when c is very small. Based on this property, we assign the following priors for λ :

$$\lambda_1 \sim \text{gamma}(a^\lambda, b^\lambda) \quad \text{and} \quad [\lambda_{t+1} | \lambda_t] \sim \text{Laplace-gamma}(\lambda_t, a^\lambda, b^\lambda, c^\lambda), \quad (13)$$

for $t = 1, \dots, T-1$. As a priori, λ_{t+1} is assumed to follow a distribution characterized by λ_t , where the difference between $E[\lambda_{t+1} | \lambda_t]$ and λ_t is controlled by $c^\lambda > 0$. This prior specification implies that the number of HIV infections in the current year can be dependent on that of the previous year to a certain extent. This further assists better posterior inference on the HIV testing rate. We demonstrate this in simulation studies. For hyperparameters in (13), we choose a^λ and b^λ such that $E(\lambda_1)$ is close to the mean of the annual numbers of total

diagnoses. Similar to c^H , the range of c^λ is determined by the coefficient of variation of λ_{t+1} given λ_t and the choice of the c^λ can be determined via Bayes factors. More details will be discussed in Section 2.4.

The proposed Laplace-beta and Laplace-gamma distributions provide an alternative way to other methods that incorporate serial dependence. The notable features of these distributions include: (1) model parameters are easily interpreted and can be straightforwardly specified and estimated; (2) the prior specifications lead to computationally feasible posterior inference and we developed an MCMC algorithm based on the adaptive rejection sampling along with a random walk updating scheme; (3) the special case of the proposed model can be considered as the Bayesian counterpart of the penalized likelihood approach with the fused lasso penalty, which has a good theoretical foundation and been widely used in many applications; and (4) compared with the fused lasso approach, the Bayesian approach automatically achieves the post-selection inference that takes into account all source of uncertainty and produces more reliable results.

2.4. Posterior inference

To simplify the posterior computation, we consider an equivalent model representation by integrating out the latent quantities $\mathbf{N}_i^{AHU}$ and N_i in models (3) and (4).

Because N_i follows a Poisson distribution with mean λ_i , it is straightforward to show that A_{it} and H_{it} follow Poisson distributions with means $q_{it}^A \lambda_i$ and $q_{it}^H \lambda_i$, respectively, that is,

$$[A_{it} | \lambda_i, q_{it}^A] \sim \text{Poisson} \left(q_{it}^A \lambda_i \right) \quad \text{and} \quad [H_{it} | \lambda_i, q_{it}^H] \sim \text{Poisson} \left(q_{it}^H \lambda_i \right). \quad (14)$$

See the proof in the Appendix. Note that A_{it} and H_{it} are mutually independent given λ_i , q_{it}^A and q_{it}^H . Given $\mathbf{p}^H$ and λ , the observed total numbers of cases diagnosed with AIDS ($A_t = \sum_{i=1}^t A_{it}$) and HIV ($H_t = \sum_{i=1}^t H_{it}$) follow Poisson distributions with means $\sum_{i=1}^t q_{it}^A \lambda_i$ and $\sum_{i=1}^t q_{it}^H \lambda_i$, respectively, that is,

$$[A_t | \mathbf{p}^H, \lambda] \sim \text{Poisson} \left(\sum_{i=1}^t q_{it}^A \lambda_i \right) \quad \text{and} \quad [H_t | \mathbf{p}^H, \lambda] \sim \text{Poisson} \left(\sum_{i=1}^t q_{it}^H \lambda_i \right), \quad (15)$$

where both q_{it}^A and q_{it}^H are functions of $\mathbf{p}^H$ according to models (6) and (5). The joint posterior distribution of $\mathbf{p}^H$ and λ given data $\mathbf{A}$ and $\mathbf{H}$ and hyperparameters (c^H, c^λ) is given by

$$\pi \left(\mathbf{p}^H, \lambda | \mathbf{A}, \mathbf{H}, \mathbf{c}^H, \mathbf{c}^\lambda \right) \propto \prod_{t=1}^T \pi \left(A_t, H_t | \mathbf{p}^H, \lambda \right) \times \pi \left(p_1^H \right) \prod_{t=1}^{T-1} \pi \left(p_{t+1}^H | p_t^H, c^H \right) \times \pi \left(\lambda_1 \right) \prod_{t=1}^{T-1} \pi \left(\lambda_{t+1} | \lambda_t, c^\lambda \right).$$

The posterior distributions of parameters given the data are complicated and have no closed form solutions. Thus, to sample from the posterior distributions for given c^λ and c^H , we resort to the adaptive rejection metropolis sampling within Gibbs sampling [31]. Details of

the full conditional distributions of p_t^H and λ_t are provided in the Appendix. To achieve a better mixing of the simulated Markov chain, we suggest a random walk step to jointly update all the elements in $\mathbf{p}^H$ and $\boldsymbol{\lambda}$ given all other parameters [32]. The proposal distributions are independent normal distributions with mean zero, and the proposal variances can be determined by adjusting the acceptance rate to be around 30%. This updating scheme is helpful to produce reliable credible intervals of parameters, especially when there exists high posterior correlation among parameters.

For the choice of hyperparameters (c^H, c^λ) , we first determine the ranges of c^H and c^λ based on the ranges of the coefficient of variation (CV) for p_{t+1}^H given p_t^H and λ_{t+1} given λ_t respectively. The ranges of the CV were chosen based on the desired variances, that is, the standard deviation not to exceed a certain percentage of the mean. Thus, the desired variance drives the choice of the range for hyperparameters. Given all other parameters, we have

$$CV(p_{t+1}^H | p_t^H) \approx \frac{\sqrt{L(E[p_1^H], a^H+2, b^H, c^H) L(E[p_1^H], a^H, b^H, c^H) - L(E[p_1^H], a^H+1, b^H, c^H)^2}}{L(E[p_1^H], a^H+1, b^H, c^H)},$$

where $E[p_1^H] = \frac{a^H}{a^H + b^H}$, and

$$CV(\lambda_{t+1} | \lambda_t) \approx \frac{\sqrt{K(E[\lambda_1], a^\lambda+2, b^\lambda, c^\lambda) K(E[\lambda_1], a^\lambda, b^\lambda, c^\lambda) - K(E[\lambda_1], a^\lambda+1, b^\lambda, c^\lambda)^2}}{K(E[\lambda_1], a^\lambda+1, b^\lambda, c^\lambda)},$$

where $E[\lambda_1] = \frac{a^\lambda}{b^\lambda}$. Based on our experience, it is reasonable to assume that CV ranges from 0.1 to 0.3 for both p_{t+1}^H given p_t^H and λ_{t+1} given λ_t . We, thus, determine the ranges and specify a set of values for c^H and c^λ , respectively. Then, on a set of pre-specified values

$\{(c^{H(k)}, c^{\lambda(k)})\}_{k=1}^K$, we maximize the approximate Bayes factors, where the reference model is the case when $(c^H, c^\lambda) = (0, 0)$, that is, we choose

$$(\widehat{c^H}, \widehat{c^\lambda}) = (c^{H(\hat{k})}, c^{\lambda(\hat{k})}) \quad \text{with} \quad \hat{k} = \arg \max_k \left[\sum_{s=1}^S \pi^{-1}(\mathbf{A}, \mathbf{H} | \mathbf{p}^{H(k,s)}, \boldsymbol{\lambda}^{(k,s)}) \right]^{-1},$$

where $\{\mathbf{p}^{H(k,s)}, \boldsymbol{\lambda}^{(k,s)}\}_{s=1}^S$ are the simulated samples from the posterior distribution $\pi(\mathbf{p}^H, \boldsymbol{\lambda} | \mathbf{A}, \mathbf{H}, c^{H(k)}, c^{\lambda(k)})$.

3. Simulation study

To demonstrate the performance of the proposed model, we conducted simulation studies to estimate the HIV testing rates and the expected time-since-infection. We specify the AIDS diagnosis rate $(p^A(x))$, shown in Table II, as the conditional probability $P(x < A < x+1 | A > x)$ based on the distribution of A, AIDS incubation period, given by gamma(2,4). To

simulate the observed numbers of AIDS-free HIV and AIDS diagnoses over the years ($\mathbf{A}$ and $\mathbf{H}$), we specify the true values for the mean numbers of new HIV infections over the years (λ) and the HIV testing rates (p^H) (Table A.1 in Appendix). In particular, we have two scenarios for estimating testing rates. In Scenario 1, we consider a 34-year period with a gradual increasing trend in the HIV testing rate. In Scenario 2, we consider a 20-year period with an increasing trend followed by a decreasing trend in the HIV testing rate.

Given a set of values of λ , p^H and p^A , the HIV infections and diagnoses data are simulated from a process that mimics data generation and collection in real-life; a person becomes infected with HIV in year i , and he or she gets diagnosed in a later year $t \geq i$ or remains undiagnosed as of the most recent year T . At the time of diagnosis, he or she can be diagnosed with AIDS or AIDS-free HIV. The diagnosis date and disease status are determined and reported to a national surveillance registry. Annual numbers of AIDS-free HIV and AIDS diagnoses are thus summarized. This process is simulated as follows:

Step 1: For each year i , $i = 1, \dots, T$, the number of new HIV infections N_i is generated through a Poisson distribution based on a mean λ_i .

Step 2: For each case of infection in year i ,

- (1) Simulate the time of HIV infection in the year from uniform(0,1), assuming an HIV infection happens uniformly throughout the year.
- (2) Simulate the time interval from HIV infection to AIDS diagnosis (i.e., the AIDS incubation period) using a gamma(2, 4) distribution.
- (3) Determine the year of diagnosis and categorize the case as either 'AIDS-free HIV' or 'AIDS' at the time of diagnosis.
 - (a) If the AIDS incubation period is smaller than one (i.e., AIDS diagnosis happens in the same year of HIV infection), the case is categorized as 'AIDS' and the year of diagnosis is the year of HIV infection.
 - (b) If the AIDS incubation period is greater than one (i.e., AIDS is diagnosed in years after the year of HIV infection), determine whether the case had an HIV test in a year before the year of AIDS diagnosis based on the HIV testing rates in each year before AIDS diagnosis.
 - If a case has an HIV test before AIDS diagnosis, it is categorized as 'AIDS-free HIV' and the year of diagnosis is the year of HIV test;
 - Else if the year of AIDS diagnosis is earlier than the most recent year, the case is an 'AIDS' case, and the year of diagnosis is the year of AIDS diagnosis.
 - Otherwise, the case remains undiagnosed as of the most recent year.

Step 3: After looping through each infection and each year, summarize the diagnosed AIDS-free HIV cases ($\mathbf{H}$) and AIDS cases ($\mathbf{A}$) over years.

Given the simulated $\mathbf{A}$ and $\mathbf{H}$, we set the initial values for λ as a half of the annual observed numbers of AIDS-free HIV and AIDS diagnoses and set p^H as random values between 0 and 1, respectively. We choose the hyperparameters (c^H, c^λ) by maximizing the Bayes factors as discussed in Section 2.4 on a set of pre-specified values. The selected values for c^H are 30, 45, and 60, which imply the coefficients of variation of p_{t+1}^H given p_t^H are 0.30, 0.17, and 0.12 respectively. The values for c^λ are 0.001, 0.002, and 0.004, leading to the coefficients of variation of λ_{t+1} given λ_t of 0.31, 0.23, and 0.14, respectively. We run the proposed posterior simulation algorithm 2,000 iterations with 200 burn-in for each combination of (c^H, c^λ) in both scenarios. We check the convergence of the simulated Markov chains using the Gelman and Rubin diagnostic [33] by running five additional Markov chains with different initial values. The potential scale reduction factors of the log-likelihood for Scenarios 1 and 2 are respectively 0.99 and 1.06, which are both close to 1, indicating the convergence of the posterior simulations.

The selected value of (c^H, c^λ) is (60, 0.002) for both Scenario 1 and Scenario 2. The posterior mean and 95% credible interval of p_t^H and η_t are shown in Figure 1. For Scenarios 1 and 2, the estimated posterior means of p_t^H and η_t for $t = 1, \dots, T$, are quite close to the true values of the HIV testing rates, and the expected time-since-infection and the associated 95% credible intervals cover the true values for all years. The results show that our model can provide accurate estimates under different trends and different periods of time. In Table III, for both scenarios, we compare the model fitting results for different choices of hyperparameters (c^H, c^λ) . For both p_t^H and η_t , Table III summarizes the average mean square error (AMSE) over years, the average length of 95% credible intervals (ACI) over years, and the approximate Bayes factors (BF). A special case (shown in Figure 1) is when $(c^H, c^\lambda) = (0, 0)$, corresponding to a regular choice of independent beta priors for p_t^H and independent gamma priors for λ_t , compared with which our method has a better model fitting (larger BF) and provides more accurate estimates and inference on the HIV testing rate and the time-since-infection (smaller AMSE and ACI).

4. Application

In this section, we apply the proposed Bayesian hierarchical model to the data from national HIV surveillance in USA.

4.1. Analysis of the US HIV surveillance data

Since 1982, all 50 states and the District of Columbia have reported AIDS cases to the Centers for Disease Control and Prevention (CDC) using a standardized case report form. In 1994, the CDC implemented data management for national reporting of HIV integrated with AIDS case reporting, at which time 25 states with confidential name-based HIV surveillance started submitting case reports to the CDC. Over time, additional states implemented name-based HIV surveillance, and all states had implemented such surveillance in 2008.

In this study, we use HIV and AIDS data reported to the CDC through June 2012. The data are adjusted for incomplete reporting, reporting delay, detection and elimination of duplicate reports, and misclassification of the diagnosis dates [34–36]. The resulting estimated annual numbers of AIDS-free HIV and AIDS diagnosed cases each year from 1977 (the beginning of the HIV epidemic) to 2010 are presented in Table IV.

The initial values for HIV testing rates are drawn from uniform distribution on $[0, 1]$. The annual numbers of new HIV infections are initially assigned a half of the observed numbers of AIDS-free HIV and AIDS diagnoses. We choose the hyperparameters (c^H, c^λ) as (45, 0.0005), which has the maximal value (9.1) of the Bayes factor among a set of pre-specified values. We allow a wide range for the coefficients of variation and hyperparameters to ensure a less chance to miss the best hyperparameters. The selected values for c^H are 15, 30, 45, 60, corresponding to the coefficients of variation of 0.69, 0.30, 0.17, 0.12 and the values for c^λ are 0.0001, 0.0002, 0.0003, 0.0005, and 0.0008, corresponding to the coefficients of variation of 0.58, 0.18, 0.12, 0.07, and 0.04, respectively. We run the posterior simulation algorithm 2,000 iterations with 200 burn-in. The potential scale reduction factors of the loglikelihood is 1.04 from running five additional chains, indicating the convergence of the posterior simulations.

Figure 2 presents the posterior means and 95% credible intervals for the HIV testing rate and the expected time-since-infection (in years) from 1985 when the first HIV test became available in the USA, to 2010. In the first few years after HIV test became available, HIV testing was widely adopted and it continued to increase until 1990. The testing rate went down in early 1990s. This is likely caused by the change in the CDC AIDS definition during that time resulting in a high proportion of simultaneous AIDS diagnoses, which could indicate low HIV testing rate. Another possible reason could be a sudden increase in the number of new HIV infections in early 1990s resulting in a high number of undiagnosed HIV infections and consequently low HIV testing rate. After that, the HIV testing rate gradually increased and sustained the increasing trend ever since. In the most recent years since 2007, the annual HIV testing rate has been stable around 0.22. As for the expected time interval (in years) since HIV infection to HIV diagnosis among individuals diagnosed in a specific calendar year, there was an increasing trend followed by a decreasing trend. The expected time-since-infection was short among those diagnosed in the early years of the epidemic, which is likely because the early infections were mainly concentrated among men who have sex with men and the targeted HIV testing among this population could result in shorter time interval from infection to diagnoses. As time went by, with the HIV epidemic spread to a more general population and the treatment improving, the expected time-since-infection gradually increased and reached the peak of 4.5 years among cases diagnosed in 1997. Since 1997, because of the increased HIV testing rate, the estimated expected time-since-infection decreased and was 3.3 years in 2010.

The estimated HIV testing rates and expected time-since-infection reflect the impact of important public health initiatives and recommendations on HIV testing. As shown in the results, the HIV testing rate increased when the first HIV test became available in 1985. In 1987, the United States Public Health Service issued guidelines making HIV counseling and testing a priority as a prevention strategy for people with high risk behaviors. [37] As a

result, the HIV testing rate increased in the late 1980s. Although HIV testing went down during 1991 to 1993, the HIV testing rate started increasing since 1993 when CDC updated the recommendations regarding HIV counseling and testing of patients in acute-care hospital settings. [38] In 1995, when National HIV Testing Day was observed, the HIV testing rate sustained the upward trend until 2000. Throughout the first decade of 2000, a few important recommendations were published in 2001 [39], 2003 [40], and 2006 [1] respectively to emphasize routine HIV testing as an important HIV prevention tool. The HIV testing rate increased after each recommendation, and it maintained an increasing trend since 2001. As a result of the increased HIV testing, the expected time-since-infection decreased for cases diagnosed since 2001. These results indicate that public health recommendations on HIV testing have a consistently positive impact on people's HIV testing awareness and testing behavior.

4.2. Model assessment

We conduct the posterior predictive model assessment using two approaches. First, we calculate the χ^2 discrepancy, which is a summary statistic for the sum of squares of standardized residuals of the data with respect to their expectations under the model [41]. For our model, the χ^2 discrepancy is defined as:

$$\chi^2(\mathbf{H}; \mathbf{p}^H, \lambda) = \sum_{t=1}^{34} \frac{(H_t - E(H_t | \mathbf{p}^H, \lambda))^2}{\text{Var}(H_t | \mathbf{p}^H, \lambda)}.$$

We calculate the posterior predictive p -value based on χ^2 as $p = P(\chi^2(\mathbf{H}^{rep}, \mathbf{p}^H, \lambda) \geq \chi^2(\mathbf{H}; \mathbf{p}^H, \lambda))$, where $\mathbf{H}^{rep}$ represents the predictive replication and $\mathbf{H}$ represents the observed data. The p -value of the predictive versus realized χ^2 discrepancies is 0.48. This implies that the model fits the data pretty well.

We also assess the validity of the 95% credible intervals for the annual HIV testing rates and expected time-since-infection from 1985 to 2010. We generate 100 simulated datasets given the estimated HIV testing rates and expected time-since-infection. For each simulated dataset, we refit the model and obtain the estimated HIV testing rates and expected time-since-infection. Then we count the number of times that the newly estimated HIV testing rates and expected time-since-infection in the estimated 95% credible intervals for each year. We found that for both HIV testing rates and the expected time-since-infection, the newly estimated HIV testing rates and the expected time-since-infection fall in the estimated 95% credible intervals more than 95 times for 24 of the 26 years. This demonstrates the 95% credible intervals are plausible.

5. Discussion

In this paper, we develop a Bayesian hierarchical model to estimate the intensities of HIV testing from 1985 to 2010 using annual numbers of AIDS-free HIV and AIDS diagnosed cases collected through national HIV surveillance in the USA. Our model takes the most general form and makes no parametric assumptions for HIV testing rates. We assume that the HIV testing rate is only dependent on the calendar year, and these annual probabilities

can be considered the discrete-time analogue of the HIV testing intensity. We propose Laplace-beta and Laplace-gamma priors to characterize the temporal dependence for annual HIV testing rates and annual HIV incidence rates, respectively, which greatly improve the estimation accuracy and the model fitting. The simulation studies show that our model can make much more accurate inference on HIV testing rates of different trends for either long or short periods of time compared with a regular choice of priors.

The proposed Laplace-beta, completely different from the beta-Laplace distribution by Cordeiro and Lemonte [42], and Laplace-gamma distributions are motivated by the need of incorporating the prior temporal dependence among HIV testing rates and incidence rates in the model; however, they are not the only way in which temporal dependence could have been incorporated. The proposed priors are general and can have different applications. Further applications will help to determine the utility of this approach compared with other more traditional approaches. For example, in spatial statistics, these two prior distributions can impose the smoothness over the spatial parameters, which are alternatives to the use of Gaussian random fields requiring the normality assumption that are not valid in certain cases. In the spatial modeling of disease mapping, the disease infection probabilities over space can be assigned with Laplace-beta priors, and the intensity of the disease clusters can be modeled by Laplace-gamma priors. Also, in the analysis of functional neuro-imaging data, the voxel-wise probabilities of activation can be modeled with Laplace-beta priors and the Laplace-gamma model should be a good choice for the intensity of peak activation locations.

There are several possible future directions that extend our current work. One extension is to include covariates such as sex, race/ethnicity, or transmission category in the model, which can adjust for the confounding factors that might affect the HIV testing rates. Also, in contrast to the current modeling of the whole population in the USA, this extension can provide stratified estimates for sub-populations, for example, HIV testing rates for demographic groups or different regions in the country, which are of particular interest to public health officials and program evaluation. Another direction is that we can develop alternative strategies to choose the hyperparameters (c^H, c^λ) that are strongly related to the performance of model fitting and parameter estimation. A fully Bayesian approach can be considered by jointly updating (c^H, c^λ) in the posterior simulation and using the Bayesian model averaging to make the inference. The key steps are to choose appropriate priors for (c^H, c^λ) and to develop an efficient posterior sampling strategy that is worthy of investigation in that this approach would take into account more sources of variation in the model and potentially produce better posterior inference on the model parameters.

Appendix A

Derivations for marginal distributions for A_{it} and H_{it}

Noting that if $(X_1, X_2, X_3) \sim \text{multinomial}(p_1, p_2, p_3, N)$ and $N \sim \text{Poisson}(\lambda)$, then the joint distribution of (X_1, X_2, X_3) and N is given by

$$P(X_1, X_2, X_3, N) = \frac{N!}{X_1! X_2! X_3!} p_1^{X_1} p_2^{X_2} p_3^{X_3} \frac{\lambda^N}{N!} e^{-\lambda}.$$

Integrating out N from the previous joint probability density, we have

$$\begin{aligned} P(X_1, X_2) &= \sum_{N=X_1+X_2}^{\infty} \frac{p_1^{X_1} p_2^{X_2} (1-p_1-p_2)^{N-X_1-X_2}}{X_1! X_2! (N-X_1-X_2)!} \lambda^{N-X_1-X_2} e^{-\lambda} \lambda^{X_1+X_2} \\ &= \sum_{N=X_1+X_2}^{\infty} \frac{[(1-p_1-p_2)\lambda]^{N-X_1-X_2}}{(N-X_1-X_2)!} e^{-\lambda(1-p_1-p_2)} e^{(p_1+p_2)\lambda} \frac{p_1^{X_1} p_2^{X_2}}{X_1! X_2!} \lambda^{X_1+X_2} \\ &= \frac{(p_1\lambda)^{X_1}}{X_1!} e^{-p_1\lambda} \frac{(p_2\lambda)^{X_2}}{X_2!} e^{-p_2\lambda} \end{aligned}$$

This implies that X_1 and X_2 follow independent Poisson distributions. In a similar fashion of the derivation, it is straightforward to show that if

$$(A_{ii}, \dots, A_{iT}, H_{ii}, \dots, H_{iT}, U_{iT}) \sim \text{multinomial} \left(q_{ii}^A, \dots, q_{iT}^A, q_{ii}^H, \dots, q_{iT}^H, q_{iT}^U, N_i \right)$$

and

$$N_i \sim \text{Poisson}(\lambda_i),$$

then

$$A_{it} \sim \text{Poisson}(q_{it}^A \lambda_i) \text{ and } H_{it} \sim \text{Poisson}(q_{it}^H \lambda_i), t=i, \dots, T,$$

where A_{it} and H_{it} are mutually independent.

Full conditional distributions

- Full conditional distribution of $\mathbf{p}^H$

$$\begin{aligned} \pi(\mathbf{p}^H | \lambda, \mathbf{A}, \mathbf{H}) &\propto \prod_{t=1}^T \frac{e^{-\sum_{i=1}^t q_{it}^A \lambda_i} \left(\sum_{i=1}^t q_{it}^A \lambda_i \right)^{A_t}}{A_t!} \frac{e^{-\sum_{i=1}^t q_{it}^H \lambda_i} \left(\sum_{i=1}^t q_{it}^H \lambda_i \right)^{H_t}}{H_t!} \\ &\times \prod_{t=1}^T \frac{(p_t^H)^{a_2-1} (1-p_t^H)^{b_2-1}}{B(a_2, b_2)} \\ &\times \prod_{t=2}^T \exp \left\{ -c^H |p_t^H - p_{t-1}^H| \right\} \end{aligned}$$

- Full conditional distribution of λ

$$\pi(\lambda|\mathbf{p}^H, \mathbf{A}, \mathbf{H}) \propto \prod_{t=1}^T \frac{e^{-\sum_{i=1}^t q_{it}^A \lambda_i}}{A_t!} \left(\sum_{i=1}^t q_{it}^A \lambda_i \right)^{A_t} \frac{e^{-\sum_{i=1}^t q_{it}^H \lambda_i}}{H_t!} \left(\sum_{i=1}^t q_{it}^H \lambda_i \right)^{H_t} \frac{b_0^{a_0}}{\Gamma(a_0)} \lambda_t^{a_0-1} \exp(-b_0 \lambda_t) \\ \times \prod_{t=2}^T \exp\{-c^\lambda |\lambda_t - \lambda_{t-1}|\}$$

Proofs for Proposition 2.1

Note that $X \sim \text{Laplace-beta}(\mu, a, b, c)$.

(1) The density function of $Y = 1 - X$ is

$$f(y) = \pi(1-x; \mu, a, b, c) \propto (1-x)^{a-1} x^{b-1} \exp(-c|1-x-\mu|),$$

which implies that $1 - X \sim \text{Laplace-beta}(1 - \mu, b, a, c)$.

(2)

$$E(X^n) = \int_0^1 \frac{1}{L(\mu, a, b, c)} x^{n+a-1} (1-x)^{b-1} \exp(-c|x-\mu|) dx = \frac{L(\mu, a+n, b, c)}{L(\mu, a, b, c)}$$

(3) Given $a, b > 0$, when $c \rightarrow \infty$, $\pi(x; a, b, c) \rightarrow I[x = \mu]$, thus, $E(X) \rightarrow \mu$.

Table A.1

Values for the parameters used in the simulation studies.

year	Scenario 1				Scenario 2			
	λ	p^H	A	H	A	p^H	A	H
1	24	0.060	0	1	24	0.060	0	1
2	86	0.060	2	4	86	0.060	2	4
3	86	0.060	6	8	86	0.060	6	8
4	244	0.060	14	17	244	0.060	14	17
5	244	0.096	28	46	244	0.096	28	46
6	862	0.096	49	91	862	0.096	49	91
7	862	0.096	92	156	862	0.096	92	156
8	2521	0.120	161	361	2521	0.120	161	361
9	2521	0.120	285	586	2521	0.120	285	586
10	3337	0.120	439	815	3337	0.120	439	815
11	3337	0.156	618	1356	3337	0.156	618	1356
12	4675	0.156	780	1649	4675	0.156	780	1649
13	4675	0.156	965	1970	4675	0.156	965	1970
14	5305	0.156	1151	2262	5305	0.156	1151	2262
15	5305	0.156	1335	2529	5305	0.156	1335	2529
16	5305	0.156	1500	2728	5305	0.144	1500	2518

year	Scenario 1				Scenario 2			
	λ	p^H	A	H	A	p^H	A	H
17	3429	0.156	1619	2730	3429	0.144	1640	2547
18	3429	0.156	1647	2582	3429	0.144	1687	2431
19	3429	0.180	1621	2840	3429	0.120	1678	1944
20	2000	0.180	1522	2542	2000	0.120	1674	1835
21	2000	0.180	1379	2196				
22	1500	0.180	1227	1895				
23	1500	0.192	1074	1739				
24	2346	0.192	934	1596				
25	2346	0.192	852	1576				
26	2346	0.192	808	1569				
27	2346	0.192	784	1568				
28	2642	0.192	775	1597				
29	2642	0.204	783	1750				
30	2642	0.204	786	1772				
31	2400	0.204	789	1763				
32	2400	0.204	785	1733				
33	2400	0.204	777	1711				
34	2400	0.204	769	1694				

λ is the mean annual number of new HIV infections, p^H is the annual HIV testing rate, A is the observed annual number of AIDS diagnoses and H is the observed annual number of HIV diagnoses. Scenario 1 is for a 34-year period with a gradual increasing trend in p^H and Scenario 2 is for a 20-year period with an increasing trend followed by a decreasing trend in p^H .

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Figure 1. Estimated posterior mean and 95% credible intervals for HIV testing rates and expected time-since-infection with different choices of (c^H, c^λ) in simulation Scenarios 1 and 2.

Figure 2.
Estimated posterior mean and 95% credible intervals for the annual HIV testing rates and expected time-since-infection from 1985 to 2010 in United States.

Table 1
Illustration of the relationship between observed data and latent quantities in the model.

Year of infection (<i>i</i>)	Year of AIDS or HIV diagnosis (<i>t</i>)					Incidence
	1	2	...	<i>T</i>	Undiagnosed by <i>T</i>	
1	A_{11}	A_{12}	...	A_{1T}	U_{1T}	N_1
2		A_{22}	...	A_{2T}	U_{2T}	N_2
...			...	...	...	...
<i>T</i>				A_{TT}	U_{TT}	N_T
Observed	A_1	A_2	...	A_T	U_T	

The column totals represent the number of persons diagnosed with AIDS and AIDS-free HIV in each year and those undiagnosed by the end of the most recent year. Row totals represent the number of new infections in each year. In each cell, A_{it} represents the number of persons infected in year i and diagnosed with AIDS in year t and H_{iT} represents the number of persons infected in year i and diagnosed with AIDS-free HIV in year t . Only column totals $\{A_t\}_{t=1}^T$ and $\{H_t\}_{t=1}^T$ are observed, and all other quantities are latent.

Table II

Values of AIDS diagnosis rate generated from the AIDS incubation time period given by a gamma distribution with shape parameter of 2 and scale parameter of 4.

$t-i$	p_{t-i}^A	$t-i$	p_{t-i}^A	$t-i$	p_{t-i}^A	$t-i$	p_{t-i}^A	$t-i$	p_{t-i}^A
0	0.00934	7	0.14701	14	0.17670	21	0.18941	28	0.19648
1	0.04761	8	0.15346	15	0.17910	22	0.19066	29	0.19724
2	0.07934	9	0.15889	16	0.18126	23	0.19181	30	0.19795
3	0.10124	10	0.16351	17	0.18321	24	0.19288	31	0.19863
4	0.11727	11	0.16749	18	0.18498	25	0.19387	32	0.19926
5	0.12952	12	0.17095	19	0.18659	26	0.19480	33	0.19986
6	0.13919	13	0.17400	20	0.18806	27	0.19567	34	0.20043

t is year of AIDS diagnosis and i is year of infection.

Table IIISimulation model fitting results for different choices of hyperparameters (c^H, c^λ).

(c^H, c^λ)	Scenario 1					Scenario 2				
	p^H		η			p^H		η		
	BF	AMSE	ACI	AMSE	ACI	BF	AMSE	ACI	AMSE	ACI
(0,0)	1.00	3.1e-05	0.032	0.008	0.30	1.00	2.8e-05	0.036	0.009	0.32
(30,0.001)	61.49	2.7e-05	0.027	0.006	0.29	3.51	2.8e-05	0.030	0.006	0.29
(30,0.002)	36.33	2.8e-05	0.026	0.006	0.27	2.58	2.8e-05	0.031	0.008	0.29
(30,0.004)	36.05	3.0e-05	0.026	0.007	0.25	2.53	2.8e-05	0.031	0.007	0.29
(45,0.001)	62.15	2.8e-05	0.025	0.006	0.29	3.74	3.1e-05	0.028	0.008	0.30
(45,0.002)	122.01	2.6e-05	0.025	0.005	0.26	10.05	2.5e-05	0.030	0.007	0.28
(45,0.004)	99.69	2.7e-05	0.024	0.007	0.24	5.49	2.5e-05	0.031	0.007	0.28
(60,0.001)	116.94	2.2e-05	0.025	0.006	0.27	13.91	4.4e-05	0.028	0.008	0.29
(60,0.002)	648.10	2.3e-05	0.024	0.005	0.26	18.14	2.3e-05	0.027	0.008	0.27
(60,0.004)	169.48	2.9e-05	0.024	0.006	0.24	2.45	3.1e-05	0.029	0.007	0.28

BF is the approximate Bayes factor, AMSE is the average mean square error, and ACI is the average length of 95% credible intervals.

Table IV

The estimated annual numbers of HIV (H_t) and AIDS (A_t) diagnoses from 1977 to 2010 from the National HIV Surveillance System in the USA.

Year	A_t	H_t	Year	A_t	H_t	Year	A_t	H_t
1977	2	3	1989	23225	53650	2001	20407	40962
1978	8	10	1990	25785	61233	2002	20024	39652
1979	13	17	1991	26013	58726	2003	18094	36028
1980	75	162	1992	28297	62485	2004	17585	36036
1981	307	144	1993	32276	51410	2005	16600	35568
1982	1144	725	1994	29813	46438	2006	15418	35260
1983	3039	1387	1995	30122	43850	2007	15360	36986
1984	6122	3211	1996	27312	40258	2008	14940	37295
1985	11515	30242	1997	23890	40692	2009	13946	33250
1986	14994	40777	1998	21582	39066	2010	13686	32356
1987	17593	46323	1999	19846	38098			
1988	21698	50522	2000	22126	44360			