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A Bayesian approach to estimate changes in condom use from limited HIV prevalence data

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Abstract

Evaluation of HIV large scale interventions programme is becoming increasingly important, but impact estimates frequently hinge on knowledge of changes in behaviour such as the frequency of condom use (CU) over time, or other self-reported behaviour changes, for which we generally have limited or potentially biased data. We employ a Bayesian inference methodology that incorporates a dynamic HIV transmission dynamics model to estimate CU time trends from HIV prevalence data. Estimation is implemented via particle Markov Chain Monte Carlo methods, applied for the first time in this context. The preliminary choice of the formulation for the time varying parameter reflecting the proportion of CU is critical in the context studied, due to the very limited amount of CU and HIV data available. We consider various novel formulations to explore the trajectory of CU in time, based on diffusion-driven trajectories and smooth sigmoid curves. Extensive series of numerical simulations indicate that informative results can be obtained regarding the amplitude of the increase in CU during an intervention, with good levels of sensitivity and specificity performance in effectively detecting changes. The application of this method to a real life problem illustrates how it can help evaluate HIV intervention from few observational studies and suggests that these methods can potentially be applied in many different contexts.

1 Introduction

Significant resources are being committed to implement large-scale interventions against infectious diseases, such as HIV/AIDS that killed an estimated two million individuals in 2008 [UNAIDS et al., 2009]. Although such interventions are implemented on a large scale because they are expected to work, increasing attention is given to the evaluation of these large-scale intervention programmes to understand what still needs to be done to control the epidemic and eventually achieve elimination, ensuring that resources are not waisted on strategies that do not work.

Even if antiretroviral therapy has become an important component of large scale prevention interventions, condom use and circumcision remain important strategies for reducing HIV transmission. While there are difficulties in estimating condom use trends accurately, due to biases inherent in self-reported
behaviour (Turner and Miller, 1997; Zenilman et al., 1995; Hanck et al., 2008), its average level closely determines the spread of HIV (Boily et al., 2007). Thus, it is important to assess if trends in epidemiological data such as HIV prevalence can be used to infer the impact of interventions on risk behaviours that are susceptible to self-reported bias. This is motivated by the fact that directly observed quantities as HIV prevalence do not provide straightforward indications on the impact of an intervention. Indeed, an epidemic has an intrinsic dynamic, which can cause the prevalence to grow although an efficient intervention is being led if the intervention is introduced early in an epidemic. Alternatively, in a mature epidemic the prevalence can decrease even though ongoing interventions are inefficient (Boily et al., 2002). However, the trajectory of CU over time, and especially since the beginning of a prevention programme, can shed light on the impact of the intervention and on the future trajectory of the epidemic. In this light, we apply a Bayesian methodology to trends in HIV prevalence data, focusing on the specific example of Avahan, India AIDS initiative, a large-scale HIV/AIDS intervention targeted to high-risk groups.

The Avahan intervention was motivated by high levels of HIV prevalence amongst high-risk groups observed in southern India (typically > 20%) (Ramesh et al., 2008), which lead to concerns about infections bridging to their long-term partners and the general population. The programme was launched by the Bill & Melinda Gates Foundation in 2003 (BMGF, 2008), and has targeted high-risk groups for HIV infection, in particular female sex workers (FSWs), by promoting and distributing free condoms. Different studies have been conducted to examine the impact of Avahan (Boily et al., 2007; Deering et al., 2008; Boily et al., 2008; Lowndes et al., 2010; Pickles et al., 2010), and to learn from it in order to inform future large-scale interventions. A key part of such evaluations is examining how risk behaviours, chiefly condom use (CU), defined as the proportion of sex acts protected by condoms at a given time, have changed over the course of the intervention. However, this can be difficult to measure in practice. Baseline CU may be difficult to record when an intervention needs to be implemented rapidly, as happened with Avahan, or may be recorded only on few occasions. While those targeted by the intervention may be asked about their CU history (Lowndes et al., 2010), their answers may be subject to social desirability and recall biases. In principle, the total number of condoms sold or distributed can be enumerated (Bradley et al., 2010), but accurate records may not be available, condoms may be used for family planning by lower-risk individuals, and the distribution of condoms is not a guarantee of their correct usage (Bradley et al., 2010; Kumar et al., 2011). Thus, in addition to direct approaches through quantitative behavioural surveys or records of condom availability, model-based methods can be used to infer unobserved quantities of interest, such as CU, and complete the partial information available from observed quantities such as HIV prevalence, using knowledge of the dynamics of large-scale epidemics.

A first study in the context of Avahan was presented in Pickles et al. (2010). In this work, a deterministic dynamic model for HIV/sexually transmitted infection was formulated based on a compartmental representation incorporating heterogeneous sexual behaviour. The model included various parameters for which informative prior distributions were used. Prior elicitation was based on various data sources, such as previous literature (see Pickles et al. 2010) for more details) and serial cross-sectional surveys termed integrated behavioural and biological assessment (IBBA) conducted in the districts of India targeted by the intervention. The objective was to utilise this model and assess its ability to fit the available prevalence observations under three different hypothesised scenarios of evolution of CU.

The work we present in this paper operates in the same context as in Pickles et al. (2010), but focus is given on exploring the entire space of CU trajectories, rather than considering three scenarios regarding its evolution. Similarly, the model formulation can also be put in a state space setting where an underlying latent process (CU trajectory) is observed through the prevalence data, and the link between these quantities is given by the deterministic model for the HIV infections. Inference in this context is a challenging task given the limited amount of HIV prevalence data aside from initial conditions (three or four observations in total) that are concentrated over a period of 6 years, and are utilised to estimate a 25-years long trajectory. Various models for the CU trajectories were considered, including smooth and
non-differentiable (yet continuous) choices. In the remainder of this paper, the term ‘trajectory prior’ is used to refer to these models in order to avoid confusion with the deterministic HIV model. Note however that the trajectory priors include parameters for which there exist some information in the data. We also present a general and efficient computational scheme using Markov Chain Monte Carlo (MCMC) techniques based on the particle MCMC algorithm (Andrieu et al., 2010); see Dureau et al (2012) for an application in a similar context. Focus is given on estimating the amplitude of the change in CU since 2003 (the start of Avahan) in order to assess the impact of the Avahan intervention on CU. The properties of the estimators arising from the MCMC are studied via simulations, and the performance is assessed from a decision-making perspective through their sensitivity and specificity in detecting strong changes in CU.

The next section presents the models introduced in this paper, the data that are typically available for such studies, and the way in which prior information is incorporated. The computational techniques, mainly the particle MCMC algorithm, are also presented. The developed methodology to compare the performance of the proposed trajectory priors is presented in Section 3 and the results from this study are introduced in Section 4 along with an application to real data from the Indian AIDS initiative Avahan. Finally Section 5 concludes with some relevant discussion.

2 Models and Methods

2.1 HIV transmission model for female sex workers

We use a deterministic model of HIV transmission in a stable but open population of sex workers and their clients. The model structure accounts for high-risk and low-risk FSWs, who have different numbers of clients. This model is parameterised using data from serial cross-sectional bio-behavioural surveys (IBBAs) in Mysore district in southern India (Ramesh, et al., 2008). Some uncertainty remains about these biological and behavioural parameters, which is reflected on the estimates of CU using a Bayesian approach (De Angelis et al., 1998). As motivated in Vickerman et al. (2010), low-risk individuals uninvolved directly in sex work are ignored as they have little influence on the dynamics of the epidemic. Each individual in these three groups is either susceptible to HIV infection, infectious, or retired either due to death or ceasing commercial sexual activity. The flow-diagram corresponding to high-risk FSWs is shown in Figure 1. In addition, individuals that either decease or stop being involved in commercial sex are replaced by susceptible ones, maintaining the population at risk at a constant size. As illustrated in the figure, the force of infection \( \beta \) is a function of a number of different parameters:

- \( NbClients^{HR} \) and \( NbClients^{LR} \): number of clients of FSWs per month, which differs for high risk and low risk FSW
- \( NbEncounters \): mean number of encounters with a FSW per client per month
- \( NbActs \): number of acts per client encounter
- \( p_{M\rightarrow F}^{HR} \) or \( p_{F\rightarrow M}^{HR} \): probability of HIV transmission from male to female or female to male respectively during an unprotected sex act
- \( Cond_{eff} \): efficacy of condoms in protecting against transmission of HIV per sex act
- \( CU(t) \): proportion of FSWs’ sex acts that are protected by condoms, that we allow to vary in time (parameter that we want to estimate)

Additionally, the transmission dynamics of HIV will depend on the following lengths of time:

- \( \mu_F^{-1} \) or \( \mu_F^{-1} \): average length of sexual activity as a sex worker / client
Figure 1: Flow-diagram of the model for high-risk FSWs. Transmission dynamics for low-risk FSWs and clients are defined similarly

- $\alpha^{-1}$: average life expectancy with HIV

In mathematical terms, the model can be defined with a set of differential equations:

$$
\begin{align*}
\frac{dS_F1}{dt} &= -\beta F1 S_F1 HIV_F1 + (\mu_F + \alpha) HIV_F1 \\
\frac{dHIV_F1}{dt} &= \beta F1 S_F1 HIV_M Tot + (\mu_F + \alpha) HIV_F1 \\
\frac{dS_F2}{dt} &= -\beta F2 S_F2 HIV_M Tot + (\mu_F + \alpha) HIV_F2 \\
\frac{dHIV_F2}{dt} &= \beta F2 S_F2 HIV_M Tot + (\mu_F + \alpha) HIV_F2 \\
\frac{dS_M}{dt} &= -\beta M S_M \left( PropF1 \left( \frac{HIV_F1}{Tot_F1} \right) + PropF2 \left( \frac{HIV_F2}{Tot_F2} \right) \right) \\
&+ (\mu_M + \alpha) HIV_M \\
\frac{dHIV_M}{dt} &= \beta M S_M \left( PropF1 \left( \frac{HIV_F1}{Tot_F1} \right) + PropF2 \left( \frac{HIV_F2}{Tot_F2} \right) \right) \\
&- (\mu_M + \alpha) HIV_M
\end{align*}
$$

with:

$$
\beta F1 = [1 - (1 - P^{tr}_{M\rightarrow F})^{NbActs}] NbClients^{HR} (1 - Cond_eff CU1) \\
\beta F2 = [1 - (1 - P^{tr}_{M\rightarrow F})^{NbActs}] NbClients^{LR} (1 - Cond_eff CU1) \\
\beta M = [1 - (1 - P^{tr}_{F\rightarrow M})^{NbActs}] \left( \frac{NbClients^{HR} + NbClients^{LR}}{2} \right) \frac{Tot_F}{Tot_M} (1 - Cond_eff CU1) \\
PropF1 = \frac{NbClients^{HR} Tot_F + NbClients^{LR} Tot_F}{NbClients^{HR} Tot_F + NbClients^{LR} Tot_F} \\
PropF2 = \frac{NbClients^{LR} Tot_F + NbClients^{LR} Tot_F}{NbClients^{HR} Tot_F + NbClients^{LR} Tot_F}
$$

In the model above, the state of the epidemic over time is described by the number of susceptibles among clients ($S_M$), among the low-risk female sex workers ($S_F1$) among the high-risk female...
sex workers ($S_{F_1}$), and the corresponding numbers of infected individuals ($HIV_{M}$, $HIV_{F_1}$ and $HIV_{F_2}$).

Three types of constant parameters are involved: the initial prevalence among the different groups of interest in 1985 ($\theta_{c0} = \{S_{F_1}(1985), HIV_{F_1}(1985), S_{F_2}(1985), HIV_{F_2}(1985), S_{M}(1985), HIV_{M}(1985)\}$), time-invariant parameters describing the biological and behavioural determinants of HIV transmission ($\theta_{tr} = \{\mu_F, \mu_M, \alpha, NbClient_{sHR}, NbClient_{sLR}, p^I_{M \rightarrow F}, p^I_{F \rightarrow M}, NbActs, CondEff\}$) and the parameters that play a role in the trajectory priors for CU between 1985 and 2010 ($\theta_{CU}$). All three components $\theta_{c0}$, $\theta_{tr}$, and $\theta_{CU}$ are integrated into a global vector of constant parameters, denoted by $\theta$. Under this notation, the trajectory $X_{1,n}$ of the space vector $X_t = \{S_{F_1}(t), HIV_{F_1}(t), S_{F_2}(t), HIV_{F_2}(t), S_{M}(t), HIV_{M}(t)\}$ is defined as a deterministic function of $\theta$ and CU ($X_{1,n} = f(\theta, CU)$) through an HIV transmission model, and is compared with the available observations, denoted by $y_{1,n}$. Note that the function $f(\cdot)$ is not available in closed form but can be obtained given the trajectory of CU by solving the above ordinary differential equations (ODE).

More specifically, we introduce a time discretisation with equidistant points of time step $\delta$ resulting in a discretised skeleton of CU denoted $CU^{discr} = \{CU_{t_0}, CU_{t_0+\delta}, CU_{t_0+2\delta}, \ldots, CU_{t_n}\}$. The partition of the CU trajectory can be made arbitrarily fine by the user-specified parameter $\delta$ to limit the approximation error induced by the time discretisation.

Assigning a model for the observation error provides the likelihood of the observation $prev_{1,n}^{obs}$ conditional on the CU trajectory $p(prev_{1,n}^{obs} | \theta, CU)$. In this paper we use a binomial distribution, considering that prevalence estimates are derived from a random sample of 425 FSWs or clients in the Mysore district. More specifically if we denote $prev_{i}^{model}$ the value of the prevalence estimated through the HIV transmission model ($prev_{i}^{model} = (HIV_{F_1}(t_i) + HIV_{F_2}(t_i))/2$) if prevalence among FSWs is observed at time $t_i$, $prev_{i}^{model} = HIV_{M}(t_i)$ if prevalence among clients is observed at time $t_i$, the distribution will be the following:

$$425 \times prev_{i}^{obs} \sim Bin(425, prev_{i}^{model})$$

Overall, the model appearing of Figure 1 and Equations 1 and 2 is a simplified version of the one in (Pickles, et al., 2010). This was done mainly for parsimony reasons; models of increased complexity can be used provided that there is adequate information on their parameters. More details on informative priors are provided in Section 2.3.

### 2.2 Trajectory priors for condom use

In this paper we introduce three different formulations for the evolution of the CU trajectory. Our first trajectory prior assigns a Brownian motion to CU, transformed to take values in the real line, aiming to impose little restrictions to its shape. Initial considerations in (Pickles et al., 2010) and classic literature on smoothly growing quantities also motivated the introduction of alternative formulations based on sigmoid-shaped growth curves. Hence, the second trajectory prior, denoted by dBR, is based on the generalised Bertalanffy-Richards model; see for example (Garcia, 1983; Yuancai et al., 1997). In order to enrich this context and address estimation issues that can be encountered with the dBR (Lei and Zhang, 2004), we also consider an alternative empirical sigmoid curve (dSigm). In what follows, we denote with $x$ the latent process that drives the CU trajectory, which in turn provides the link with the prevalence observations through the model in Section 2.1.

#### 2.2.1 Brownian motion (BM)

The first formulation assigns a Brownian motion to a transformed version of the CU trajectory. As the latter has to be constrained in the $[0,1]$ region, we work with the logit transformation of $CU_i$, denoted
The use of diffusion processes to describe time varying quantities in contexts associated with uncertainty has been used in epidemic models; see for example Cazelles and Chau (1997), Cori et al. (2009) and Dureau et al. (2012). It can also be seen as a prior according to which \( x_t \) is a random walk with continuous, yet non-differentiable trajectories. It is used here in an attempt to incorporate a limited amount of prior information on the shape of the trajectory. It can also be used as an exploration tool for potential modelling-remodelling steps towards more informative formulations. Variations of this formulation may include smoother diffusion models, by taking integrals of the Brownian motion, or alternative transformations such as the probit link. We note at this point that very little information is available on the volatility in (3) which is determined mostly by its prior. More details are provided in Sections 2.3 and 3.

2.2.2 Deterministic Bertallanfy-Richards function (dBR)

Qualitatively, CU trends reconstructions by alternative methods (Lowndes et al., 2010; Bradley et al., 2010) suggest that CU was quite low in 1985, and has grown over the recent year. The above motivated the use of a growth curve parametric model instead of the Brownian motion diffusion. This is in line with various approaches in modelling quantities that are smoothly growing in time in different contexts such as biology (Zwietering et al., 1990), marketing (Lessne and Hanumara, 1988) and epidemiology (Omran, 1971). We use the generalised Bertalanffy-Richards (BR) family (Richards, 1959; Garcia, 1983) that can be written as:

\[
CU_t = \eta (1 - Be^{-kt})^{1/m}
\]

or else, in differential equation framework:

\[
CU_t = [(1-m)x_t + \eta^{1-m}]^{1/m}
\]

\[
dx_t = -kx_t dt
\]

This family contains various growth curves, including the logistic \((m = 2)\) and Gompertz \((m \to \infty)\) functions. The growth curve can be parameterised by four quantities: the initial value of \(CU_0\), the time of inflection \(t_{in}\), the value of CU after an infinite time \((\eta\), also termed as the asymptote), and the ‘shape’ or ‘allometric’ parameter \(m\). Note that the time of inflection can be related to the parameter \(k\) by the following equation:

\[
k \times t_{in} = \log\left(\frac{B}{1-m}\right)
\]

Furthermore, this definition implies that the initial value \(CU_0\) is lower than \(m^{1/m} \eta\). In order to focus on sigmoid-shaped growth curves, we restrict our attention to cases where \(m \geq 1\) (Yuancai et al., 1997). For illustration, the slope of the curve at its inflection point is a non-monotonous function of \(m\):

\[
\frac{dC}{dt}(t_{in}) = \eta km^{m-1/m} = \frac{\eta}{t_{in}} \log\left(\frac{1 - \left(\frac{CU_0}{\eta}\right)(1-m)}{1 - m}\right) m^{1/m}
\]

2.2.3 Deterministic empirical sigmoid curve (dSigm)

An empirical sigmoid model is also considered to address the potential difficulties that can arise with the parameterisation of the dBR. Since growth models are used to study intrinsically growing objects,
trajectories that are inexplicably stable for a long period of time and that eventually start picking at a rapid pace are not typical under the BR formulations. Moreover, inference on the allometric parameter \( m \) in dBR can be problematic (Lei and Zhang, 2004). These may lead to underestimating the amplitude of a shift in CU under the potential extrinsic influence of the Avahan intervention. For this reason, we also consider an alternative sigmoid curve, defined in the following way:

\[
CU_t = a + \frac{b}{c(1 + x_t)} \\
\text{dx}_t = -kx_t\text{dt}
\]  

Here the model is parameterised by its baseline \((CU_0)\), its asymptote \((\eta)\), its time of inflection \((t_{in})\), and the increase rate \((r)\), from which \(a\), \(b\) and \(c\) can be computed:

\[
a = CU_0 - b \\
b = (\eta - CU_0)c \\
c = \frac{1}{1 + e^{(t_{in})/r}}
\]

The slope of the curve at its inflection point is now a simpler function of the model parameters:

\[
\frac{dCU}{dt}(t_{in}) = \frac{\eta - CU_0}{4r}
\]

### 2.2.4 Stochastic growth curves

It is also possible to combine the Brownian motion and the growth curve approaches using diffusions. Stochastic extensions of the dBR and dSigm model can be considered, in which the mean behaviour remains intact while some random perturbations are introduced through a stochastic differential equation. In order to ensure positivity, restrict \(CU_t\) below one and retain the link with deterministic dBR curve, a geometric Brownian motion can be used to replace equations (5) and (6)

\[
\text{dx}_t = -kx_t\text{dt} + \sigma x_t\text{dB}_t
\]

The stochastic growth curve defined by (4) and (8) was also mentioned in Garcia (1983). A convenient feature for both stochastic extension of dBR and dSigm is the fact that since

\[
x_t = \frac{1}{1-m} (CU_t^{1-m} - \eta^{1-m}),
\]

and \(x_t\) is strictly negative, the resulting CU trajectory is maintained strictly below \(\eta\). Given the limited data at our disposal, these models can hardly be fitted in the context of this paper. Nevertheless, they may be helpful in cases where more observations are available.

### 2.3 Priors

The parameters contained in \(\theta_{i.c.}\) and \(\theta_{i.c.}\) cannot be identified from the prevalence observations only, so we assign informative priors on them. These are summarised in Table 1 and are similar with the priors used in Pickles et al. (2010). They were either based on previous literature regarding general quantities as transmission probability for unprotected acts, or life expectancy with HIV, whereas the ones concerning quantities that are more sociologically and geographically specific were estimated from cross-sectional individual-based surveys (IBBAs) in Mysore.
The parameter vector $\theta$ includes an additional component, $\theta_{CU}$, that contains the parameters for different models describing the CU trajectories, $\theta = \{\theta_{c.c.}, \theta_{\tau}, \theta_{CU}\}$. Although there is some information in the data for $\theta_{CU}$, the posterior will depend on the prior to a large extent. As mentioned earlier, there is very little information on the volatility parameter of the BM formulation. Throughout this paper we used a Uniform prior between 0 and 0.5. As explained in more detail in Section 3.3, the parameter of main interest in this study is the quantity $\Delta CU = CU_{2009} - CU_{2003}$. Simulations suggest that, if we combine the BM approach with a $\text{Unif}(0, 1)$ prior for $CU_0$ (CU in 1985), this results in a symmetric prior on $\Delta CU$ that is centered around 0 with 2.5% and 97.5% points at ±0.6 respectively. We considered it as a reasonably vague prior for $\Delta CU$ and evaluated the performance of the resulting model via the simulation experiments of Section 3. More diffuse priors can also be used by setting a larger value for the upper limit of the Uniform prior for $\sigma$. Regarding the parameters of the sigmoid curves, we used vague priors that are also shown in Table 1.

### 2.4 Computational schemes for implementation

The joint posterior distribution can be obtained up to proportionality by the HIV transmission model of Section 2.1, which links the prevalence observations with the CU trajectories, the trajectory priors of Section 2.2 and the remaining priors of Section 2.3. For the dBR and dSigm trajectory priors, it can be put in a non-linear regression framework, with the non-linear function being the solution of the ODE, and can therefore be implemented with standard software such as WinBUGS through WBDiff [Lunn, 2004]. However this is not possible for the BM case where more involved techniques are required. Since the posterior probability density function is intractable, a data augmentation scheme can be utilised. This inference problem poses some challenges due to the high dimension of the discretised representation of $CU_{1,n}$ and its strong correlation with the vector of constant parameters, $\theta$. This correlation imposes problems to Gibbs schemes on $\theta$ and $CU_{1,n}$, leading to extremely poor mixing and convergence properties. The Particle MCMC algorithm (PMCMC, see [Andrieu et al., 2010]) algorithm offers a solution by updating the two components jointly, thus reducing the problem to a small-dimensional MCMC on $\theta$. Implementation is based on the estimates of the likelihood $\hat{p}(\text{prev}_{\text{obs}} | \theta)$ that are provided by a particle filter.

The particle filter and the PMCMC are described in Algorithms 1 and 2 in terms of the quantities introduced in the previous sections. More details about this algorithm and its practical implementation can be found in [Dureau et al., 2012] (through an application in a similar context) and [Andrieu et al., 2010].

#### Algorithm 1 Particle Filter algorithm

With $N$ being the number of particles and $n$ the number of observations.

Initialise $L^0(\theta) = 1$, $W^j_0 = \frac{1}{N}$, sample $(\tilde{C}\hat{U}^j_{t_0})_{j=1,...,N}$ from $p(CU_{t_0} | \theta)$

for $i = 0$ to $n - 1$ do

for $j = 1$ to $N$ do

Sample $(\tilde{C}\hat{U}^j_{i+1})$ from $p(CU_{i+1} | \theta, C\hat{U}^j_i)$

Calculate the resulting prevalence $\hat{\text{prev}}_{\text{obs}}^{i,\text{model}}$ by solving the ODE (for example with the Euler step)

Set $\alpha^j = p(\hat{\text{prev}}_{\text{obs}}^{i+1} | \hat{\text{prev}}_{\text{prev}}^{i,\text{model}})$

end for

Set $W_{i+1}^j = \frac{\alpha^j}{\sum_{j=1}^N \alpha^j}$, and $L^{i+1}(\theta) = L^i(\theta) \times \frac{1}{N} \sum \alpha^j$

Resample $(\tilde{C}\hat{U}^j_{i+1}, \hat{\text{prev}}_{\text{obs}}^{i,\text{model}})_{j=1,...,N}$ according to $(W_{i+1}^j)$,

end for
| HIV transmission model parameters definition | Notation | Range of uniform priors for the district of Mysore (Pickles et al. 2010) |
|---------------------------------------------|----------|-------------------------------------------------------------------------|
| Probability of transmission from M. to F. per act | $p_{M\rightarrow F}^r$ | 0.0006-0.0055 |
| Probability of transmission from M. to F. per act | $p_{F\rightarrow M}^r$ | 0.0001-0.007 |
| Condom efficacy per act | $\text{Cond}_{eff}$ | 80%-95% |
| Mean number of acts per clients | $\text{NbActs}$ | 1-2 |
| Mean number of clients per high-risk FSW | $\text{NbClients}^{HR}$ | 46.6-54.0 clients/month |
| Mean number of clients per low-risk FSW | $\text{NbClients}^{LR}$ | 20-23.7 clients/month |
| Toral number of FSWs | $\text{Tot}_{F_1} + \text{Tot}_{F_2}$ | 2144 |
| Cliens/FSW population ratio | $\frac{\text{Tot}_{F_1} + \text{Tot}_{F_2}}{\text{Tot}_{F_1} + \text{Tot}_{F_2}}$ | 7-19 |
| Mean length of sexual activity as FSW | $\mu_{F}^{-1}$ | 45-54 months |
| Mean length of sexual activity as client | $\mu_{M}^{-1}$ | 154-191 months |
| Mean life expectancy after infection with HIV | $\alpha^{-1}$ | 87-138.5 months |
| Initial proportion of infected FSWs in 1985 | $\frac{\text{HIV}_{F_1}+\text{HIV}_{F_2}}{\text{Tot}_{F_1} + \text{Tot}_{F_2}}$ | 0%-5% |
| Initial proportion of infected clients in 1985 | $\frac{\text{HIV}_{M}}{\text{Tot}_{M}}$ | 0%-5% |

| Condom trajectory priors parameters definition | Notation | Prior |
|-----------------------------------------------|----------|-------|
| Allometric parameters (dBR) | $m$ | $\mathcal{N}(1,10^6) \times \mathbb{I}_{[1,\infty[}$ |
| Growth rate (dSigm) | $r$ | $\mathcal{N}(0,10^6) \times \mathbb{I}_{[1,\infty[}$ |
| Asymptote (dBR, dSigm) | $\eta$ | $\text{Unif}(0,1)$ |
| Initial Value (all trajectory priors) | $\text{CU}_0$ | $\text{Unif}(0,1)$ |
| Time of inflection (dBR, dSigm) | $t_{in}$ | $\text{Unif}(1985,2009)$ |
| Allometric parameters, initial conditions and asymptote (dBR) | $(\text{CU}_0, \eta, m)$ | $0$ if $\text{CU}_0 \geq m^{t_{in}} \eta$ |
| Volatility (BM) | $\sigma$ | $\text{Unif}(0,0.5)$ |
Algorithm 2 Particle MCMC algorithm (particle Marginal Metropolis Hastings version)

With M being the number of iterations
Set current θ value, ˜θ, to an initial value
Use Particle Smoother (PS) according to Algorithm [1] to compute ˆp(prevobs1:n| ˜θ) = L(˜θ) and sample ˜CU1:n from p(CU1:n|prevobs1:n, ˜θ)
for l = 1 to M do
Sample ˜θ∗ from Q( ˜θ, )
Use Particle Filter to compute L( ˜θ∗) and sample ˜CU1:n from ˆp(CU1:n|prevobs1:n, ˜θ∗)
Set ˜θ = ˜θ∗ (and ˜CU1:n = ˜CU1:n) with probability 1 ∧ L( ˜θ∗)Q( ˜θ∗, ˜θ) / L(˜θ)Q(˜θ, ˜θ∗)
Record ˜θ and ˜CU1:n
end for

Regarding the choice of Q(.) in Algorithm 2 we use a random walk Metropolis-Hastings algorithm in a transformed parameter space (log or logit) to ensure positivity. Each iteration of the MCMC algorithm requires an execution of the particle filter, which induces substantial computational cost if the importance sampling covariance matrix Σ is ill-adapted. Adaptive approaches (Roberts and Rosenthal, 2009) can be used to tune Σ but they require lengthy explorations of the target space. We propose to speed up this process by pre-exploration of a proxy posterior density pEKF(θ|prevobs) relying on a Gaussian approximation of the dynamic system and the Extended Kalman filter methodology (Dureau et al., 2012). A simple bootstrap version of the particle filter is used as it is not straightforward to consider data-driven transition proposals given complex observation regime of our model. Note that given the short length of the observed time series, simpler alternatives to PMCMC may perform reasonably well. For example, the resampling step can be omitted and the particle filter output can be used to approximate p(CU1:n|prevobs1:n, θ). In our application however, it turns out that additional particles are needed for this approach, thus not offering a great reduction to the computational cost when compared to PMCMC. We therefore suggest the use of PMCMC as a robust computational tool that still does not require a large amount of time in applications of this type.

3 Evaluation methodology based on ensemble simulations

Given the limited amount of information in available data (four or five prevalence observations, including initial conditions), it is very likely that the posterior output will be influenced substantially by the choice of CU priors and their parameters. In this section we explore the performance of the proposed inferential mechanism via simulation-based experiments designed to mimic the behaviour of datasets typically encountered in the context of application studied. Clearly, the approach of this paper heavily relies on the HIV infection model and the results will be quite sensitive to its specification. We therefore set up the simulation experiments under the assumption that the model of Section 2.1, parameterised according to the priors of Section 2.3, is correct. Focus is given on quantities related with the CU trajectories, under the different choices of Section 2.2, that can be estimated from the samples of the posterior distribution provided by the MCMC algorithms of Section 2.4. We also provide some discussion regarding the static parameters appearing in the CU trajectory priors.

3.1 Parameter of interest

By fitting each of the previously introduced models we obtain samples from the marginal posterior density pmet(CU1|y) (meth ∈ {dBR, dSigm, BM}). However, our interest mainly lies in the amplitude of the shift in CU between 2003 and April 2009 measuring the estimated increase in CU during the
interception, henceforth denoted by $\Delta CU$. The posterior draws of CU trajectories can be transformed to provide samples from the posterior of this parameter of interest. The samples can then be used to form an estimator $\hat{\Delta CU}^{meth}$ of $\Delta CU$ such as the posterior median of $\hat{\mu}_{ CU}^{meth}(CU_t|y)$. In what follows we explore the frequentist properties of this estimator derived from each of the trajectory priors.

It may also be of interest to assess the estimating capabilities, given the limited amount of data, for the hyperparameters of the various CU priors ($CU_0, \eta, r, m, t_m$ and $\sigma$). As it turns out there is information for some of them ($CU_0, \eta, t_m$), whereas some others are hard to estimate and are determined mostly by their prior ($r, m$ and $\sigma$). Nevertheless, from a subject matter point of view, interest lies mainly on $\Delta CU$, whereas the remaining quantities (in CU priors) can be regarded as nuisance parameters. Another appealing feature of $\Delta CU$ is that it appears in all models and therefore provides an omnibus quantity for comparison. Hence, inference properties of these parameters ($CU_0, \eta, r, m, t_m$ and $\sigma$) are only studied indirectly through inference properties of $\Delta CU$.

3.2 Measures of performance

The performance of each estimator $\hat{\Delta CU}^{meth}$ in estimating $\Delta CU$ is evaluated from the following criteria (where $L = 100$, the number of simulations):

\[
\begin{align*}
\text{Bias}^{meth} &= \frac{1}{L} \sum_i (\hat{\Delta CU}^{meth}_i - \Delta CU_t) \\
\text{MSE}^{meth} &= \frac{1}{L} \sum_i (\hat{\Delta CU}^{meth}_i - \Delta CU_t)^2 \\
\text{Std}^{meth} &= \sqrt{\text{MSE}^{meth} - (\text{Bias}^{meth})^2}
\end{align*}
\]

In addition to the quantities above we are also interested in assessing the discriminative ability of each model in detecting increases in CU. Focus is given to increases in CU that are at least as high as a predefined threshold $T$, which reflects the minimum practical increase. When analysing the data a researcher may decide that CU did increase more than $T$ if the value of the estimator $\hat{\Delta CU}^{meth}$ is higher than a user-specified threshold $t$. Each decision mechanism may lead to different types of error and is therefore associated with a particular sensitivity and specificity. More specifically we can define the true and false positives in the following way

- **Sensitivity** (true positives rate) for $t$: \[
\frac{\#(\hat{\Delta CU}^{meth}>T, \Delta CU>T)}{\#(\Delta CU>T)}\]

- **Specificity** (1 - false positives rate) for $t$: \[
\frac{\#(\hat{\Delta CU}^{meth}<T, \Delta CU<T)}{\#(\Delta CU<T)}\]

We proceed by first reporting sensitivities and specificities corresponding to the case of $t = T$. This corresponds to saying that $\Delta CU$ is higher than $T$ if its estimator is higher than $T$. We then use a range of different $t$’s and obtain the sensitivity-specificity pair that corresponds to each of them. A lower detection threshold $t$ will increase the sensitivity of the method, but it also increases the risk for false positives, and vice versa. These pairs are combined to form the Receiver Operating Characteristics ROC curve by plotting sensitivity versus 1-specificity. The area under the ROC curve (AUC) provides an overall measure of discriminatory power as it reflects the probability of correctly classifying a randomly chosen positive instance as higher than a randomly chosen negative one (Fawcett, 2006). For example, an AUC value of 50% indicates no power (i.e random choice) This detailed procedure is repeated to assess the ability to detect two different levels of increase in CU, with $T$ set to 20% and 40% respectively.

3.3 Simulation procedure

The performance of the estimators derived from the different models is measured using a set of simulated experiments where CU trajectories are sampled from a given growth curve model, and parameters from $\theta_{c, c}$ and $\theta_{r}$, are sampled following their prior distributions. To maximise the utility of this test procedure for future application of this methods to help evaluate Avahan in different districts (manuscript in
preparation), only plausible and realistic CU trajectories are considered: cases with prevalence in 2010 between 2% and 40% and with CU shifts that occurred after 1995. Furthermore, the test trajectories have been sampled so that $\Delta CU$ regularly spans the [0; 0.6] interval.

For each of these experiments, an epidemic is simulated to provide observations ($y_{\text{sim}}^{\text{rep}}$) replicating the observation framework applied in Mysore: three prevalence estimates among female sex workers and one among clients, concentrated during the period of the intervention (step 2 of Figure 2). From these observations, the MCMC algorithm is applied to each method $\text{meth}$ to sample from $p(CU_{\text{meth}}^{\text{rep}} | y_{\text{sim}}^{\text{rep}})$ (step 3 of Figure 2). Then, given the posterior CU samples the estimators $\hat{\Delta}CU_{\text{meth}}$ can be computed, and compared to their true counterparts $\Delta CU$ (step 4 of Figure 2) by calculating the measures of performance of the previous subsection. Examples of ROC curves obtained in such manner are provided for the Brownian motion trajectory prior in Figure 5.

4 Results

4.1 Comparison of the CU trajectory models from ensemble simulations

The results of the simulation experiments are presented in Tables 2 and 3. Table 2 focuses on the frequentist properties of the estimators, derived from the median of the posterior densities provided by each trajectory prior, and reports the bias, the standard deviation and the MSE of each estimator. Table 3 concentrates on the ability of the model to classify shift amplitudes of CU from 2003 to 2009 in the right order (AUCs), and more specifically on the risk of overstating versus understating the quantity of interest. In other words, we aim to address questions such as ‘was the shift in CU during the intervention over 0.2 (0.4)?’, via the corresponding sensitivity and specificity and the resulting AUC.

The first table of this section (Table 2) suggests that no model tends to consistently overstate $\Delta CU$ as...
all biases are negative. More precisely, the dBR model tends to strongly understate the shift in amplitude, by up to 0.23. The biases of the dSigm model is smaller (-0.17), but optimal results are obtained with the Brownian Motion model (-0.13). Similarly, in terms of MSE, the performance of the BM model is better. Figure 4 shows the bias, estimated from 100 simulations, of each model as a function of the true amplitude of the shift in CU. It suggests that the bias increases as a function of the size of the true amplitude of the shift in CU, and that the ranking of the different models is consistent across different configurations (from no shift in CU to moderate and high shifts in CU). If, for example, the true shift is 50%, it is on average underestimated by 0.15 with the best method (BM) and more than 0.35 points with the BR method.

Table 3 and Figure 4 suggest that all estimators based on the median of the posterior density of $p(\Delta CU | y_1:n)$ have good distinguishing power: the AUC is between 0.82 and 0.91 in all cases. In line with the results of Table 2, the estimates provided by the BM model achieve better sensitivity (68% and 49%) than the other models (between 5% and 51%), and very good specificity (over 94%). The performance, particularly the sensitivity, decreases as the level of increase in CU that is being tested for increases.

The results presented in these tables provide an informative qualitative assessment for the ability of the different models to capture $\Delta CU$ from limited prevalence data on an important and diverse set of likely scenarios (100 experiments). First of all MSE and AUC figures suggest that although the number of prevalence observations is low and some elements of the transmission process are uncertain, it is still possible to extract information on our time varying parameter and provide estimates of the amplitude of the shift in CU during the intervention. Furthermore, there seems to be a possibility to control the risk of overstating these quantities by analysing the outputs of the three models that offer different levels of compromise between sensitivity and specificity. Thus, although the procedure may fail to identify some shifts in CU, we have the reassurance that if it is detected it is likely to be true, which, in the context of interest, results in conservative estimates of intervention impact on CU trends.

The bias in estimating $\Delta CU$ under each of the CU priors can be attributed to a large extent to the prior implied by each formulation on $\Delta CU$. As mentioned in Section 2.3, the BM approach results in a symmetric prior on $\Delta CU$ that is centered around 0 with 2.5% and 97.5% points at ±0.6 respectively. The posterior median is therefore pulled towards 0 resulting in conservative estimates. The amount of shrinkage depends on the upper limit of the Uniform prior on $\sigma$. The corresponding priors under the dBR and dSigm formulations result it priors for $\Delta CU$ that put more mass around 0, although this heavily depends on the values of $r$ and $m$ that are hard to estimate. The resulting biases are therefore higher but
Figure 4: Bias of each model as a function of the true amplitude of the shift in condom use, estimated from 100 simulations.

Table 2: Frequentist properties of the different estimators of the amplitude of the shift in condom use during the intervention, estimated from 100 simulations

|                       | Deterministic Bertalanffy- Richards | Deterministic empirical sigmoid | Brownian motion |
|-----------------------|-------------------------------------|---------------------------------|-----------------|
| Bias                  | -0.23                               | -0.17                           | -0.13           |
| Error standard deviation | 0.16                                 | 0.17                            | 0.17            |
| Mean Squared Error (MSE) | 0.078                                | 0.0057                          | 0.045           |

they have been obtained without placing informative priors on their hyperparameters, as was done with $\sigma$ under the BM formulation.

The two models with the higher overall performance, BM and dSigm, are quite different in nature: the dSigm trajectories are smooth, whereas under the Brownian motion prior they are non-differentiable. Hence, the choice between the two models can also be based on prior beliefs of the researcher regarding the smoothness of the CU trajectories.

4.2 Application: what can we infer on the trajectory of CU in Mysore?

Mysore is one of the districts targeted by the Avahan intervention, and Avahan was the first HIV prevention intervention in this region. Four HIV prevalence estimates have been obtained between 2003 and 2009, three among female sex workers, and one among clients. Results from the inference procedure using a Brownian motion model are shown in Figure 5, suggesting a strong impact of the intervention. The purpose of this paper was to assess what level of increase of CU between 2003 and 2009 can be inferred while controlling the risk of overstating it. As it was shown in section 4.1, dSigm models could provide a good alternative to the BM formulation. Hence, we also present here results obtained with this model for the Mysore dataset (see figure 5). Table 4 shows the estimates of $\Delta CU$ for each of the three presented models. The results indicate a positive increase in all cases. In particular, for the BM and dSigm models the corresponding posterior means are 0.54 and 0.55 while the 95% credible intervals are [0.04;0.99] and [0.14;0.99] respectively.

A stronger conclusion regarding a lower bound for the CU shift between 2003 and 2009 can be made by comparing the posteriors medians to the results of Table 3. If the underlying set of simulations is to
Table 3: General distinctive power (AUC) of the median estimator of the shift, and specific sensitivity and specificity when answering: is the shift in CU during the intervention stronger than 0.2? than 0.4? These quantities were estimated over 100 simulations.

|                        | Deterministic | Deterministic | Brownian |
|------------------------|---------------|---------------|----------|
|                        | Bertalanffy-  | Empirical     | motion   |
|                        | Richards      | Sigmoid       |          |
| AUC                    | 0.91          | 0.9           | 0.9      |
| ΔCU > 0.2?             | 46%           | 51%           | 68%      |
| Specificity            | 100%          | 100%          | 96%      |
| AUC                    | 0.85          | 0.83          | 0.82     |
| ΔCU > 0.4?             | 5%            | 38%           | 49%      |
| Specificity            | 100%          | 95%           | 94%      |

Table 4: Estimates of the change in CU in Mysore between 2003 and 2009.

|                        | Posterior mean | Posterior median | 95% credible interval |
|------------------------|----------------|------------------|-----------------------|
| Deterministic Bertalanffy-Richards | 0.30           | 0.28             | [0.11;0.73]           |
| Deterministic Sigmoid   | 0.53           | 0.54             | [0.14;0.99]           |
| Brownian motion         | 0.52           | 0.55             | [0.04;0.99]           |

be considered realistic, an argument in favour of a CU increase being at least 0.4 can be made. Since the posterior medians are more than 0.4 under both BM and dSigm models (.54 and .55 respectively), Table 3 suggests that a statement for ΔCU > 0.4 will be correct with probability given by the specificity of each model (94% BM and 95%-dSigm). While being more informative than the credible intervals obtained directly from the posterior densities (over 0.04 and 0.14 respectively with BM and dSigm), these numbers are heavily dependent on the assumption that the simulations of Section 3 provided an adequate approximation of the reality.

Finally, Figure 5 and Table 4 show that the results obtained from the deterministic Sigmoid and Brownian motion models strongly coincide: they suggest that CU was stable over the 1985-2003 period, remaining below 0.5, sharply increased between 2003 and 2007, and stabilised between 0.8 and 0.9.

5 Discussion

In this article, we presented a Bayesian approach to draw conclusions regarding the evolution of time-varying behavioural parameters in the context of HIV such as CU among FSWs. Inference can be based on prevalence estimates while a substantial amount of information from additional sources can be incorporated via prior distributions. In order to describe the behaviour of CU trajectories we introduced three different formulations based on Brownian motion and growth curves such as the generalised Bertalanffy Richards and empirical sigmoid models. To our knowledge, these formulations are new in this context. The presented computational framework allows estimation of CU trajectories as well as functionals thereof, using advanced MCMC methods and following ideas of Dureau et al. (2012); Cazelles and Chau (1997); Rasmussen et al. (2011). Nevertheless, in comparison to these approaches, the problem of evaluating the Avahan intervention by estimating its impact on CU from prevalence estimates is of additional difficulty due to the limited amount of information; the application to Mysore district was based on three observations of prevalence among FSWs and one among clients, plus hypothesis on the initial value of prevalence in 1985. Various simulation experiments were conducted in order
Figure 5: Estimates obtained for Mysore district.

a) reconstructed prevalence trajectory among female sex workers when condom use modelled with Brownian motion

b) reconstructed prevalence trajectory among clients when condom use modelled with Brownian motion

c) reconstructed condom use trajectory when modelled with Brownian motion

d) reconstructed condom use trajectory when modelled with deterministic Sigmoid

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to assess the validity of the procedure, examining the frequentist properties of the underlying estimators and the ability of the model to avoid overestimation via conducting ROC analysis. The evidence from the simulation experiments is encouraging, suggesting that the approach can be used in this context for making conservative estimates of changes in CU both with the Brownian motion and the deterministic sigmoid trajectory priors. However, the overall performance is bound to depend on the deterministic HIV infection model which was parameterised based on a substantial amount of prior information, as in Pickles et al. (2010), as well as on assumptions such as the very low HIV prevalence in 1985. Most of the prior information utilised in this study was obtained from additional data sources (IBBAs). In the presence of all these data sources, it would be interesting to consider and contrast a joint inferential scheme through an evidence synthesis framework in the spirit of Goubar et al. (2008); Presanis et al. (2011).

While the representation of HIV transmissions in this paper is simpler in behavioural terms in comparison with the model presented in Pickles et al. (2010), the model is enriched as it explores the CU trajectories space rather than working with three pre-determined scenarios. Nevertheless, there are reasons for a potential overestimation of the shift amplitude in this simpler model as coinfection with other sexually transmitted diseases were ignored (although higher transmission probability per unprotected act were allowed to compensate for the latter), and no acute phase was considered. However, diffusion driven models aim at capturing and compensating for structural mis-specifications while capturing the main dynamics of the system and have been shown here to provide conservative estimates. Overall it may be viewed as a different and complementary choice in the trade-off between richness and tractability of the model compared to Pickles et al. (2010). Lastly, this approach relies on the hypothesis that changes in transmission probabilities are solely related to changes in CU, ignoring for example potential changes in the frequency of commercial sex partnerships. This choice can be motivated by the strong focus of the Avahan intervention on prevention measures and the relative stability in the frequency of commercial sex exhibited by the series of cross-sectional bio-behavioural surveys that were conducted during the period of the intervention.

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