

Online Appendix 1: Model fitting procedure

Likelihood function

Two data sources are used when fitting the model: the provincial HIV prevalence levels in the antenatal clinic surveys (1990–2013) and the provincial HIV prevalence levels in the HSRC household surveys (conducted in 2005, 2008 and 2012). The sections that follow explain how the likelihood function is defined for each of these data sets.

Firstly, the antenatal likelihood is calculated by comparing model estimates of HIV prevalence in pregnant women and corresponding survey estimates. In the national version of the Thembisa model, these comparisons were performed separately for pregnant women in each 5-year age group. However, because this age-specific prevalence information is not reported for each province in most of the antenatal survey reports, our approach in the calibration of the provincial models is to calibrate only to the overall antenatal HIV prevalence (not disaggregated by age). Suppose that $H_{i,t}(\boldsymbol{\phi})$ is the model estimate of HIV prevalence in pregnant women in province i , in year t , where the vector $\boldsymbol{\phi}$ represents the values of the model input parameters. The corresponding prevalence of HIV actually measured in the antenatal survey is represented by $y_{i,t}$. It is assumed that if $\boldsymbol{\phi}$ is the true set of parameter values, then the difference between the logit-transformed model estimate and the logit-transformed observed prevalence is normally distributed. The mean of this normal distribution represents the extent of the antenatal bias, which arises because of a number of factors, such as the exclusion of women receiving private antenatal care from the antenatal survey. The variance of the distribution is assumed to be composed of a 'survey error' term – representing the uncertainty around the survey estimate because of binomial variation and cluster variation in the survey – and a 'model error' term. More formally, it is assumed that

$$\log\left(\frac{y_{i,t}}{1-y_{i,t}}\right) = \log\left(\frac{H_{i,t}(\boldsymbol{\phi})}{1-H_{i,t}(\boldsymbol{\phi})}\right) + b_i + m_{i,t} + \varepsilon_{i,t}, \quad [\text{Eqn 1}]$$

where b_i is the antenatal bias parameter in province i , $m_{i,t} \sim N(0, \sigma_i^2)$ and $\varepsilon_{i,t} \sim N(0, \sigma_{i,t}^2)$. The latter two terms represent the model error and the survey error, respectively. The logit transformations ensure that the error terms are closer to normality and that the model error terms are roughly independent of the level of HIV prevalence.

In the initial calibration of the national model,¹ the antenatal bias was a free parameter and it was allowed to change over time, from a theoretical maximum in 1991 (when antenatal surveillance was biased towards urban areas) to an ultimate level that applied in

1997 and all subsequent years (following the introduction of standard sampling protocols). The resulting estimates of the maximum antenatal bias (0.48, 95% CI: 0.41–0.56) and the ultimate antenatal bias (0.43, 95% CI: 0.39–0.46) were similar, suggesting little change in the extent of the antenatal bias over time. In calibrating the provincial models, we therefore, assume that levels of antenatal bias are constant over time, but make implicit allowance for the possibility of error because of non-constant bias by including the 'model error' term defined previously. To adopt the same approach as in the national model, of treating the antenatal bias as a free parameter, would lead to too much variation in the extent of the antenatal bias between provinces, and initial attempts to apply this approach led to implausible HIV estimates in some provinces. Our approach is therefore to constrain the extent of the antenatal bias by specifying prior distributions on the antenatal bias parameters, similar to the approach adopted in other recent modelling studies.^{2,3} The mean of the prior distribution is assumed to differ between provinces, depending on the fraction of the population that uses private healthcare facilities, because much of the antenatal bias is attributable to the exclusion of pregnant women attending private facilities from the antenatal survey. Mathematically, the prior mean is estimated by assuming that

$$\bar{b}_i = \psi + \chi \omega_i, \quad [\text{Eqn 2}]$$

where \bar{b}_i is the mean of the prior distribution on b_i , ψ is the antenatal bias that would be expected if all pregnant women used public health facilities, χ is the difference in HIV prevalence between women using private antenatal services and women using public antenatal services (on the logit scale) and ω_i is the proportion of pregnant women in province i who use private antenatal services. Estimates of differences in HIV prevalence between pregnant women using private and public antenatal services are very limited, but a 1998 survey in KwaZulu-Natal found a prevalence of 14.0% in pregnant women using private facilities,⁴ which compared with a prevalence of 32.5% in public antenatal clinics in KwaZulu-Natal in the same year.⁵ This suggests a value of χ equal to 1.08. Estimates of the ω_i values are not directly reported, but we have approximated these values using the proportions of adults who reported being members of medical schemes in the 2003 DHS,⁶ as shown in Table 1. Given that this proportion is 14.2% for the country as a whole, and given the previously estimated antenatal bias of 0.426 for the country as a whole, we estimate the ψ parameter as 0.272 ($0.426 - 1.08 \times 0.142$). These parameter values are entered into Equation 2 to obtain the prior means for each province, as shown in Table 1. As might be expected, the estimated antenatal bias levels are greatest in Gauteng and the Western Cape, the two provinces with the highest levels of medical scheme membership.

To represent the uncertainty around the antenatal bias parameters, we use gamma prior distributions. The coefficient

TABLE 1: Antenatal bias levels by province.

Province	EC	FS	GT	KZ	LP	MP	NC	NW	WC
% in medical schemes (ω_i)	10.3%	11.0%	22.0%	9.6%	8.4%	12.5%	15.8%	9.4%	20.3%
Antenatal bias (\bar{b}_i)	0.383	0.391	0.510	0.376	0.363	0.407	0.443	0.374	0.492

EC, Eastern Cape; FS, Free State; GT, Gauteng; KZ, KwaZulu-Natal; LP, Limpopo; MP, Mpumalanga; NC, Northern Cape; NW, North West; WC, Western Cape.

of variation around the antenatal bias parameter estimated for the country as a whole is 3.9%, so to represent the slightly greater uncertainty that exists at a provincial level because of the private sector adjustments, we assume a coefficient of variation of 5% for all provinces when assigning the prior distributions.

The $\sigma_{i,t}^2$ parameters have been estimated from the published 95% confidence intervals around the antenatal survey estimates, in 1998 and subsequent years. Prior to 1998, the published 95% confidence intervals were calculated on the assumption of simple random sampling (SRS), that is, not reflecting the clustering associated with the sampling of antenatal clinics. As these confidence intervals would have exaggerated the precision associated with the prevalence estimates, we recalculated the standard errors by inflating the published standard errors up to 1998 by province-specific adjustment factors. The adjustment factor was calculated as the average ratio of the published standard error to the SRS standard error over the 2003–2005 period (the only period for which we had sufficient data to calculate both standard error estimates in all provinces). The $\sigma_{i,t}^2$ parameters up to 1998 were then estimated from these inflated standard error estimates.

Having obtained the $\sigma_{i,t}^2$ parameters, the variance of the model error (σ_i^2) is estimated using the formula

$$\hat{\sigma}_i^2 = \frac{1}{24} \sum_t \left(\log \left(\frac{y_{i,t}}{1 - y_{i,t}} \right) - \log \left(\frac{H_{i,t}(\phi)}{1 - H_{i,t}(\phi)} \right) - b_i \right)^2 - \sigma_{i,t}^2 \quad [\text{Eqn 3}]$$

The likelihood in respect of the antenatal data is then calculated based on the assumption that the error terms are normally distributed:

$$L_i(y_i | \phi, b_i) = \prod_t \left(2\pi(\hat{\sigma}_i^2 + \sigma_{i,t}^2) \right)^{-0.5} \exp \left[-\frac{\left(\log \text{it}(y_{i,t}) - \log \text{it}(H_{i,t}(\phi)) - b_i \right)^2}{2(\hat{\sigma}_i^2 + \sigma_{i,t}^2)} \right] \quad [\text{Eqn 4}]$$

where y_i represents the vector of $y_{i,t}$ values, across calendar years 1990–2013.

The approach followed in defining the likelihood in respect of the household survey data is similar to that for the antenatal data, with a few key differences. Firstly, instead of using only the total HIV prevalence in the likelihood definition, we calculate the likelihood separately for 15–24 year olds and adults aged 25 and older, as the age breakdown provides useful information on trends in HIV incidence. Secondly, the bias term (b_i) and model error term ($m_{i,t}$) are both omitted from the expression for the observed prevalence. The bias term is omitted because there is

no evidence to suggest that antiretroviral exposure is understated in the South African household surveys,^{7,8} which implies that individuals who know they are HIV-positive (and are receiving ART) are no less likely to participate in the household surveys. The model error term is omitted because there is no need to make implicit allowance for changes in survey bias over time if the surveys are truly unbiased.

Posterior analysis

The posterior distributions, representing the parameter sets that were most consistent with both the province-specific HIV prevalence data and the prior beliefs about the most plausible parameter values (Table 1 of the main text) were approximated using the Incremental Mixture Importance Sampling (IMIS) method.⁹ For each province, an initial set of 5000 parameter combinations were sampled from the prior distributions and the likelihood function was calculated for each parameter combination. In subsequent IMIS steps, the regions of the parameter space with the highest posterior density were sampled more heavily, with an additional sample of 500 parameter combinations being evaluated in each IMIS step. The procedure was repeated until a sufficiently mixed posterior sample was generated, containing 1000 parameter combinations. All posterior means and 95% confidence intervals are calculated from this sample of 1000 parameter combinations.

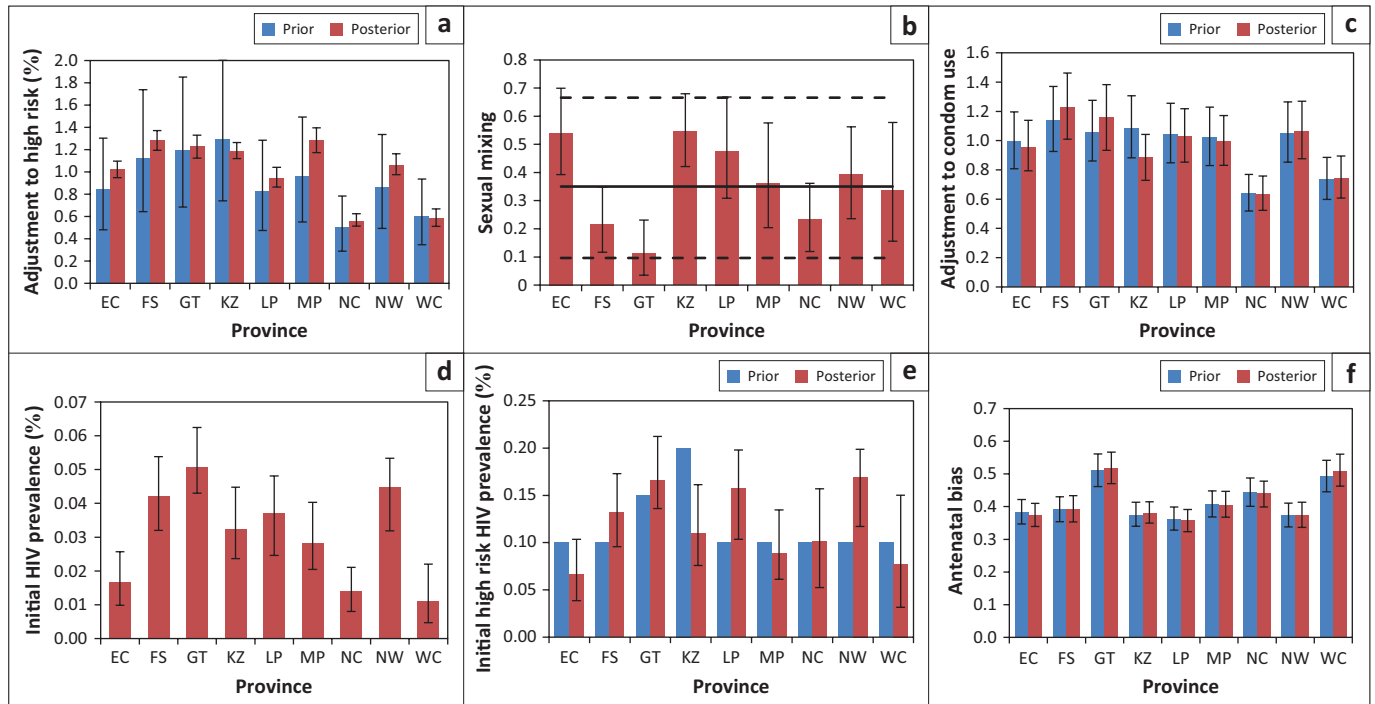
Figure 1 compares the posterior distributions and prior distributions for each province. There is generally close correspondence between the prior and posterior means in the case of the antenatal bias and condom adjustment factors. However, the posterior means are in some cases very different from the prior means when comparing the high-risk adjustment factors, the sexual mixing parameters and the initial HIV prevalence levels.

Sensitivity analyses

Because the model confidence intervals are relatively wide for North West and Mpumalanga, and because the model fit to the Gauteng data is not as good as for the other provinces, we consider the effect of a number of possible changes to the model fitting procedure for these three provinces.

Exclusion of antenatal survey data collected prior to 1997

Antenatal survey data collected prior to 1997 did not follow a standard sampling methodology, and it is believed that this may explain some of the anomalous provincial HIV prevalence estimates in the early surveys. We, therefore, assess the effect of running the model fitting procedure when the pre-1997 antenatal data are excluded. Table 2 compares the posterior estimates of the model parameters and shows that excluding the pre-1997 data does lead to some changes in the posterior estimates of the model parameters, particularly the initial HIV prevalence in 1985 and the sexual mixing parameter. However, these have little effect on the average estimates of HIV prevalence in pregnant women in 2000 and subsequent years



EC, Eastern Cape; FS, Free State; GT, Gauteng; KZ, KwaZulu-Natal; LP, Limpopo; MP, Mpumalanga; NC, Northern Cape; NW, North West; WC, Western Cape.

Note: Bar heights represent means and vertical error bars represent 2.5 and 97.5 percentiles (95% confidence intervals) of the relevant distributions. In panel (b), the prior distributions are the same for all provinces, and the horizontal lines, therefore, represent the prior mean and 95% confidence interval.

FIGURE 1: Comparison of prior and posterior distributions.

TABLE 2: Posterior estimates of model parameters before and after excluding pre-1997 data.

Parameter	High-risk adjustment factor		Sexual mixing parameter		Condom use adjustment factor		Initial HIV prevalence in women aged 15–49		Antenatal bias (logit scale)	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Gauteng										
Including all data	1.23	1.12–1.33	0.11	0.04–0.23	1.16	0.93–1.38	0.051	0.043–0.062	0.52	0.47–0.57
Excluding pre-97 data	1.17	1.09–1.26	0.19	0.08–0.32	1.17	0.97–1.41	0.074	0.053–0.088	0.52	0.47–0.57
Mpumalanga										
Including all data	1.28	1.17–1.40	0.36	0.20–0.58	0.99	0.83–1.17	0.028	0.021–0.040	0.41	0.37–0.45
Excluding pre-97 data	1.22	1.13–1.37	0.44	0.25–0.62	0.94	0.76–1.14	0.038	0.018–0.057	0.40	0.36–0.44
North West										
Including all data	1.06	0.98–1.16	0.39	0.24–0.56	1.06	0.88–1.27	0.045	0.032–0.053	0.37	0.34–0.41
Excluding pre-97 data	1.05	0.98–1.12	0.41	0.26–0.55	1.03	0.85–1.23	0.042	0.024–0.052	0.37	0.34–0.41

CI, confidence intervals.

TABLE 3: Model estimates of antenatal HIV prevalence (public sector).

Province	1990		1995		2000		2005		2010		2013	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Gauteng												
Including all data	1.0	0.9–1.2	10.0	9.2–10.7	26.1	24.9–27.1	30.1	29.0–31.1	30.9	29.8–32.1	31.3	30.2–32.5
Excluding pre-97 data	1.4	1.1–1.6	11.4	9.8–12.8	26.6	25.3–27.7	30.1	29.1–31.0	30.7	29.6–31.9	31.0	29.9–32.1
Mpumalanga												
Including all data	0.9	0.8–1.0	12.5	11.2–14.1	30.7	29.0–32.6	34.6	32.9–36.5	34.8	32.8–36.8	34.4	32.5–36.4
Excluding pre-97 data	1.0	0.6–1.4	12.6	10.4–15.2	30.3	28.8–31.9	34.4	33.3–35.6	34.8	33.4–36.0	34.3	33.1–35.6
North West												
Including all data	0.9	0.7–1.1	10.5	8.7–12.8	26.2	24.2–28.3	29.8	27.7–32.0	29.8	27.5–32.1	29.1	26.9–31.3
Excluding pre-97 data	0.8	0.6–1.0	9.6	8.5–10.6	25.4	24.5–26.3	29.6	28.9–30.2	29.8	29.0–30.6	29.1	28.4–29.9

CI, confidence intervals.

(Table 3). The exclusion of the pre-1997 data does lead to wider confidence intervals around the model estimates of antenatal HIV prevalence in the period before 1997, but for Mpumalanga and North West, the exclusion of the pre-1997 data leads to substantially narrower confidence intervals around model

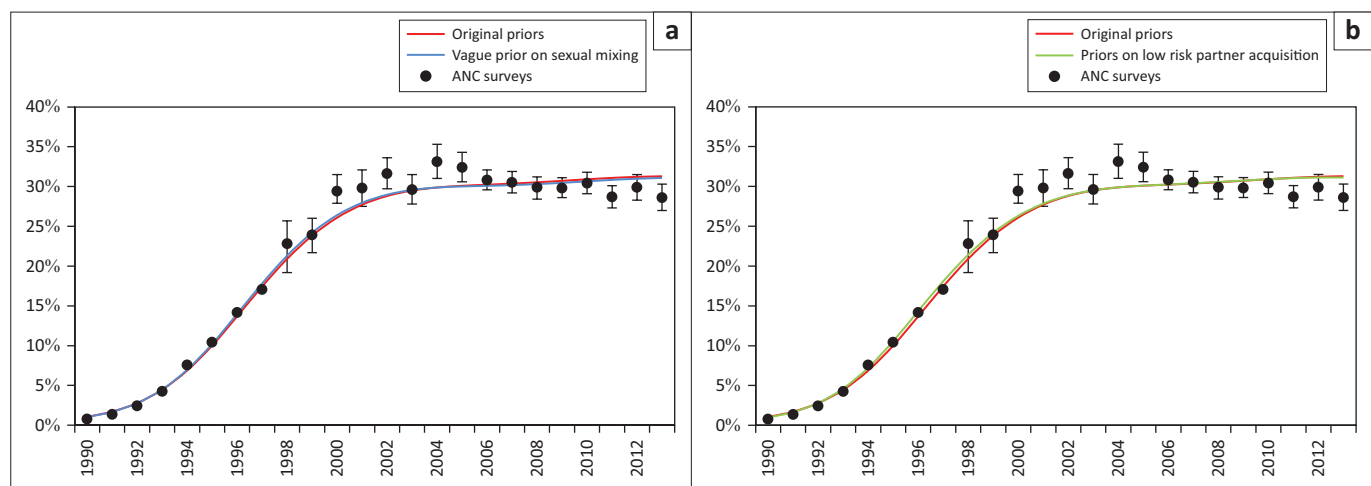
estimates in 2000 and subsequent years (Table 3). The anomalous antenatal survey measurements in North West and Mpumalanga in the early 1990s are, therefore, responsible for the relatively wide confidence intervals around the model estimates in recent years.

TABLE 4: Posterior estimates for Gauteng with different prior distributions.

Parameter	Using original priors		Using vague prior on sexual mixing parameter		Using priors on relative rates of partner acquisition in low-risk group	
	%	95% CI	%	95% CI	%	95% CI
High-risk adjustment factor	1.23	1.12–1.33	1.25	1.16–1.34	1.02	0.75–1.26
Sexual mixing parameter	0.11	0.04–0.23	0.06	0.01–0.18	0.29	0.09–0.58
Condom use adjustment factor	1.16	0.93–1.38	1.16	0.94–1.40	1.18	0.98–1.40
Initial HIV prevalence, women aged 15–49	0.051	0.043–0.062	0.048	0.042–0.057	0.039	0.026–0.053
Antenatal bias parameter (logit scale)	0.52	0.47–0.57	0.52	0.48–0.57	0.52	0.48–0.56
Relative rate of partner acquisition						
Low risk males	0.37†	–	0.37†	–	0.19	0.03–0.49
Low risk females	0.16†	–	0.16†	–	0.17	0.02–0.38

†, Parameter is fixed in the uncertainty analysis.

CI, confidence intervals.

**FIGURE 2:** Antenatal HIV prevalence in Gauteng: Effect of alternative priors on (a) sexual mixing and (b) low risk activity.

Alternative priors on sexual behaviour parameters

We consider two hypotheses for the poor model fit to the antenatal survey data in Gauteng. The first hypothesis is that the choice of prior on the sexual mixing parameter may exert too much influence, effectively preventing very low sexual mixing parameters from being included in the posterior sample. It might be expected that with lower sexual mixing parameter values, we could improve the model fit to the antenatal data, because a lower sexual mixing parameter would tend to push up the HIV prevalence in the early 2000s and reduce the HIV prevalence in more recent years. To test this hypothesis, we consider an alternative prior, which is uniform on the interval (0, 1); this vague prior attaches greater weight to the possibility of very low sexual mixing parameter values. Table 4 shows that the use of this vague prior does indeed lead to a lower posterior estimate of the sexual mixing parameter. However, the change in prior leads to almost no change in the posterior estimates of HIV prevalence in pregnant women (Figure 2a). The choice of prior on the sexual mixing parameter is, therefore, not responsible for the poor model fit to the data.

The second hypothesis is that the model may not be allowing for sufficient heterogeneity in sexual behaviour. As with the effect of reducing the sexual mixing parameter, we would expect the effect of increasing heterogeneity to be a more rapid early increase in HIV prevalence followed by a more rapid decline in HIV prevalence,¹⁰ that is, closer to the pattern observed in the Gauteng antenatal HIV

prevalence data. To test the hypothesis, we extend the model fitting procedure to include priors on two additional parameters: the relative rate of partnership formation in low-risk males (compared to high-risk males) and the corresponding parameter for females. The lower these relative rates, the greater is the heterogeneity on sexual risk behaviour in the population. Including these parameters in the uncertainty analysis, therefore, creates flexibility to model increased or reduced levels of heterogeneity in sexual risk behaviour. Table 4 shows that when these parameters are allowed to vary in the model fitting procedure, the relative rate of partnership formation in low-risk males is halved relative to the levels previously assumed, implying greater heterogeneity in sexual risk behaviour. However, this is offset by a substantial increase in the fitted sexual mixing parameter (from 0.11 to 0.29). The net effect is that there is negligible change to the model estimate of HIV prevalence in pregnant women (Figure 2). The relative inflexibility regarding the assumptions about heterogeneity in behaviour is, therefore, not the explanation for the poor model fit to the antenatal survey data in Gauteng.

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