Appendix to "Integrated nested Laplace approximations for extended latent Gaussian models with application to the Naomi HIV model"

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1 Modified Naomi model description

1.1 Notation

1.1.1 Indexing

Consider a given country in sub-Saharan Africa. Let x refer to a district located within the Spectrum region R_x. We restrict our attention to the time period $t = T_1$ of the most recent national household survey with HIV testing. Let $s \in \{\text{F}, \text{M}\}$ be sex, and $a \in \{\text{0-5}, \text{5-10}, \ldots, \text{75-80}, \text{80+}\}$ be five-year age bands. As short-hand, we write $a = l$ to refer to the age band with lower bound l, e.g. $a = 20$ for $a = \text{20-25}$. We index the following quantities by district, sex and age-band: population size $N_{x,s,a}$, HIV prevalence $\rho_{x,s,a}$, ART coverage $\alpha_{x,s,a}$, annual HIV incidence rate $\lambda_{x,s,a}$, and proportion of HIV positive persons recently infected $\kappa_{x,s,a}$. Sometimes data are observed at an aggregate level, rather then the level of granularity at which the model operates. In this instance, we use $\{\cdot\}$ to generically refer to a aggregate set over which an observation is made, e.g. $\{a\} = \{\text{15-19}, \ldots, \text{45-49}\}$ for adults.

1.1.2 Structured random effects

Consider a generic random effect u. We use use structured random effects to share information across units assessed as being similar, such as districts next to each other or adjacent age-bands. We use $u \sim \text{ICAR}(\sigma)$ to refer to the Besag intrinsic conditional auto-regressive model (ICAR) (Besag, York, and Mollié 1991) with full conditionals

$$u_i \,|\, u_{-i} \sim \mathcal{N}\left(\frac{\sum_{j:j\sim i} u_j}{n_{\delta i}}, \frac{\sigma^2}{n_{\delta i}}\right),$$

where u_{-i} is u with the ith unit removed, $j \sim i$ if the units are defined as adjacent, $n_{\delta i} = |\{j : j \sim i\}|$ is the total number of adjacent units, and $\sigma > 0$ is the marginal standard deviation. We follow recommendations of Freni-Sterrantino, Ventrucci, and Rue (2018) on scaling of precision matrices, disconnected adjacency graph components, and islands regarding the ICAR model. For the reparameterised Besag-York-Mollie model (BYM2) (Simpson et al. 2017) we write $u \sim \text{BYM2}(\sigma, \phi)$, where u is comprised of a spatially structured ICAR component $v^\star$ with proportion $\phi \in (0, 1)$ and spatially unstructured IID component $w^\star$ with proportion $1 - \phi$, both scaled to have generalised variance equal to one, and $\sigma > 0$ is the marginal standard deviation such that

$$u = \sigma\left(\sqrt{\phi} \cdot v^\star + \sqrt{1-\phi} \cdot w^\star\right).$$

We specify the first order auto-regressive model by $u \sim \text{AR1}(\sigma, \phi)$ such that

$$\begin{aligned} u_1 &\sim \left(0, \frac{1}{1-\rho^2}\right), \\ u_i &= \rho u_{i-1} + \epsilon_t, \quad i = 2, \ldots \end{aligned}$$

where $\epsilon_i \sim \mathcal{N}(0, 1)$ is Gaussian white noise, $|\rho| < 1$ is the lag-one correlation parameter.

1.2 Process specification

1.2.1 HIV prevalence

We model HIV prevalence on the logit scale using

$$\text{logit}(\rho_{x,s,a}) = \beta_0^\rho + \beta_S^{\rho,s=\text{M}} + u_a^\rho + u_a^{\rho,s=\text{M}} + u_x^\rho + u_x^{\rho,s=\text{M}} + u_x^{\rho,a<15} + \eta_{R_x,s,a}^\rho$$

where β_0^ρ is an intercept term, $\beta_s^{\rho,s=\text{M}}$ is the difference in logit prevalence for men compared to women, $u_a^\rho \sim \text{AR1}(\sigma_A^\rho, \phi_A^\rho)$ are age random effects for women, $u_a^{\rho,s=\text{M}} \sim \text{UNKNOWN}$ are age random effects for the difference in logit prevalence for men compared to women age a, $u_x^\rho \sim \text{BYM2}(\sigma_X^\rho, \phi_X^\rho)$ are spatial random effects for women, $u_x^{\rho,s=\text{M}} \sim \text{BYM2}(\sigma_{XS}^\rho, \phi_{XS}^\rho)$ are spatial random effects for the difference in logit prevalence for men compared to women in district x, $u_x^{\rho,a<15} \sim \text{ICAR}(0, \sigma_{XA}^\rho)$ are spatial random effects for the ratio of paediatric prevalence to adult women prevalence, and $\eta_{R_x,s,a}^\rho$ are fixed offsets specifying assumed odds ratios

for prevalence outside the age ranges for which data are available. We use the prior distributions $\mathcal{N}(0,5)$ for the fixed effects β_0^ρ and $\beta_s^{\rho,s=\mathrm{M}}$, $\mathcal{N}^+(0,2.5)$ for all standard deviation terms, $\mathcal{U}(-1,1)$ for all AR1 correlation parameters, and $\mathrm{Beta}(0.5,0.5)$ for all BYM2 proportion parameters.

1.2.2 ART coverage

We model ART coverage by

$$\mathrm{logit}(\alpha_{x,s,a}) = \beta_0^\alpha + \beta_S^{\alpha,s=\mathrm{M}} + u_a^\alpha + u_a^{\alpha,s=\mathrm{M}} + u_x^\alpha + u_x^{\alpha,s=\mathrm{M}} + u_x^{\alpha,a<15} + \eta_{R_x,s,a}^\alpha$$

with terms and priors analogous to the HIV prevalence model above.

1.2.3 HIV incidence rate

We model HIV incidence rate by

$$\log(\lambda_{x,s,a}) = \beta_0^\lambda + \beta_S^{\lambda,s=\mathrm{M}} + \log(\rho_x^{\text{15-49}}) + \log(1-\omega\cdot\alpha_x^{\text{15-49}}) + u_x^\lambda + \eta_{R_x,s,a}^\lambda$$

where β_0^λ is an intercept term proportional to the average HIV transmission rate for untreated HIV positive adults, $\beta_S^{\lambda,s=\mathrm{M}}$ is the log incidence rate ratio for men compared to women, $\rho_x^{\text{15-49}}$ is the HIV prevalence among adults 15-49 calculated by

$$\rho_x^{\text{15-49}} = \frac{\sum_{s\in\{\mathrm{F,M}\}}\sum_{a=15}^{45} N_{x,s,a}\cdot\rho_{x,s,a}}{\sum_{s\in\{\mathrm{F,M}\}}\sum_{a=15}^{45} N_{x,s,a}},$$

$\alpha_x^{\text{15-49}}$ is the ART coverage among adults 15-49 calculated by

$$\alpha_x^{\text{15-49}} = \frac{\sum_{s\in\{\mathrm{F,M}\}}\sum_{a=15}^{45} N_{x,s,a}\cdot\rho_{x,s,a}\cdot\alpha_{x,s,a}}{\sum_{s\in\{\mathrm{F,M}\}}\sum_{a=15}^{45} N_{x,s,a}\cdot\rho_{x,s,a}},$$

ω is the average reduction in HIV transmission rate per 1% increase in population ART coverage and is fixed at $\omega = 0.7$ via the EPP model, $u_x^\lambda \sim \mathcal{N}(0,\sigma^\lambda)$ with $\sigma^\lambda \sim \mathcal{N}^+(0,1)$ are IID spatial random effects, and $\eta_{R_x,s,a}^\lambda$ specify log incidence rate ratios by sex and age group calculated from Spectrum model output

1.2.4 ANC testing

HIV prevalence $\rho_{x,a}^{\mathrm{ANC}}$ and ART coverage $\alpha_{x,a}^{\mathrm{ANC}}$ among pregnant women modelled with logit-linear models

$$\mathrm{logit}(\rho_{x,a}^{\mathrm{ANC}}) = \mathrm{logit}(\rho_{x,F,a}) + \beta^{\rho^{\mathrm{ANC}}} + u_x^{\rho^{\mathrm{ANC}}} + \eta_{R_x,a}^{\rho^{\mathrm{ANC}}} \tag{1}$$

$$\mathrm{logit}(\alpha_{x,a}^{\mathrm{ANC}}) = \mathrm{logit}(\alpha_{x,F,a}) + \beta^{\alpha^{\mathrm{ANC}}} + u_x^{\alpha^{\mathrm{ANC}}} + \eta_{R_x,a}^{\alpha^{\mathrm{ANC}}}, \tag{2}$$

where $\eta_{R_x,a}^{\theta^{\mathrm{ANC}}}$ for $\theta\in\{\rho,\alpha\}$ are offsets for the log fertility rate ratios for HIV positive women compared to HIV negative women and for women on ART to HIV positive women not on ART, calculated from Spectrum model outputs for region R_x, $\beta^{\theta^{\mathrm{ANC}}}$ for $\theta\in\{\rho,\alpha\}$ are the average differences between population and ANC outcomes after removing the offset, and $u_x^{\theta^{\mathrm{ANC}}} \sim \mathcal{N}(0,\sigma_X^{\theta^{\mathrm{ANC}}})$ for $\theta\in\{\rho,\alpha\}$ are district random effects.

1.2.5 ART attendance

Let $\gamma_{x,x'}\in[0,1]$ be the probability that a person on ART residing in district x recieves ART in district x'. We assume that $\gamma_{x,x'}=0$ for $x\notin\{x,\mathrm{ne}(x)\}$ such that individuals seek treatment only in their residing district and its neighbours $\mathrm{ne}(x)=\{x' : x'\sim x\}$, where $\sim$ is an adjacency relation and $\sum_{x'\in\{x,\mathrm{ne}(x)\}}\gamma_{x,x'}=1$.

To model $\gamma_{x,x'}$ for $x\sim x'$ we use a multinomial logistic regression model where $\tilde{\gamma}_{x,x'}$ is the log odds ratio of seeking ART

$$\tilde{\gamma}_{x,x'} = \tilde{\gamma}_0 + u_x^{\tilde{\gamma}} \tag{3}$$

$$\tilde{\gamma}_0 = -4 \tag{4}$$

$$u_x^{\tilde{\gamma}} \sim \mathcal{N}(0,\sigma_X^{\tilde{\gamma}}) \tag{5}$$

where $\tilde{\gamma}_0$ is an intercept specifying the prior mean for the log odds of seeking ART in each neighbouring district compared to the home district, and $u_x^{\tilde{\gamma}}$ are district random effects. We fix $\tilde{\gamma}_{x,x} = 0$ and recover the multinomial probabilities using the softmax

$$\gamma_{x,x'} = \frac{\exp(\tilde{\gamma}_{x,x'})}{\sum_{x^\star \in \{x, \text{ne}(x)\}} \exp(\tilde{\gamma}_{x,x^\star})}$$

Then, given the number of PLHIV on ART $A_{x,s,a} = N_{x,s,a} \cdot \rho_{x,s,a} \cdot \alpha_{x,s,a}$, the number of ART clients who reside in district x and obtain ART in district x' are

$$A_{x,x',s,a} = A_{x,s,a} \cdot \gamma_{x,x'},$$

and the total attending ART facilities in district x' are

$$\tilde{A}_{x',s,a} = \sum_{x \in \{x', \text{ne}(x')\}} A_{x,x',s,a}.$$

1.3 Likelihood specification

1.3.1 Household survey data

Let ν be a household survey occurring at T_1, furnishing weighted observations $\hat{\theta}_{\{x\},\{s\},\{a\},\nu}$ for $\theta \in \{\rho, \alpha, \kappa\}$ with respective Kish effective sample sizes $M^{\hat{\theta}}_{\{x\},\{s\},\{a\},\nu}$, and observed number of cases

$$Y^{\hat{\theta}}_{\{x\},\{s\},\{a\},\nu} = M^{\hat{\theta}}_{\{x\},\{s\},\{a\},\nu} \cdot \hat{\theta}_{\{x\},\{s\},\{a\},\nu}.$$

For HIV prevalence and ART coverage we use binomial working likelihoods as follows

$$Y^{\hat{\rho}}_{\{x\},\{s\},\{a\},\nu} \sim \text{xBin}(M^{\hat{\rho}}_{\{x\},\{s\},\{a\},\nu}, \rho_{\{x\},\{s\},\{a\},T_1}) \tag{6}$$

$$\rho_{\{x\},\{s\},\{a\}} = \frac{\sum_{x \in \{x\}} \sum_{s \in \{s\}} \sum_{a \in \{a\}} N_{x,s,a} \cdot \rho_{x,s,a}}{\sum_{x \in \{x\}} \sum_{s \in \{s\}} \sum_{a \in \{a\}} N_{x,s,a}}, \tag{7}$$

and

$$Y^{\hat{\alpha}}_{\{x\},\{s\},\{a\},\nu} \sim \text{xBin}(M^{\hat{\alpha}}_{\{x\},\{s\},\{a\},\nu}, \alpha_{\{x\},\{s\},\{a\},T_1}) \tag{8}$$

$$\alpha_{\{x\},\{s\},\{a\}} = \frac{\sum_{x \in \{x\}} \sum_{s \in \{s\}} \sum_{a \in \{a\}} N_{x,s,a} \cdot \rho_{x,s,a} \cdot \alpha_{x,s,a}}{\sum_{x \in \{x\}} \sum_{s \in \{s\}} \sum_{a \in \{a\}} N_{x,s,a} \cdot \rho_{x,s,a}}. \tag{9}$$

For recent infections we also use a binomial working likelihood

$$Y^{\hat{\kappa}}_{\{x\},\{s\},\{a\},\nu} \sim \text{xBin}(M^{\hat{\kappa}}_{\{x\},\{s\},\{a\},\nu}, \kappa_{\{x\},\{s\},\{a\},T_1}) \tag{10}$$

$$\kappa_{x,s,a} = 1 - \exp(-\lambda_{x,s,a} \cdot \frac{1 - \rho_{x,s,a}}{\rho_{x,s,a}} \cdot (\Omega_T - \beta_T) - \beta_T) \tag{11}$$

$$\Omega_T \sim \mathcal{N}(\Omega_{T_0}, \sigma^{\Omega_T}) \tag{12}$$

$$\beta_T \sim \mathcal{N}(\beta_{T_0}, \sigma^{\beta_T}) \tag{13}$$

where $\kappa_{x,s,a}$ are the predicted proportion recently infected among HIV positive persons, Ω_T is the mean duration of recent infection (MDRI), and β_T is the false recent ratio (FRR). We use an informative prior on Ω_T based on the characteristics of the recent infection testing algorithm (RITA). For PHIA surveys this is $\Omega_{T_0} = 130$ days and $\sigma^{\Omega_T} = 6.12$ days. For PHIA surveys we assume there is no false recency, such that $\beta_{T_0} = 0.0$ and $\sigma^{\beta_T} = 0.0$.

1.3.2 ANC testing data

We include ANC testing data for the year of the most recent survey $Y[T_1]$. Let $W^{\text{ANC}}_{\{x\},Y[t]}$ be the number of ANC clients, $X^{\text{ANC}}_{\{x\},Y[t]}$ the number of those with ascertained status, $Y^{\text{ANC}}_{\{x\},Y[t]}$ the number of those with positive status (either known or tested) and $Z^{\text{ANC}}_{\{x\},Y[t]}$ the number of ANC clients already on ART prior to first ANC, such that $W^{\text{ANC}}_{x,Y[t]} \geq X^{\text{ANC}}_{x,Y[t]} \geq Y^{\text{ANC}}_{x,Y[t]} \geq Z^{\text{ANC}}_{x,Y[t]}$ When ANC testing data are only available for part of a given year, we denote $M^{\text{ANC}}_{Y[t]} \in \{1, \ldots, 12\}$ the number of months of reported data reflected in counts for year $Y[t]$.

The observed number of HIV positive and already on ART among ANC clients at $Y[T_1]$ is modelled by

$$Y^{\text{ANC}}_{\{x\}Y[T_1]} \sim \text{Bin}\left(X^{\text{ANC}}_{\{x\}Y[T_1]}, \rho^{\text{ANC}}_{\{x\},\{15,\ldots 45\}}\right)$$
$$Z^{\text{ANC}}_{\{x\}Y[T_1]} \sim \text{Bin}\left(Y^{\text{ANC}}_{\{x\}Y[T_1]}, \alpha^{\text{ANC}}_{\{x\},\{15,\ldots 45\}}\right)$$

where predicted prevalence and ART coverage are aggregated weighted by the predicted number of pregnant women by age $\Psi_{x,a}$

$$\rho^{\text{ANC}}_{\{x\}\{a\}} = \frac{\sum_{x\in\{x\}}\sum_{a\in\{a\}} \Psi_{x,a} \cdot \rho^{\text{ANC}}_{x,a}}{\sum_{x\in\{x\}}\sum_{a\in\{a\}} \Psi_{x,a}}$$
$$\alpha^{\text{ANC}}_{\{x\}\{a\}} = \frac{\sum_{x\in\{x\}}\sum_{a\in\{a\}} \Psi_{x,a} \cdot \rho^{\text{ANC}}_{x,a} \cdot \alpha^{\text{ANC}}_{x,a}}{\sum_{x\in\{x\}}\sum_{a\in\{a\}} \Psi_{x,a} \cdot \rho^{\text{ANC}}_{x,a}}$$

1.3.3 Number receiving ART

Let $\dot{A}_{\{x\},\{s\},\{a\}}$ be data for the number receiving ART

$$\dot{A}_{\{x\},\{s\},\{a\}} = \sum_{s\in\{s\}}\sum_{a\in\{a\}}\sum_{x\in\{x\}}\sum_{x\sim x', x=x'} \dot{A}_{x',x,s,a},$$

We model the unobserved numbers of ART clients travelling from x' to x as

$$\dot{A}_{x',x,s,a} \sim \text{Bin}(N_{x',s,a}, \pi_{x',x,s,a})$$

where $\pi_{x',x,s,a} = \rho_{x',s,a} \cdot \alpha_{x',s,a} \cdot \gamma_{x',x,s,a}$. This likelihood is approximated using a normal for the sum of binomials by

$$\dot{A}_{\{x\},\{s\},\{a\}} \sim \mathcal{N}(\tilde{A}_{\{x\},\{s\},\{a\}}, \sigma^{\tilde{A}}_{\{x\},\{s\},\{a\}})$$

where

$$\tilde{A}_{\{x\},\{s\}\{a\}} = \sum_{s\in\{s\}}\sum_{a\in\{a\}}\sum_{x\in\{x\}}\sum_{x\sim x', x=x'} N_{x',s,a} \cdot \pi_{x',x,s,a},$$

and

$$\sigma^{\tilde{A}}_{\{x\},\{s\}\{a\}} = \sqrt{\sum_{s\in\{s\}}\sum_{a\in\{a\}}\sum_{x\in\{x\}}\sum_{x\sim x', x=x'} N_{x',s,a} \cdot \pi_{x',x,s,a} \cdot (1 - \pi_{x',x,s,a})}.$$

1.4 Identifiability constaints

If data are missing, some parameters are fixed to default values to help with identifiability. In particular:

- If survey data on ART coverage by age and sex are not available then we set $u^{\alpha}_{a} = 0$ and $u^{\alpha}_{a,s=\text{M}} = 0$ and use the average age/sex pattern of ART coverage from the Spectrum offset $\eta^{\alpha}_{R_x,s,a}$.
- If no ART data (survey or ART programme) are available at T_1 but data on ART coverage among ANC clients are available, the level of ART coverage is not identifiable, but spatial variation is identifiable. In this instance, overall ART coverage is determined by the Spectrum offset, and only area random effects are estimated

$$\text{logit}\left(\alpha_{x,s,a}\right) = u^{\alpha}_{x} + \eta^{\alpha}_{R_x,s,a}$$

- If survey data on recent HIV infection are not included in the model, then $\beta_0^\lambda = \beta_S^{\lambda,s=\mathrm{M}} = u_x^\lambda = 0$. The sex ratio for HIV incidence is determined by the sex incidence rate ratio from Spectrum in the same years and the incidence rate in all districts is modelled assuming the same average HIV transmission rate for untreated adults, but varies according to district estimates of HIV prevalence and ART coverage.

2 C++ template

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