

UCLA

UCLA Previously Published Works

Title

Measuring concurrency using a joint multistate and point process model for retrospective sexual history data

Permalink

<https://escholarship.org/uc/item/04s7j38z>

Journal

Statistics in Medicine, 35(24)

ISSN

0277-6715

Authors

Aralis, Hilary J
Gorbach, Pamina M
Brookmeyer, Ron

Publication Date

2016-10-30

DOI

10.1002/sim.7013

Peer reviewed



Published in final edited form as:

Stat Med. 2016 October 30; 35(24): 4459–4473. doi:10.1002/sim.7013.

Measuring concurrency using a joint multistate and point process model for retrospective sexual history data

Hilary Aralis^{a,*}, Pamina M. Gorbach^b, and Ron Brookmeyer^a

^aDepartment of Biostatistics, UCLA Fielding School of Public Health, University of California, Los Angeles, CA 90095, USA

^bDepartment of Epidemiology, UCLA Fielding School of Public Health, University of California, Los Angeles, CA 90095, USA

Abstract

Understanding the impact of concurrency, defined as overlapping sexual partnerships, on the spread of HIV within various communities has been complicated by difficulties in measuring concurrency. Retrospective sexual history data consisting of first and last dates of sexual intercourse for each previous and ongoing partnership is often obtained through use of cross-sectional surveys. Previous attempts to empirically estimate the magnitude and extent of concurrency among these surveyed populations have inadequately accounted for the dependence between partnerships and used only a snapshot of the available data. We introduce a joint multistate and point process model in which states are defined as the number of ongoing partnerships an individual is engaged in at a given time. Sexual partnerships starting and ending on the same date are referred to as one-offs and modeled as discrete events. The proposed method treats each individual's continuation in and transition through various numbers of ongoing partnerships as a separate stochastic process and allows the occurrence of one-offs to impact subsequent rates of partnership formation and dissolution. Estimators for the concurrent partnership distribution and mean sojourn times during which a person has k ongoing partnerships are presented. We demonstrate this modeling approach using epidemiological data collected from a sample of men having sex with men and seeking HIV testing at a Los Angeles clinic. Among this sample, the estimated point prevalence of concurrency was higher among men later diagnosed HIV positive. One-offs were associated with increased rates of subsequent partnership dissolution.

Keywords

multistate; concurrency; HIV; sexual history; point process

1. Introduction

Sexual partnership dynamics known to impact HIV transmission include the number and duration of partnerships, the frequency and type of sexual intercourse engaged in, and the

*Correspondence to: Hilary Aralis, Department of Biostatistics, UCLA Fielding School of Public Health, University of California, Los Angeles, CA 90095, USA. hilary.aralis@gmail.com.

The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH.

length of time between partnerships [1, 2, 3]. However, the question of whether or not concurrency, defined as overlapping dates of sexual partnership, impacts HIV transmission independent of these other factors remains unanswered [4, 5].

In identifying concurrency, a frequently used operational definition involves classifying consecutive partnerships as having either a negative or a positive partnership gap [6]. For example, assume an individual is sampled from the population of interest and reports on his or her previous sexual partnerships by providing the number of days elapsed since the partnership started and stopped. For each set of consecutive partnerships, it is then possible to subtract the number of days corresponding to the beginning of the more recent partnership from the number of days corresponding to the end of the previous partnership. If the resulting difference is positive, we classify these partnerships as serially monogamous. If the difference is negative, we classify these partnerships as occurring concurrently. Thus, the question becomes whether or not concurrent partnership patterns result in increased rates of HIV transmission relative to serially monogamous patterns, when holding all other sexual partnership dynamics fixed.

A number of frequently cited studies have used mathematical models to demonstrate that the risk of HIV transmission is theoretically greater when partnerships are concurrent rather than serially monogamous [7, 8]. However, strong empirical evidence to support the effect of concurrency on HIV transmission has been difficult to obtain resulting in an ongoing debate among experts in the field of HIV transmission research [9, 10, 11].

The statistical analysis of sexual partnership dynamics, and concurrency in particular, is complicated because data is frequently obtained from cross-sectional surveys in which participants record recent sexual histories over a specified time interval. Furthermore, sexual histories may include both partnerships that last over a prolonged period of time as well as isolated sexual encounters that occur on a single day. The objective of this paper is to develop a statistical modeling approach for the analysis of retrospective sexual history data in order to identify and characterize covariates that impact concurrency and to provide estimates of the magnitude and extent of concurrency within a population. The present work was motivated by the MetroMates study in which men who have sex with men (MSM) who attended a clinic in Los Angeles and received HIV testing were asked to provide sexual history data. In section 2, we describe retrospective sexual history data and review some existing methods of analysis. In section 3, we propose a modeling approach based on a joint multistate model and point process allowing incorporation of explanatory variables. We derive estimators for two important concurrency metrics in section 4. The proposed methods are applied to the MetroMates study in section 5. We discuss the results and utility of the proposed model in section 6.

2. Background

2.1. Concurrency Metrics

Many of the challenges in establishing empirical evidence supporting the impact of concurrency on HIV transmission can be traced back to difficulties in accurately measuring concurrency. To assess the effect of concurrent partnership patterns on the trajectory of the

HIV epidemic in a population, it is necessary to estimate both the extent and the magnitude of concurrency. Specifically, interest lies in estimating the point prevalence of concurrency, referred to more generally as the *concurrent partnership distribution*, and the mean duration of concurrency, referred to here as the *mean concurrent partnership sojourn time* during which a person has k ongoing partnerships. We assume both these metrics can be estimated using sexual history data obtained by independently sampling individuals from a population existing in a stationary state with respect to its partnership patterns. Thus, the concurrent partnership distribution and the mean concurrent partnership sojourn times are estimated for a population at steady state and are not expressed as a function of time.

- *Concurrent partnership distribution* π_k is the probability that an individual member of a population is engaged in k ongoing partnerships at any given point in calendar time for $k \in \{0, 1, 2, \dots\}$
- *Mean concurrent partnership sojourn time* for an individual engaged in k ongoing partnerships ρ_k is the the mean duration of time the individual will remain in k ongoing partnerships before experiencing the next partnership formation or dissolution for $k \in \{0, 1, 2, \dots\}$

Estimation of these two population concurrency metrics enables researchers to draw inferences about specific populations from which data were collected and to ultimately compare patterns of concurrency across different populations or subpopulations. Further, empirical estimates of these population concurrency metrics could be used as input when constructing infectious disease mathematical models, such as agent-based and social network models, which would allow researchers to examine the viability and trajectory of the HIV epidemic over time and under variable conditions [12, 13, 14, 15].

2.2. Retrospective Sexual History Data

An optimal study design for estimating these population concurrency metrics would involve recruitment of a cohort of individuals prior to sexual debut followed by ongoing collection of partnership information from each participant throughout the duration of his or her life. Unfortunately, such designs are prohibitively expensive and typically infeasible due to implementation obstacles. Instead, partnership data is typically collected retrospectively in the form of sexual history information obtained using an approach known as the calendar method [16]. Following this approach, researchers administer a cross-sectional survey to a sample of individuals from the target population asking respondents to identify each sexual partnership, either ongoing or concluded, that occurred in part or in full during the previous year or other pre-specified elapsed interval of time. For each identified partnership, respondents are then asked to provide the first and last dates of sexual intercourse.

A drawback of the calendar method is that careful consideration needs to be taken when attempting to appropriately analyze data obtained using this technique. Traditionally, attempts to analyze retrospective sexual history data have used the partnership as the unit of observation and have thus ignored heterogeneity across individuals and time. For example, the mean partnership duration is usually calculated by averaging across partnership durations reported by all individuals across all time points, assuming partnerships to be independent and identically distributed [17]. In some instances, these partnership-level

analyses have also inadequately addressed right censoring and length-biased sampling[18]. Another shortcoming of current analytical approaches is the tendency to use only a snapshot of the available information. For example, to obtain an estimate of the concurrent partnership distribution, a specific time point is selected, such as one month prior to the survey date, and the observed distribution at that time is taken as the estimated distribution thereby discarding a large portion of the available data [19, 20]. In 2010, a UNAIDS working group developed guidelines for measuring concurrency and recommended that the point prevalence at six months prior to the interview be used as an indicator of concurrency within a population [21]. Following the dissemination of these guidelines, numerous articles were published questioning the validity of the proposed indicator citing issues of recall bias and demonstrating the variability in point prevalence estimates across differing points in time [20, 22].

Another concern rarely addressed when analyzing retrospective sexual history data is the handling of individual partnerships reported as having the same first and last dates of sexual intercourse. These partnerships are usually assumed to represent one-time sexual encounters and will be referred to as *one-offs*. Here we distinguish one-offs from other partnerships which we will refer to throughout this paper as *ongoing partnerships*. The high rate of one-offs reported among many of the populations targeted for prevention and treatment efforts necessitates the consideration of these events in the statistical analysis stage. Regardless of the per-one-off transmission probabilities, the cumulative effect of relatively high rates of one-offs on HIV transmission within a community may be substantial. Another advantage of explicitly modeling these one-off events is to account for the potential impact of one-off events engaged in by an individual on the likelihood of a subsequent partnership formation or dissolution event.

3. Methods

3.1. Modeling Objectives

Based on the challenges described above, the present study aims to develop a modeling framework that meets four criteria. The proposed model should:

1. Treat individuals as the independent units of observation rather than partnerships which may exhibit dependence when engaged in by the same individual at the same or different points in time.
2. Allow estimation of population metrics of interest for measuring concurrency: the *concurrent partnership distribution* and the *mean concurrent partnership sojourn time* for an individual engaged in k ongoing partnerships.
3. Be flexible enough to incorporate explanatory variables in order to identify and characterize factors affecting concurrency.
4. Account for one-offs and allow the occurrence of one-offs to potentially impact the subsequent formation and dissolution of ongoing partnerships.

3.2. The Joint Model

To address the modeling objectives, a joint multistate and point process model is proposed. A multistate model is a model for a continuous-time stochastic process which may, at any time, occupy one of a number of discrete states [23, 24]. Typically, multistate models are fit to longitudinal observations of a categorical variable. For sexual history data, each individual's continuation in and transition through differing states, where state is defined as the number of ongoing partnerships an individual is engaged in at a given point in time, can be modeled using a multistate modeling approach. In this manner, each individual's partnership patterns over time are treated as a single stochastic process. Figure 1(a) depicts data for an individual who reported the first and last dates of sexual intercourse for three partnerships occurring within the past year. Figure 1(b) demonstrates the way in which the reported partnership information can be translated into process data appropriate for use in fitting a multistate model. The depicted individual begins the year interval in a state of zero ongoing partnerships. He then experiences three partnership formation events followed by two dissolution events and ends the year in a state of one ongoing partnership.

The multistate component of the joint model addresses one of our modeling objectives by treating each individual's sexual history as its own stochastic process. Partnerships engaged in by the same individual at the same and different points in time are inherently linked by the modeling of transition intensities associated with partnership formation and dissolution. However, the point process component of the joint model is necessary to accommodate one-offs. By proposing a joint model, the state occupied by the multistate process for an individual at a given time can influence the rate of occurrence of one-offs. Additionally, the joint nature of the model allows the occurrence of one-offs to affect the subsequent intensity of transition from one state to another. Joint modeling of a multistate process and a discrete event process has been recently demonstrated using medical record data with random informative observation times [25].

Let $Y(t)$ denote the number of ongoing partnerships an individual is engaged in at calendar time t such that $Y(t)$ takes values in $\{0, 1, 2, \dots\}$ for all t where t corresponds to external or calendar time. We let $Y(t)$ represent the count of ongoing partnerships, which excludes the occurrence of one-offs that are alternatively modeled by the count process component of the joint model. Jumps in $Y(t)$ thus correspond to partnership formation or dissolution events. Assume multiple partnership formation or dissolution events cannot occur at the exact same point in time such that $Y(t)$ can only jump to adjacent states resulting in a birth-death-type process. If we assume $Y(t)$ is a time homogeneous continuous-time Markov multistate process, $Y(t)$ can be fully characterized by specification of either the transition probabilities from state k to state l

$$p_{kl}(\Delta t) = P(Y(t + \Delta t) = l | Y(t) = k)$$

for all $t \geq 0$ and $k, l \in \{0, 1, 2, \dots\}$, or by the transition intensities,

$$\alpha_{kl} = \lim_{\Delta t \rightarrow 0} \frac{p_{kl}(\Delta t)}{\Delta t}$$

for $k, l \in \{0, 1, 2, \dots\}$, which represent the instantaneous probability of transition to state l given occupation of state k . Under the Markov assumption, these transition intensities are assumed constant with respect to time yielding exponentially distributed sojourn times. In order for the occurrence of one-offs to influence the subsequent intensity of transition we must relax this assumption by allowing transition intensities to vary within occupancy of a state. We adopt a phase-type Markov model with intensities that fluctuate in response to each one-off event that occurs during occupancy of a state [26]. To implement this, we choose to parametrically model transition intensities by

$$\alpha_{kl}(t) = \beta_{kl0} \exp(\beta_{kl1} N(t) + \beta_{kl2}^T \mathbf{X}(t)) \quad (1)$$

where $N(t)$ represents the count of one-off events at calendar time t having occurred since the last transition in $Y(t)$ and $\mathbf{X}(t)$ denotes a vector of explanatory variables. For an individual who enters a state of k ongoing partnerships, $N(t)$ counts the occurrence of one-offs since entry into the current state. Each time an ongoing partnership is formed or dissolved an individual transitions to a new state and the counting process for one-offs, $N(t)$, starts over at zero. To make the definition of $N(t)$ precise, let $\nu(t)$ represent the cumulative count of one-offs having occurred at time t such that $\nu(t)$ represents a true counting process. Let $N(t) = \nu(t) - \nu(s(t))$ where $s(t) = \max_{0 \leq x < t} \{x : Y(x) = Y(t)\}$, 0 such that $s(t)$ represents the calendar time at which the last partnership formation or dissolution occurred prior to time t . $N(t)$ takes values in $\{0, 1, 2, \dots\}$ for all t . Assume no two one-offs can occur at the exact same time such that $N(t)$ is a counting process within each state occupied. In general, the α_{kl} transition intensities may depend on the history of the process, \mathcal{H} , which includes the trajectories associated with $N(t)$ and $\mathbf{X}(t)$ over time ranging from 0 to t . Here we consider the special case in which the history of the process can be ignored and $\alpha_{kl}(t|\mathcal{H})$ can be reduced to $\alpha_{kl}(t)$ and expressed as a function of $\mathbf{X}(t)$ and $N(t)$ observed at time t . Thus, the intensity of transition at time t may depend log-linearly on the number of one-offs having occurred, baseline characteristics of the individual, and time-dependent characteristics of the individual or his ongoing partners. Time-dependent variables are restricted, however, in that they are only allowed to vary along with the phase-type intensities which vary only at the instant a partnership is formed or dissolved or a one-off occurs. For example, $\mathbf{X}(t)$ could contain an indicator for engagement in a main partnership or occurrence of a one-off with a commercial sex worker but could not contain information on an individual's CD4 count as measured at arbitrary time points.

We choose to model $N(t)$ as a Markov-modulated Poisson process which allows variation in the rates of one-offs over time according to the number of ongoing partnerships an individual is engaged in. Markov-modulated Poisson processes are doubly stochastic in that the Poisson process rate varies according to a continuous-time Markov chain [27]. In our proposed model, the continuous-time Markov chain regulating the rates of one-offs

corresponds to the multistate process $Y(t)$ representing the number of ongoing partnerships an individual is engaged in at time t . The interaction of both components of the proposed joint model are visually depicted in Figure 2. At each day prior to the survey date corresponding to time t , an individual can be said to be in a state of $Y(t)$ ongoing partnerships and to have experienced $N(t)$ one-offs which can be read from the left and right vertical axes of Figure 2, respectively. The dashed line which increments along with each partnership or one-off event depicts the times at which the transition intensities for partnership formation or dissolution may vary. A Markov-modulated Poisson process can be fully characterized through specification of the intensity function $\lambda(t)$ which represents the infinitesimal rate at which events are expected to occur around time t . Thus, in modeling $N(t)$ it suffices to model $\lambda(t)$. We parametrically model intensity functions for individuals in a state of k ongoing partnerships by

$$\lambda_k(t) = \gamma_{k0} \exp(\boldsymbol{\gamma}_{k1}^T \mathbf{X}(t)) \quad (2)$$

where $\mathbf{X}(t)$ is a vector of potentially time-dependent explanatory variables with the same restrictions as described previously. $\mathbf{X}(t)$ does not need to consist of the same explanatory variables across the two components of the model and careful consideration of the joint nature of the model should be taken prior to selecting covariates for inclusion in both components of the model. In choosing to consider the two components of the joint model together as a two-dimensional vector, $(Y(t), N(t))$, the overarching modeling framework can alternatively be described as a bivariate continuous-time Markov process in which the Markov property holds for states defined through specification of both $Y(t)$ and $N(t)$.

3.3. Parameter Estimation

We fit the joint model described in section 3.2 and specifically given by equations (1) and (2) using maximum likelihood estimation. Let $\boldsymbol{\beta}_{kl} = \{\beta_{kl0}, \beta_{kl1}, \beta_{kl2}\}$ denote the vector of regression parameters expressed in equation (1). In theory, transition intensity regression parameters $\boldsymbol{\beta}_{kl}$ can be estimated for each $k, l \in \{0, 1, 2, \dots\}$. In practice, we choose to specify a limited number of unique transition intensities. For modeling of sexual history data, we will estimate parameters $\boldsymbol{\beta}_{kl}$ associated with transition from a state of k ongoing partnerships to a state of l ongoing partnerships for three distinct types of transitions:

Formation of a monogamous partnership	$(k=0, l=1)$
Formation of a concurrent partnership	$(k>0, l=k+1)$
Dissolution of any ongoing partnership	$(k>0, l=k-1)$

To clarify use of the term monogamous, here we define a *monogamous partnership* as any partnership that is the sole ongoing partnership that an individual has reported being engaged in at a given point in time. Thus, engagement in a monogamous partnership does not preclude the occurrence of one-offs or the formation of additional concurrent partnerships at a future point in time. To simplify notation, let $\boldsymbol{\beta}_0$, $\boldsymbol{\beta}_1$, and $\boldsymbol{\beta}_2$ denote the parameters to be estimated for the intensity of formation of a monogamous partnership,

formation of a concurrent partnership, and dissolution of a partnership, respectively. Additionally, we choose to estimate $\boldsymbol{\gamma}_k = \{\gamma_{k0}, \gamma_{k1}\}$ from equation (2) separately for states of no ongoing partnership ($k = 0$), one ongoing partnership ($k = 1$) and concurrent partnerships ($k = 2$). For simplicity, we will denote these parameters as $\boldsymbol{\gamma}_0$, $\boldsymbol{\gamma}_1$ and $\boldsymbol{\gamma}_2$, respectively. Therefore, the full likelihood will be maximized to obtain parameter estimates $\hat{\boldsymbol{\theta}} = \{\hat{\boldsymbol{\beta}}_0, \hat{\boldsymbol{\beta}}_1, \hat{\boldsymbol{\beta}}_2, \hat{\boldsymbol{\gamma}}_0, \hat{\boldsymbol{\gamma}}_1, \hat{\boldsymbol{\gamma}}_2\}$.

In constructing the likelihood we must calculate the probability of survival across intervals of time during which the transition probabilities remain constant. The term *event* will be used to signify any one of the following: a partnership formation, a partnership dissolution, or the occurrence of a one-off. We assume that multiple events cannot occur at the same instant in time. Due to the Markov modeling approach, inter-event times are exponentially distributed. For an individual in a state of k ongoing partnerships who experiences an event at time t_1 , the probability of that individual remaining in state k until time t_2 without experiencing another event is

$$S_k(t_1, t_2) = \begin{cases} \exp(-\{(\alpha_{01}(t_1) + \lambda_0(t_1))(t_2 - t_1)\}) & \text{if } k=0 \\ \exp(-\{(\alpha_{k,k+1}(t_1) + \alpha_{k,k-1}(t_1) + \lambda_k(t_1))(t_2 - t_1)\}) & \text{if } k>0 \end{cases}$$

where α_{01} , $\alpha_{k,k+1}$, and $\alpha_{k,k-1}$ denote the transition intensities associated with the formation of a monogamous partnership, formation of a concurrent partnership, and dissolution of any ongoing partnership, respectively. λ_k denotes the rate of one-offs for an individual in a state of k ongoing partnerships. To construct the likelihood, we must also calculate the instantaneous probability of an event occurring at time t . Given an individual in a state of k ongoing partnerships experienced an event at time t_1 and remained in state k until time t_2 , the probability of a specific event occurring at time $t_2 > t_1$ is assumed constant and equal to

$$q_{kl}(t_1) = \begin{cases} \alpha_{01}(t_1) & \text{if } k=0, l=1 \\ \alpha_{k,k+1}(t_1) & \text{if } k>0, l=k+1 \\ \alpha_{k,k-1}(t_1) & \text{if } k>0, l=k-1 \\ \lambda_k(t_1) & \text{if } k \geq 0, l=k \end{cases}$$

where $q_{kk}(t_1)$ indicates no change in the number of ongoing partnerships and is used to denote the occurrence of a one-off. Let $i = 1, \dots, n$ index each respondent in an independent sample of size n . For each individual i , let m_i indicate the total number of events experienced, either ongoing partnership events or one-off events, over the course of the year interval. Let $T_i = \{t_{i0}, t_{i1}, \dots, t_{im_i}, t_{i(m_i+1)}\}$ be the set of event times for individual i such that t_{i0} indicates the time at which the year interval begins, t_{i1} the time when the first event occurs, t_{im_i} the time when the last event occurs and $t_{i(m_i+1)}$ the time at which the year interval ends. Event times are ordered such that $t_{i0} < t_{i1} < \dots < t_{i(m_i+1)}$. Similarly, let $Y_i = \{y_{i0}, y_{i1}, \dots, y_{im_i}\}$ be the sequence of states for individual i such that y_{i0} and y_{im_i} indicate the numbers of ongoing partnerships individual i is engaged in at the start and end of the year interval, respectively. Importantly, adjacent elements of Y_i need not differ, for example,

y_{2i} would equal y_{3i} in the instance that the third event experienced by individual i was a one-off. An example demonstrating use of this notation for a single individual is depicted in Figure 3.

The likelihood can then be expressed as the product over all individuals and all events

$$L = \prod_{i=1}^n \left[\prod_{j=0}^{m_i} S_{y_{ij}}(t_{ij}, t_{i(j+1)}) \right] \left[\prod_{j=0}^{m_i-1} q_{y_{ij}y_{i(j+1)}}(t_{ij}) \right]$$

Following maximization of the log likelihood function using numerical optimization techniques, the covariance matrix for the parameter estimates can be obtained by inverting the negative Hessian. The square root of the diagonal elements of this covariance matrix are asymptotically equal to the standard errors for the corresponding parameter estimates.

4. Concurrency Metric Estimators

As a result of the bivariate Markov model specification, which implies constant event intensities, the concurrency metric estimators can be expressed in terms of the model parameter estimates. Let C_k be an integer valued random variable representing the number of one-offs that occur from the moment an individual enters a state of k ongoing partnerships until the individual leaves that state by either forming or dissolving an ongoing partnership. Let H_k be the random variable indicating the concurrent partnership sojourn time, that is the duration of time an individual remains in a state of k partnerships prior to an ongoing partnership formation or dissolution event. For an individual in a state of k ongoing partnerships who has experienced r one-offs since the last partnership formation or dissolution event, let μ_{kr} denote the mean duration of time until the next event (partnership formation, dissolution, or one-off). Thus, μ_{kr} is the mean inter-event time after entry into a state of k ongoing partnerships and after a total of r one-offs since entry into the current state. Inter-event times are exponentially distributed because the event occurrence intensities are constant given k and r . Therefore, for a fixed $C_k = c$, H_k will be equal to the amount of time spent in state k with a cumulative total of exactly 0 one-offs, plus the amount of time spent in state k with a cumulative total of exactly 1 one-off, summing all the way up to c one-offs. For an individual in a state of k ongoing partnerships who has experienced r one-offs, let λ_{kr} represent the probability that the next event (formation, dissolution, or one-off) that occurs is either a partnership formation or dissolution event resulting in escape from the state of k ongoing partnerships. Therefore, $P(C_k = 0) = \lambda_{k0}$ and $P(C_k = 1) = \lambda_{k1}(1 - \lambda_{k0})$ which is equal to the probability of the first event being a one-off and the second event being the formation or dissolution of an ongoing partnership. The mean concurrent partnership sojourn times for all $k \in \{0, 1, 2, \dots\}$ can then be derived as follows using iterative expectation

$$\begin{aligned}
 \rho_k &= E(H_k) \\
 &= E_{C_k}(E(H_k|C_k=c)) \\
 &= E_{C_k}\left(\sum_{r=0}^c \mu_{kr}\right) \\
 &= \sum_{c=0}^{\infty} \left(\left(\sum_{r=0}^c \mu_{kr} \right) P(C_k=c) \right) \\
 &= \mu_{k0}\Delta_{k0} + \sum_{c=1}^{\infty} \left(\left(\sum_{r=0}^c \mu_{kr} \right) \Delta_{kc} \prod_{s=0}^{c-1} (1-\Delta_{ks}) \right) \\
 \hat{\rho}_k &= \hat{\mu}_{k0}\hat{\Delta}_{k0} + \sum_{c=1}^{\infty} \left(\left(\sum_{r=0}^c \hat{\mu}_{kr} \right) \hat{\Delta}_{kc} \prod_{l=0}^{c-1} (1-\hat{\Delta}_{kl}) \right) \quad (3)
 \end{aligned}$$

To calculate $\hat{\rho}_k$, we first define

$$\hat{\alpha}_{klr} = E[\hat{\alpha}_{kl}(t)|Y(t)=k, N(t)=r] = \hat{\beta}_{kl0} \exp\left(\hat{\beta}_{kl1}r + \hat{\beta}_{kl2}^T E[\mathbf{X}(t)|Y(t)=k, N(t)=r]\right) \quad (4)$$

$$\hat{\lambda}_{kr} = E[\hat{\lambda}_k(t)|Y(t)=k, N(t)=r] = \hat{\gamma}_{k0} \exp\left(\hat{\gamma}_{k1}^T E[\mathbf{X}(t)|Y(t)=k, N(t)=r]\right) \quad (5)$$

Depending on the variables comprising $\mathbf{X}(t)$, $E[\mathbf{X}(t)|Y(t)=k, N(t)=r]$ can usually be estimated given the available data. For instance, if $X(t)$ is an indicator for engagement in a main partnership, $E[X(t)|Y(t)=k, N(t)=r]$ would simply equal the probability of being in at least one main partnership for an individual who experienced r one-offs since transition into a state of k ongoing partnerships. As a result of the homogeneous Markov assumption which implies independent and exponentially distributed inter-event times,

$$\begin{aligned}
 \hat{\mu}_{kr} &= \left[\hat{\alpha}_{k(k+1)r} + \hat{\alpha}_{k(k-1)r} + \hat{\lambda}_{kr} \right]^{-1} \\
 \hat{\Delta}_{kr} &= \frac{\hat{\alpha}_{k(k+1)r} + \hat{\alpha}_{k(k-1)r}}{\hat{\alpha}_{k(k+1)r} + \hat{\alpha}_{k(k-1)r} + \hat{\lambda}_{kr}}
 \end{aligned}$$

for all $k \in \{1, 2, \dots\}$. For $k=0$, $\hat{\mu}_{kr} = [\hat{\alpha}_{01r} + \hat{\lambda}_{0r}]^{-1}$ and $\hat{\Delta}_{kr} = [\hat{\alpha}_{01r}][\hat{\alpha}_{01r} + \hat{\lambda}_{0r}]^{-1}$. For practical purposes, in estimating the mean concurrent partnership sojourn times, infinite sums can typically be truncated such that the sum extends only until $P(C_k=c)$ becomes negligible.

Assuming stationarity of the bivariate continuous-time Markov process, an estimator for the concurrent partnership distribution can be derived by solving the equilibrium equation $\boldsymbol{\pi}\mathbf{Q} = \mathbf{0}$ for $\boldsymbol{\pi}$ where \mathbf{Q} is the infinitesimal generator matrix for the two-dimensional process [28]. We will assume maximal values for possible counts of ongoing partnerships and one-offs in order to obtain a finite dimensional \mathbf{Q} matrix and to make the calculations tractable. The resulting approximation is thus accurate up to arbitrary numerical error stemming from truncation of the state space. Allowing a maximum of K ongoing partnerships and R one-

offs, such that $\boldsymbol{\pi} = \{\boldsymbol{\pi}_{00}, \boldsymbol{\pi}_{10}, \boldsymbol{\pi}_{20}, \dots, \boldsymbol{\pi}_{K0}, \boldsymbol{\pi}_{01}, \boldsymbol{\pi}_{11}, \dots, \boldsymbol{\pi}_{KR}\}$ where $\boldsymbol{\pi}_{kr}$ denotes the probability that, at any given point in time, an individual is engaged in k ongoing partnerships after the occurrence of r one-offs since the last formation or dissolution event. For $r \in \{0, 1, \dots, R\}$, let

$$\begin{aligned} \boldsymbol{\Lambda}_r &= \text{diag}(\hat{\lambda}_{0r}, \hat{\lambda}_{1r}, \hat{\lambda}_{2r}, \dots, \hat{\lambda}_{Kr}) \\ \boldsymbol{\Gamma}_r &= \text{diag}(-\hat{\alpha}_{01r}, -\hat{\alpha}_{10r} - \hat{\alpha}_{12r}, -\hat{\alpha}_{21r} - \hat{\alpha}_{23r}, \dots, -\hat{\alpha}_{(K-1)(K-2)r} - \hat{\alpha}_{(K-1)Kr}, -\hat{\alpha}_{K(K-1)r}) \\ \boldsymbol{A}_r &= \begin{bmatrix} 0 & \hat{\alpha}_{01r} & 0 & 0 & \dots & 0 \\ \hat{\alpha}_{10r} & 0 & \hat{\alpha}_{12r} & 0 & \dots & 0 \\ 0 & \hat{\alpha}_{21r} & 0 & \hat{\alpha}_{23r} & \dots & 0 \\ 0 & 0 & \hat{\alpha}_{32r} & 0 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \hat{\alpha}_{K(K-1)r} & 0 \end{bmatrix} \end{aligned}$$

where $\boldsymbol{\Lambda}_r, \boldsymbol{\Gamma}_r$ and \boldsymbol{A}_r are $(K + 1)$ -dimensional square matrices. Then, \boldsymbol{Q} is a $(K + 1)(R + 1)$ -dimensional square matrix that can be defined using the above notation and a series of block matrices.

$$\boldsymbol{Q} = \begin{bmatrix} \boldsymbol{A}_0 + \boldsymbol{\Gamma}_0 - \boldsymbol{\Lambda}_0 & \boldsymbol{\Lambda}_0 & 0 & 0 & \dots & 0 \\ \boldsymbol{A}_1 & \boldsymbol{\Gamma}_1 - \boldsymbol{\Lambda}_1 & \boldsymbol{\Lambda}_1 & 0 & \dots & 0 \\ \boldsymbol{A}_2 & 0 & \boldsymbol{\Gamma}_2 - \boldsymbol{\Lambda}_2 & \boldsymbol{\Lambda}_2 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \boldsymbol{A}_R & 0 & 0 & 0 & 0 & \boldsymbol{\Gamma}_R \end{bmatrix}$$

The structure of \boldsymbol{Q} is such that the $\boldsymbol{A}_0 + \boldsymbol{\Gamma}_0 - \boldsymbol{\Lambda}_0$ block yields the transition rates between states $(k, 0)$ and $(l, 0)$ and the first $\boldsymbol{\Lambda}_0$ block yields the transition rates between states $(k, 0)$ and $(k, 1)$ [25, 29]. The rest of the generator matrix is structured similarly. There is insufficient information to solve the set of balance equations resulting from $\boldsymbol{\pi}\boldsymbol{Q} = 0$ and we must therefore incorporate our knowledge that $\sum_{i=0}^K \sum_{j=0}^R \pi_{ij} = 1$. After solving for $\boldsymbol{\pi}$, we obtain the concurrent partnership distribution by summing across numbers of one-offs such that $\hat{\pi}_k = \sum_{j=0}^R \pi_{kj}$ for all $k \in \{0, 1, 2, \dots, K\}$.

Estimation of standard errors for all $\hat{\rho}_k$ and $\hat{\boldsymbol{\pi}}_k$ can be completed using a nonparametric bootstrap approach for multistate processes [30, 31]. For an observed sample of size n , the approach entails sampling with replacement a total of n individuals and using all of each sampled individual's sexual history data to calculate $\hat{\rho}_k$ and $\hat{\boldsymbol{\pi}}_k$ for $k \in \{0, 1, \dots\}$ as described above. This entails fitting the proposed model, obtaining the parameter estimates and then using the formulas presented in this section to calculate the concurrency metrics of interest. This resampling process is repeated until g bootstrap samples have been drawn and estimates computed where g is usually large. The variances of $\hat{\rho}_k$ and $\hat{\boldsymbol{\pi}}_k$ can then be estimated as the empirical variances of the g replicates of $\hat{\rho}_k$ and $\hat{\boldsymbol{\pi}}_k$.

5. Application

The retrospective sexual history data that motivated the development of the proposed model came from a National Institute of Drug Abuse (NIDA)-funded research study officially titled *Transmission Behavior in Partnerships of Newly HIV Infected Southern Californians* and commonly referred to as the MetroMates study (PI: Dr. Pamina Gorbach). Between February 2009 and May 2012, MSM seeking testing for HIV through the Sexual Health Program at the Los Angeles LGBT Center were recruited to participate in the MetroMates study involving a baseline interview, testing for HIV and other sexually transmitted infections, and a year of follow-up interviews. Criteria for enrollment included: male, at least 18 years of age, report of sex with a male partner in the past 12 months, and a new HIV test. Demographic, behavioral, and other data were collected using Audio Computer-Assisted Self-Interview (ACASI). Data were collected at the respondent level and respondents could elect to provide information for up to six named partners with whom they reported having sexual intercourse within the past year. Using the calendar method, respondents reported the lengths of time since first and last intercourse in days, weeks, months, or years creating variation in precision. To distinguish between partnerships that were ongoing versus dissolved at the time of the survey, responses to an item asking how likely it is that a respondent will have sex with the partner again were used. Responses of “extremely unlikely” and “very unlikely” were assumed to indicate a terminated partnership.

Data were collected for 326 participants in the MetroMates study. Among these participants, 1,050 partnerships were reported. Invalid partnerships consisting of 64 partnerships with missing first or last dates of intercourse, 39 partnerships with a last date of intercourse preceding the first date of intercourse, and 47 partnerships with last dates of intercourse prior to the year interval were excluded. Following these exclusions, data were available for 295 male participants with at least one valid partnership. Participants ranged in age from 19 to 62 years (mean = 30.03, standard deviation = 7.85). The MetroMates study protocol called for oversampling of HIV positive men. Among the 295 respondents, 196 received a positive HIV diagnosis and the remaining 99 were HIV negative at the time of the survey. The MetroMates study also selectively enrolled men whose new HIV diagnosis suggested a recent or acute infection. As described by Gorbach et al. [32], during the initial phase of enrollment only men with a recent diagnosis were recruited. To complete enrollment, men with any new diagnosis, including chronically infected men, were recruited. Of the 295 men included in our sample, 74% reported one or more one-offs during the year interval for a total of 534 one-offs. Of the 896 partnerships reported, 60% were one-offs, 7% were of duration 30 days or less, 24% were of duration 31–365 days, and 9% were reported as lasting longer than 365 days.

The Markov nature of the proposed model assumes exponentially distributed sojourn times conditional on the number of ongoing partnerships and the number of one-offs having occurred since the last partnership event. To assess the appropriateness of this assumption for the MetroMates sample, we performed graphical diagnostics [33]. Specifically, we plotted the Nelson-Aalen estimated cumulative hazard rate versus time for each condition defined by HIV status, the number of ongoing partnerships, and number of one-offs. For conditions with a sufficient sample size, we assessed the linearity of the plotted curve.

Across most conditions, the assumption of exponentially distributed sojourn times appeared valid.

In applying the modeling approach described previously to the MetroMates data, we fit a number of models including explanatory variables such as respondent age and HIV status. In the model selection stage, explanatory variables were incorporated into either or both the multistate and point process components of the model. The model we selected for presentation included the number of one-offs and an indicator for HIV status as covariates in the multistate portion of the model. One-off event rates were estimated separately for individuals in no ongoing partnerships, one ongoing partnership, and concurrent partnerships. The log likelihood function was constructed using code written in R version 3.2.0 and available in the supplementary materials. Minimization of the negative log likelihood function was accomplished using the general-purpose optimization function *optim* available in the base R stats package. The Nelder-Mead direct search method was specified and differing sets of initial values were used to verify the results obtained. To enable calculation of standard errors, a numerical approximation to the Hessian matrix was generated using the R *numDeriv* package. Parameter estimates for the model fit to the MetroMates data are displayed in Table 1. Relative to HIV negative men, HIV positive men were estimated to have higher hazard of forming a monogamous partnership, higher hazard of forming a concurrent partnership, and lower hazard of partnership dissolution during the previous year, although these results were not statistically significant. The number of one-offs was significantly associated with rates of subsequent partnership dissolution. Following the occurrence of each additional one-off, an individual was estimated to experience a 56% increase in the hazard of dissolution of an ongoing partnership.

Using the analytic expressions derived previously and the parameter estimates in Table 1, the population concurrency metrics were estimated. The concurrent partnership distribution and the mean concurrent partnership sojourn times were estimated separately for HIV positive and negative individuals in this sample (Table 2). Standard errors for the concurrency metrics were calculated based on $g = 1000$ bootstrap samples. The concurrent partnership distribution was calculated across states ranging from 0–7 ongoing partnerships and 0–4 one-offs, as these ranges encompassed the majority of the observed data. States of 2 ongoing partnerships were combined for presentation in Table 2. At any given point in time, approximately 18% of the HIV positive sample would be expected to be engaged in concurrent partnerships as compared to 10% of the HIV negative sample. Sixteen percent of the HIV negative sample was estimated to be engaged in a monogamous partnership at any given point in time relative to 19% of the HIV positive sample.

The mean concurrent partnership sojourn times for states of 0, 1, and 2 or more ongoing partnerships are displayed in Table 2. Regardless of HIV status, the mean length of time an individual was expected to remain engaged in a state of 2 or more partnerships prior to forming or dissolving a partnership was approximately 4 months. The mean duration of time spent in a state of one ongoing partnership was also approximately 4 months and did not appear to differ substantially according to HIV status. HIV negative individuals were estimated to remain in a state of no ongoing partnerships for an average duration of 15.5 months, as compared to approximately 14.5 months among HIV positive individuals.

The mean numbers of one-offs per year for individuals engaged in no ongoing partnerships, one ongoing partnership, or concurrent partnerships were obtained by taking the inverse of each element of $\hat{\gamma}$. Not surprisingly, individuals in a single monogamous partnership had the lowest estimated rate of one-offs per year (0.81). On average, men engaged in concurrent partnerships experienced an estimated 1.40 one-offs per year and men engaged in no partnerships experienced 1.75 one-offs per year.

6. Discussion

We have described a novel approach for the joint modeling of sexual partnership patterns using retrospective sexual history data containing one-off sexual encounters. The proposed model can be applied to answer pertinent questions in the field of HIV transmission research. Implementation of this approach was demonstrated using epidemiological data collected from a sample of MSM seeking HIV testing at a Los Angeles clinic. Despite the limitations associated with retrospective sexual history survey data, we were able to estimate several important population concurrency metrics using a technique that accounted for different sources of variation and fully utilized the available data.

The joint multistate and point process model addresses all of the modeling objectives outlined previously. The proposed method accounts for dependence among partnerships engaged in by the same person at the same or different points in time by translating the data collected at the partnership-level into individual-level trajectories and modeling these trajectories as independent stochastic processes. Another advantage of the joint model is the explicit modeling of rates of partnership formation and dissolution. Many of the agent-based and other mathematical models constructed to examine the impact of concurrency on HIV transmission have relied on simple empirical estimates of the mean partnership duration or concurrent partnership distribution as input [15, 12, 34]. Our proposed method provides improved estimates of these quantities but also provides formation and dissolution rates that are perhaps more useful in creating a dynamic mathematical model involving forward simulation of concurrent partnership patterns over time. As shown in Figure 4, state transition intensities and one-off rates estimated based on the MetroMates data can be easily used to generate simulated sexual partnership trajectories at the individual level. Rates of partnership and one-off events that are dynamic with respect to time could be useful in adapting current network models such that the probabilities of a partnership formation or dissolution between two individuals in a network are variable and more accurately reflect the sexual partnership patterns observed in a population. The proposed joint model is also flexible enough to allow for the incorporation of explanatory variables to further account for heterogeneity between individuals. Lastly, we have developed a joint model that includes the random occurrence of one-offs. This important extension enables examination of the relative importance of one-offs in driving the spread of HIV within a population and also allows for one-offs to impact HIV transmission indirectly, by affecting rates of subsequent partnership formation and dissolution. Among populations such as the MSM surveyed in the MetroMates study, the high reported rate of one-offs makes this a valuable feature of the proposed model. The joint modeling approach also distinguishes between one-offs and short-term partnerships which may be important for determining factors impacting HIV transmission. One-offs could potentially have a higher probability of transmission for a

given sexual encounter due to differences in the type of sex occurring during a one-off. For example, one-offs may be more frequently associated with drug use leading to longer duration of sex or more vigorous sex which could in turn enhance infectiousness. The proposed model could enable identification of such differences in the risk of transmission.

Participants in this study do not represent a random sample of all MSM living within Los Angeles nor do they represent all MSM living within the community served by the Los Angeles LGBT Center. This sample was obtained by recruiting individuals who sought HIV testing and the recent sexual activity they reported on would be expected to include behaviors that influenced their decision to seek testing. Further, the study protocol called for the oversampling of HIV positive individuals and, in particular, recently-infected HIV positive individuals[32]. Thus, the generalizability of results presented in this study is limited. We assume that the removal of invalid partnerships resulting in exclusion of 31 respondents did not significantly bias our results although we have limited means of assessing this assumption. Sixty-one percent of the 31 excluded individuals were HIV positive as compared to 66% of individuals included in the analyzed data. In removing invalid partnerships, we further acknowledge that the partnership rate estimates presented here could be biased downward if the removed partnerships represented actual partnerships occurring during the year interval.

Several sources of uncertainty were present in our analysis of the MetroMates data. Since respondents were only allowed to report on a maximum of six sexual partnerships that occurred in part or in full during the previous year, individuals engaging in larger numbers of partnerships across the year interval may have provided incomplete partnership data that could potentially bias the estimates presented. Of the 295 participants included in the final sample, 60 (20.3%) reported on 6 partnerships. Methods to address this issue in future studies need further development but could include alternative questionnaire designs or consideration of subject-specific time intervals of observation during the analysis stage. Additionally, since respondents were allowed to choose the unit of measurement with which they reported time since first and last dates of sexual intercourse, dates used in analyses were often approximated. Future studies are required to explore the potential impact of this source of uncertainty, especially in the context of multistate models with bidirectional transitions. Similarly, this issue of coarseness in the reporting of dates introduces uncertainty surrounding the distinction between one-offs and ongoing partnerships of short duration which is an area for future work. Lastly, due to the questionnaire instructions, respondents were not asked to report partnerships occurring prior to the year interval and therefore the number of one-offs an individual had engaged in at the start of the year interval was unknown. In analyzing the MetroMates data, we assumed zero one offs having occurred since the last formation or dissolution event, which could potentially bias our results. Future studies may choose to consider attempting to capture or impute this missing data.

In considering these results, it is important to recall the sampling approach with regard to HIV status. The HIV positive sample received their positive diagnosis at the time of the survey. Thus, the sexual behaviors these individuals were reporting on occurred prior to their knowledge of their HIV status. The sexual patterns attributed to HIV positive men within this sample should not be assumed to reflect the behaviors an HIV positive man aware of his

status would engage in. Additionally, some of the behaviors reported on by recently infected HIV positive individuals within this sample may have occurred prior to the individual's acquisition of HIV. Although the retrospective reporting of the data relative to the date of diagnosis limits some of the conclusions that can be drawn, the timing of calendar method data collection may be advantageous when attempting to answer questions about the association between concurrency and acquisition of HIV. If a significant association between concurrency and subsequent diagnosis of acute HIV infection had been identified, it would not directly support the hypothesis that concurrency impacts HIV transmission at the population-level. In theory, an individual who engages in concurrent partnerships does not put him or herself at greater risk than if he or she had engaged in the same numbers and types of risky behaviors with the same individuals but in a serially monogamous setting. Therefore, we would expect an increase in the rate of transmission among individuals engaging in concurrent partnerships but not necessarily an increase in the rate of acquisition. It is, however, reasonable to consider that individuals engaging in concurrent partnerships are (1) also engaging in more total partnerships and engaging in risky behaviors at a greater rate relative to individuals in monogamous partnerships, and (2) more likely to be engaging in concurrent partnerships with individuals who themselves are engaging in concurrent partnerships. Both of which could explain an association between increased point prevalence of concurrency and subsequent diagnosis with HIV among samples reporting retrospective sexual history data at the time of screening.

We have demonstrated implementation of this joint modeling approach using model specifications that were selected to be appropriate for use with the MetroMates data and to reduce complexity in this initial presentation of the proposed model. Future applications of this model for analysis of sexual history data could select a different set of covariates, including the addition of other time-varying explanatory variables such as partnership-level characteristics. Although the assumption of stationarity is critical for calculation of the concurrency metrics as described herein, inclusion of covariates such as respondent age or calendar date at the time of interview is possible. In this instance, the concurrency metrics can be calculated for categorical age or date strata as done for HIV status in the present application, or calculations can be completed after taking the expected value of these covariates as shown in equations (4) and (5). Although the presented model for the MetroMates data did not include any explanatory variables significantly associated with the rate of one-offs, the parametric formulation of the point process rate function can easily accommodate inclusion of these variables. A simple modification to the proposed model would allow for a different definition of $N(t)$. For instance, one might elect to let $N(t)$ reflect the count of one-offs occurring only during some specific time interval prior to time t , for instance, one month, such that the impact of one-offs on subsequent events is limited in duration. The proposed model is also general enough to allow for selection of different counting processes in instances when the assumptions surrounding the Poisson process are not valid. For instance, when it is not acceptable to assume that the variance of the counts of one-offs over any given interval of time equals the mean, an alternative counting process distribution, such as the negative binomial, may be more appropriate. Another consideration is the use of zero-inflated count models in instances in which time intervals during which no one-offs occur are observed in excess. The model specified herein also assumes a bivariate

continuous-time Markov structure. This framework requires that transition intensities are constant within subintervals of time defined by the occurrence of one-offs, allowing transition intensities from one state to another to differ across the interval of time spent in a given state. Advantages of this framework are the flexibility to allow one-offs to affect subsequent intensities and ease of construction of the likelihood. Alternative non-Markovian models that do not rely on the phase-type intensities assumption are possible although the derived concurrency metric estimators would not be directly applicable.

Future applications of the proposed model to sexual history data may use the general joint multistate and point process framework presented here and alternatively adapt it to meet their needs. Researchers investigating sexual partnership dynamics impacting HIV transmission should consider analyzing sexual history data using a modeling approach such as the one proposed here, that jointly models both ongoing and one-off sexual partnerships and treats the individual, rather than the partnership, as the independent unit of observation.

Acknowledgments

The authors would like to thank Dr. Marjan Javanbakht for her efforts in preparing and transferring the MetroMates data and providing information about the study. The MetroMates project was funded by the National Institute of Drug Abuse (NIDA) under grant number 1R01DA022116-01A1 awarded to Dr. Pamina Gorbach at the University of California Los Angeles. Hilary Aralis was supported by the National Institutes of Health (NIH) Training Grant 5-T32-AI007370, Biostatistical Training in AIDS.

References

1. Foxman B, Newman M, Percha B, Holmes KK, Aral SO. Measures of sexual partnerships: lengths, gaps, overlaps, and sexually transmitted infection. *Sexually Transmitted Diseases*. 2006; 33(4):209–214. DOI: 10.1097/01.olq.0000191318.95873.8a [PubMed: 16434884]
2. Baggaley RF, White RG, Marie-Claude B. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *International Journal of Epidemiology*. 2010; 39(4):1048–1063. DOI: 10.1093/ije/dyq057 [PubMed: 20406794]
3. Royce RA, Sena A, Cates W, Cohen MS. Sexual transmission of HIV. *The New England Journal of Medicine*. 1997; 336(15):1072–1078. DOI: 10.1056/NEJM199704103361507 [PubMed: 9091805]
4. Boily M, Alary M, Baggaley RF. Neglected issues and hypotheses regarding the impact of sexual concurrency on HIV and sexually transmitted infections. *AIDS Behavior*. 2012; 16:304–311. DOI: 10.1007/s10461-011-9887-0 [PubMed: 21279678]
5. Morris M, Kurth AE, Hamilton DT, Moody J, Wakefield S. Concurrent partnerships and HIV prevalence disparities by race: linking science and public health practice. *American Journal of Public Health*. 2009; 99(6):1023–1031. DOI: 10.2105/AJPH.2008.147835 [PubMed: 19372508]
6. Mercer CH, Aicken CRH, Tanton C, Estcourt CS, Brook MG, Keane F, Cassell JA. Serial monogamy and biologic concurrency: measurement of the gaps between sexual partners to inform targeted strategies. *American Journal of Epidemiology*. 2013; 178(2):249–259. DOI: 10.1093/aje/kws467 [PubMed: 23801013]
7. Epstein H. The mathematics of concurrent partnerships and HIV: a commentary on Lurie and Rosenthal, 2009. *AIDS Behavior*. 2010; 14:29–30. DOI: 10.1007/s10461-009-9627-x [PubMed: 19866354]
8. Morris M. Barking up the wrong evidence tree. Comment on Lurie and Rosenthal, “Concurrent partnerships as a driver of the HIV epidemic in Sub-Saharan Africa? The evidence is limited. *AIDS Behavior*. 2010; 14:31–33. DOI: 10.1007/s10461-009-9639-6 [PubMed: 19997971]
9. Lurie MN, Rosenthal S. Concurrent partnerships as a driver of the HIV epidemic in Sub-Saharan Africa? the evidence is limited. *AIDS Behavior*. 2010; 14:17–24. DOI: 10.1007/s10461-009-9583-5 [PubMed: 19488848]

10. Lurie MN, Rosenthal S. The concurrency hypothesis in Sub-Saharan Africa: convincing empirical evidence is still lacking. Response to Mah and Halperin, Epstein, and Morris. *AIDS Behavior*. 2010; 14:34–37. DOI: 10.1007/s10461-009-9640-0 [PubMed: 20130786]
11. Mah TL, Halperin DT. The evidence for the role of concurrent partnerships in Africa's HIV epidemics: a response to Lurie and Rosenthal. *AIDS Behavior*. 2010; 14:25–28. DOI: 10.1007/s10461-009-9617-z
12. Goodreau SM, Cassels S, Kasprzyk D, Montano DE, Greek A, Morris M. Concurrent partnerships, acute infection and HIV epidemic dynamics among young adults in Zimbabwe. *AIDS Behavior*. 2012; 16:312–322. DOI: 10.1007/s10461-010-9858-x [PubMed: 21190074]
13. Rhee, A. Master's Thesis. Massachusetts Institute of Technology; 2006. An agent-based approach to HIV/AIDS modelling: A case study of Papua New Guinea.
14. Heuveline, P.; Sallach, D.; Howe, T. The structure of an epidemic: modelling AIDS transmission in Southern Africa. Symposium on Agent-Based Computational Modelling; Vienna, Austria. 2003;
15. Brookmeyer R, Boren D, Baral SD, Bekker L, Phaswana-Mafuya N, Beyrer C, Sullivan PS. Combination HIV prevention among MSM in South Africa: results from agent-based modeling. *PLoS ONE*. 9(11):e112 668. DOI: 10.1371/journal.pone.0112668
16. Mah TL, Haperin DT. Concurrent sexual partnerships and the HIV epidemics in Africa: evidence to move forward. *AIDS Behavior*. 2010; 14:11–16. DOI: 10.1007/s10461-008-9433-x [PubMed: 18648926]
17. Morris M, MK. A microsimulation study of the effect of concurrent partnerships on the spread of HIV in Uganda. *Mathematical Population Studies*. 2000; 8:109–133. DOI: 10.1080/08898480009525478
18. Burington B, Hughes JP, Whittington WLH, Stoner B, Garnett G, Aral SO, Holmes KK. Estimating duration in partnership studies: issues, methods and examples. *Sexually Transmitted Infections*. 2010; 86:84–89. DOI: 10.1136/sti.2009.037960 [PubMed: 20332366]
19. Morris M, Epstein H, Wawer M. Timing is everything: international variations in historical sexual partnership concurrency and HIV prevalence. *PLoS ONE*. 2010; 5(11):e14 092.doi: 10.1371/journal.pone.0014092
20. Glynn JR, Dube A, Kayuni N, Floyd S, Molesworth A, Parrott F, French N, Crampin AC. Measuring concurrency: an empirical study of different methods in a large population-based survey and evaluation of the UNAIDS guidelines. *AIDS*. 2012; 26:997–985. DOI: 10.1097/QAD.0b013e328350fc1f [PubMed: 22343965]
21. UNAIDS Reference Group on Estimates, Modelling, and Projections: Working Group on Measuring Concurrent Sexual Partnerships. HIV: Consensus indicators are needed for concurrency. *Lancet*. 2014; 375:621–622. DOI: 10.1016/S0140-6736(09)62040-7
22. Eaton JW, McGrath N, Newell M. Unpacking the recommended indicator for concurrent sexual partnerships. *AIDS*. 2012; 26(8):1037–1039. DOI: 10.1097/QAD.0b013e328351f726 [PubMed: 22313959]
23. Commenges D. Multi-state models in epidemiology. *Lifetime Data Analysis*. 1999; 5:315–327. DOI: 10.1023/A:1009636125294 [PubMed: 10650740]
24. Andersen PK, Keiding N. Multi-state models for event history analysis. *Statistical Methods in Medical Research*. 2002; 11:91–115. DOI: 10.1191/0962280202SM276ra [PubMed: 12040698]
25. Lange JM, Hubbard RA, Inoue LYT, Minin VN. A joint model for multistate disease processes and random informative observation times, with applications to electronic medical records data. *Biometrics*. 2015; 71:90–101. DOI: 10.1111/biom.12252 [PubMed: 25319319]
26. Kapetanakis V, Matthews FE, van den Hout A. A semi-Markov model for stroke with piecewise-constant hazards in the presence of left, right and interval censoring. *Statistics in Medicine*. 2013; 32:697–713. DOI: 10.1002/sim.5534 [PubMed: 22903796]
27. Fischer W, Meier-Hellstern K. The Markov-modulated Poisson process (MMPP) cookbook. *Performance Evaluation*. 1992; 18:149–171. DOI: 10.1016/0166-5316(93)90035-S
28. Bocharov, PP.; D'Apice, C.; Pechinkin, AV.; Salerno, S. *Queueing Theory*. Walter de Gruyter; New York: 2003.

29. Fearnhead P, Sherlock C. An exact Gibbs sampler for the Markov-modulated Poisson process. *Journal of the Royal Statistical Society: Series B*. 2006; 68:767–784. DOI: 10.1111/j.1467-9868.2006.00566.x
30. Efron B. Bootstrap methods: another look at the jackknife. *Annals of Statistics*. 1979; 7:1–26. DOI: 10.1214/aos/1176344552
31. Efron B. Missing data, imputation and the bootstrap. *Journal of the American Statistical Association*. 1994; 89:972–985. DOI: 10.2307/2290846
32. Gorbach PM, MJ, Kornbleth L, Bolan R, Blum ML. Behaviors associated with transmitted drug resistant HIV: Findings from a cohort of Los Angeles MSM with new HIV diagnosis. *JAIDS*. In Review.
33. Klein, JP.; Moeschberger, ML. *Survival Analysis: Techniques for Censored and Truncated Data*. 3. Springer; New York: 2010.
34. Goodreau SM, Carnegie NB, Vittinghoff E, Lama JR, Sanchez J, Grinsztejn B, Koblin BA, Mayer KH, Buchbinder SP. What drives the US and Peruvian HIV epidemics in men who have sex with men (MSM)? *PloS ONE*. 2012; 7(11):e50 522.doi: 10.1371/journal.pone.0050522

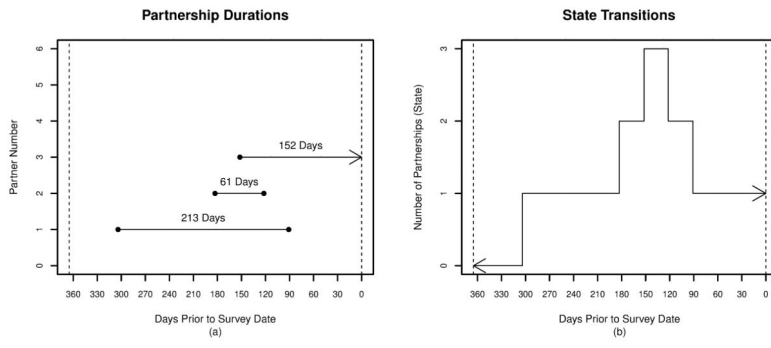


Figure 1.

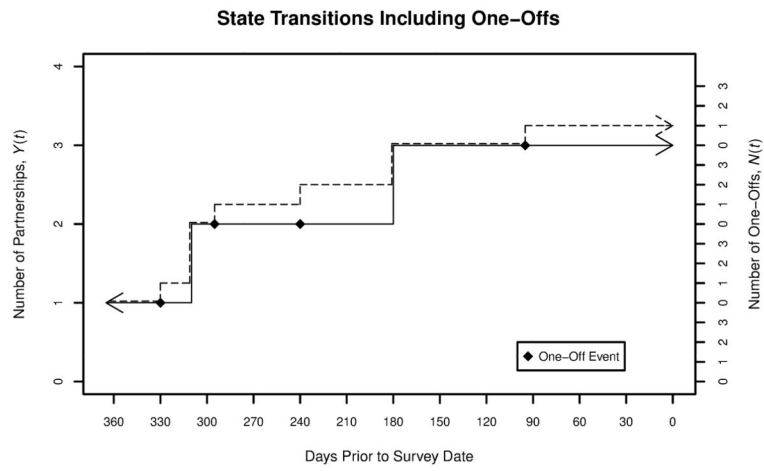


Figure 2.

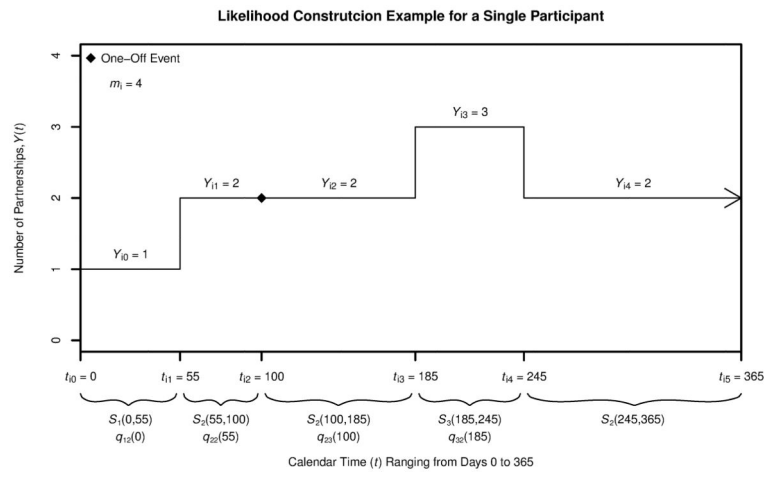


Figure 3.

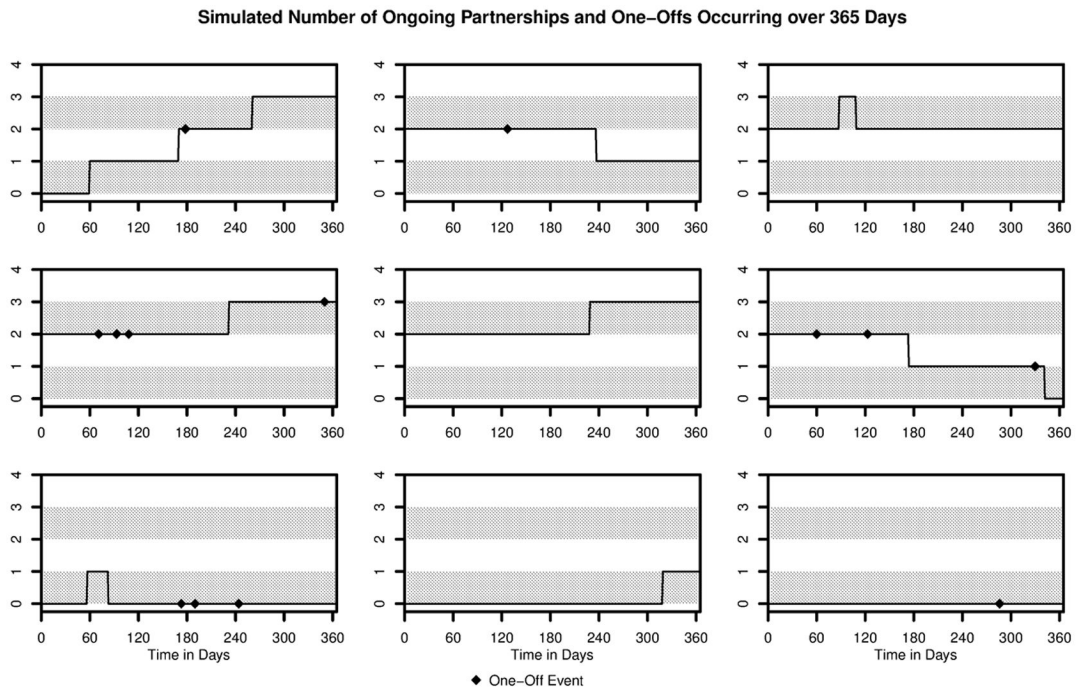


Figure 4.

Table 1
Parameter estimates for the joint multistate and Poisson process model fit to the MetroMates data

Event Type	Parameter	Description	Estimate	Standard Error	P Value	Hazard Ratio (95% CI)
Formations from State 0	β_0	Baseline Hazard	0.0019	0.0003		
	β_1	Count of One-offs	-0.1812	0.1511	0.23	0.83 (0.62, 1.12)
	β_2	HIV Status	0.1520	0.1923	0.43	1.16 (0.80, 1.70)
Formations from State 0	β_0	Baseline Hazard	0.0026	0.0004		
	β_1	Count of One-offs	-0.1529	0.2839	0.59	0.86 (0.49, 1.50)
	β_2	HIV Status	0.0704	0.1982	0.72	1.07 (0.73, 1.58)
Dissolutions	β_0	Baseline Hazard	0.0053	0.0006		
	β_1	Count of One-offs	0.4457	0.1097	< 0.01	1.56 (1.26, 1.94)
	β_2	HIV Status	-0.1615	0.1403	0.25	0.85 (0.65, 1.12)
One-off Events	γ_0	0 partnerships	0.0048	0.0003	< 0.01	
	γ_1	1 partnership	0.0022	0.0003	< 0.01	
	γ_2	2 partnerships	0.0038	0.0006	< 0.01	

Table 2
Population partnership metric estimates based on the model fit to the MetroMates data

	Number of Ongoing Partnerships		Concurrent Partnership Distribution		Mean Concurrent Partnership Sojourn Time		Mean Number of One-Offs per Year	
	k	$\hat{\pi}_k$	SE	$\hat{\rho}_k$	SE	Estimate	SE	
HIV -	0	0.7384	0.1237	466 days	80 days	1.75	0.10	
	1	0.1573	0.0524	119 days	18 days	0.81	0.10	
	2	0.1043	0.1168	114 days	18 days	1.40	0.20	
HIV +	0	0.6325	0.0800	441 days	64 days	1.75	0.10	
	1	0.1880	0.0414	129 days	12 days	0.81	0.10	
	2	0.1795	0.0565	123 days	12 days	1.40	0.20	