Supplementary materials:
The effect of HIV programmes in South Africa on national HIV incidence trends, 2000-2019

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1. Introduction

These supplementary materials provide additional detail on the Thembisa model. Our analysis is based on an adaptation of Thembisa version 4.4, which is described more fully elsewhere [1]. The purpose of these supplementary materials is to describe those aspects of the model that have been modified for the purpose of the present analysis, and to provide more detail on those aspects of the model that are most relevant to the present analysis. Although the main form of behaviour change considered in this analysis is condom use, we include in section 4 of the supplementary materials a review of trends in other risk behaviours. The final section compares our modelling approach to other approaches commonly used in estimating HIV incidence rates and intervention effects on HIV incidence.

2. Methods

2.1 Overview of the model

Thembisa is a compartmental deterministic model of HIV in South Africa. Table S1 summarizes the variables that define the compartments in the model. As noted in the main text, there are two broadly defined risk groups: high-risk individuals (those who have a propensity for concurrent partners and/or commercial sex) and low-risk individuals. Unmarried high-risk women are assumed to transition in and out of commercial sex activity, and a proportion of men are assumed to have sex with other men. Three types of sexual relationship are modelled: long-term marital/cohabiting relationships, short-term non-cohabiting relationships, and contacts between female sex workers and their clients. Rates of sexual debut and rates of entry into different relationship types depend on age, sex, risk group and marital status, and have been set with reference to South African census and survey data. Coital frequencies in long-term and short-term relationships are assumed to depend on age and relationship type, while contacts between sex workers and clients are assumed to be once-off. Partner age preferences are specified, and a ‘sexual mixing’ parameter determines the extent to which individuals select partners from outside their risk group.

Table S1: Index variables and compartments in Thembisa

Symbol	Description	Value	Definition
a	ART status	0	ART-naïve
		1	On ART or previously treated
d	Time since ART initiation	0	ART-naïve
		1	1st 6 months after ART start
		2	7-18 months after ART start
		3	19-30 months after ART start
		4	31-42 months after ART start
		5	>42 months after ART start
g	Sex	1	Male
		2	Female
i	Risk group	1	High risk
		2	Low risk
j	Partner risk group	1	High risk
		2	Low risk
l	Marital status *or* relationship type	0	Unmarried/short-term relationship
		1	Married/long-term relationship
		2	Sex worker/sex worker-client relationship
		3	MSM/same-sex short-term relationship
r	Circumcision status	0	Uncircumcised
		1	Circumcised
s	HIV stage *or* baseline CD4 count	0	Uninfected
		1	Acute HIV
		2	HIV-positive, CD4 ≥500 (after acute infection)
		3	HIV-positive, CD4 350-499
		4	HIV-positive, CD4 200-349
		5	HIV-positive, CD4 <200
v	HIV testing history	0	Never tested for HIV*
		1	Lasted tested HIV-negative*
		2	Diagnosed HIV-positive
x	Age	0-90+	Age at last birthday (at start of the year)

* In section 2.6.6 the 0 and 1 correspond to HIV-negative and undiagnosed HIV-positive respectively.

2.2 Model of trends in condom use

2.2.1 Condom use in women (excluding commercial sex)

Rates of condom use are assumed to depend on age, sex, type of relationship and knowledge of HIV-positive status. Rates of condom usage are also assumed to change over time; this time-dependency represents the effect of HIV communication programmes and condom promotion campaigns, which were introduced in the 1990s and early 2000s. The parameter $\gamma_{2,l}(x,t)$ represents the probability that an HIV-negative woman aged x uses a condom in an act of sex with a partner of type l at time t (time is measured in years since 1985). This is calculated as

$$\gamma_{2,l}(x,t) = \zeta(t)\, \nu^{(x-20)}\, \beta_l\, \theta_r, \qquad (1)$$

where $\zeta(t)$ represents the rate of condom use in unmarried women aged 20 in year t, ν is the factor by which condom use decreases per year of age, β_l is the relative rate of condom use in relationship type l, and θ_r is a scaling parameter, which we include to allow for the possibility of bias in self-reported condom use data (the value depends on the type of reporting, r). The 'base rate' of condom use, $\zeta(t)$, relates to women aged 20 who are unmarried ($l = 0$) and reporting on their condom use at last sex ($r = 0$), and the β_0 and θ_0 parameters are therefore both set to 1. The $\zeta(t)$ function is a linear combination of a constant term and two cumulative Weibull distribution functions. The constant term (k_0) represents the initial rate of condom usage, prior to the start of the HIV epidemic in South Africa, the first Weibull distribution corresponds to the increase in condom usage following the introduction of behaviour change communication programmes in the mid-1990s, and the second Weibull distribution represents a possible change in condom usage rates in recent years. In mathematical terms,

$$\zeta(t) = k_0 + k_1\left(1 - 0.5^{(t/m_1)^{\phi_1}}\right) + k_2\left(1 - 0.5^{(t/m_2)^{\phi_2}}\right). \qquad (2)$$

The k_1 parameter represents the extent of the increase in condom use following the early phase of the HIV communication programmes, and the m_1 and ϕ_1 parameters represent the median and shape parameters respectively of the first Weibull distribution. The k_2 parameter represents the extent of the change in condom use in recent years (possibly due to changes in funding for behaviour change communication programmes, and possibly due to changes in attitudes towards condom use as ART has become more widely available); the m_2 and ϕ_2 parameters represent the median and shape parameters respectively of the second Weibull distribution. We have fixed $m_2 = 2m_1$ and $\phi_2 = 2\phi_1$, similar to Thembisa version 4.2 [2], in order to simplify the model calibration.

These rates of condom use are adjusted in HIV-diagnosed individuals and individuals on ART. In a diagnosed but ART-naïve individual of sex g, the probability of condom use is calculated as $1 - (1 - \gamma_{g,l}(x,t))(1 - \delta)$, where δ is the proportionate reduction in unprotected sex after HIV diagnosis (as discussed in section 2.2.4). In ART-experienced individuals, the probability of condom use is $1 - (1 - \gamma_{g,l}(x,t))(1 - \delta)(1 - h)$, where h is the proportionate reduction in unprotected sex after ART initiation (as discussed in section 2.2.5). We have fixed $\delta = 0.18$ (the prior mean assigned to this parameter in section 2.2.4) and $h = 0.18$ (see section 2.2.5) for the purpose of the analyses that follow.

We estimate the parameters in equations (1) and (2) by fitting the model to self-reported condom usage data from national surveys conducted in South African women. For the purpose of this model fitting we do not include male data on condom usage because it is more difficult to determine the relationship type from male data (for example, if a married man reports that he used a condom the last time he had sex, it is not clear if this occurred in the context of his spousal relationship, another relationship with a non-spousal partner, or a contact with a sex worker). Another reason for not using the male data in calibration is that condoms are perceived to be a male-controlled form of contraception, and thus men might be more inclined to over-report their condom use (due to social desirability bias). Male rates of condom use are instead calculated as a function of female rates of condom use, as described in section 2.2.2.

For the purpose of the model fitting, we consider two types of self-reported condom use data: data on the reported use of condoms at last sex ($r = 0$) and data on use of condoms for contraceptive purposes ($r = 1$). In the case of the former, we set $\theta_r = 1$, so that the 'base rates' correspond to those that would be estimated if we believed reporting of condom use at last sex

to be an accurate reflection of the proportion of sex acts that are protected. In the case of the latter, we estimate a value of θ_r less than 1, assuming that there is less likely to be bias towards over-reporting condom use in the context of contraceptive use (since condoms are generally less effective than hormonal methods of contraception [3]).

A total of 71 national survey estimates of women's self-reported condom use were obtained, from 12 surveys conducted between 1986 and 2017. Of these, 49 related to condom use at last sex and 22 related to condom use for contraceptive purposes. All but 5 of the survey estimates combined married and unmarried women; the remaining 5 related only to women with non-cohabiting partners. Data were disaggregated by 5-year age group wherever possible; when this was not possible, broader age groupings were used. Table S2 summarizes the data.

For the purpose of fitting the model in equations (1) and (2) to the survey data, we use estimates of numbers of women who are married and unmarried, stratified by HIV diagnosis and receipt of ART, by age and by year, as estimated by Thembisa version 4.2 [2]. If $n_l(x, t)$ is the Thembisa estimate of the number of sexually-experienced women of marital status l, aged x in year t, and $d_l(x, t)$ and $a_l(x, t)$ are the corresponding proportions diagnosed positive and ART-experienced respectively, then the model estimate of condom use that is compared to the survey estimate is

$$\frac{\sum_{l=0}^{1} n_l(x,t)\left[\left(1-d_l(x,t)\right)\gamma_{2,l}(x,t)+\left(d_l(x,t)-a_l(x,t)\right)\left\{1-\left(1-\gamma_{2,l}(x,t)\right)\times\left(1-\delta\right)\right\}+a_l(x,t)\left\{1-\left(1-\gamma_{2,l}(x,t)\right)\left(1-\delta\right)\left(1-h\right)\right\}\right]}{n_0(x,t)+n_1(x,t)}. \quad (3)$$

For the sake of simplicity, we take x as the mid-point of the age range to which the survey estimate relates (except in the case of survey estimates for the 50+ age range, which we arbitrarily assign to age 60 for calibration purposes).

Table S2: National survey data on condom use in South Africa

Survey	Reporting type	Relationship type	Age group	Condom use
1985-87 DHS [4]	Contraception	All	15-49	0.8%
1998 DHS [5]	Last sex	All	15-19	19.5%
	Last sex	All	20-24	14.4%
	Last sex	All	25-29	7.6%
	Last sex	All	30-34	6.6%
	Last sex	All	35-39	2.6%
	Contraception	All	15-19	4.0%
	Contraception	All	20-24	4.2%
	Contraception	All	25-29	1.1%
	Contraception	All	30-34	2.7%
	Contraception	All	35-39	1.8%
	Contraception	All	40-44	0.9%
	Contraception	All	45-49	2.4%
2002 HSRC household survey [6]	Last sex	All	15-19	48.9%
	Last sex	All	20-24	47.0%
	Last sex	All	25-49	19.7%
	Last sex	All	50+	5.6%
2003 DHS [7]	Last sex	All	15-19	48.1%
	Last sex	All	20-24	48.8%
	Last sex	All	25-29	35.2%
	Last sex	All	30-34	25.1%
	Last sex	All	35-39	25.7%
	Contraception	All	15-19	17.7%
	Contraception	All	20-24	14.5%
	Contraception	All	25-29	7.6%
	Contraception	All	30-34	4.0%
	Contraception	All	35-39	4.4%
	Contraception	All	40-44	5.7%
	Contraception	All	45-49	5.1%
2003 Youth Survey [8]	Last sex	All	15-19	55.0%
	Last sex	All	20-24	44.0%
2005 HSRC household survey [9]	Last sex	All	15-24	55.7%
	Last sex	All	25-49	29.1%
	Last sex	All	50+	5.3%
2008 HSRC household survey [10]	Last sex	All	15-24	66.5%
	Last sex	All	25-49	40.8%
	Last sex	All	50+	7.8%
2009 NHCS [11]	Last sex	All	16-19	63.0%
	Last sex	All	20-24	49.0%
	Last sex	All	25-29	43.0%
	Last sex	All	30-34	32.0%
	Last sex	All	35-39	28.0%
	Last sex	All	40-44	20.0%
	Last sex	All	45-49	20.0%
	Last sex	All	50-55	11.0%
2012 HSRC household survey [12]	Last sex	All	15-24	49.8%
	Last sex	All	25-49	32.7%

	Last sex	All	50+	9.4%
2012 NHCS [13]	Last sex	All	16-19	65.0%
	Last sex	All	20-24	55.0%
	Last sex	All	25-29	52.0%
	Last sex	All	30-34	43.0%
	Last sex	All	35-39	43.0%
	Last sex	All	40-44	37.0%
	Last sex	All	45-49	28.0%
	Last sex	All	50-55	17.0%
2016 DHS [14]	Last sex	Non-marital	15-19	63.8%
	Last sex	Non-marital	20-24	61.5%
	Last sex	Non-marital	25-29	58.1%
	Last sex	Non-marital	30-39	58.5%
	Last sex	Non-marital	40-49	59.7%
	Contraception	All	15-19	24.3%
	Contraception	All	20-24	15.0%
	Contraception	All	25-29	18.0%
	Contraception	All	30-34	12.9%
	Contraception	All	35-39	18.3%
	Contraception	All	40-44	11.0%
	Contraception	All	45-49	13.2%
2017 HSRC household Survey [15]	Last sex	All	15-24	49.8%
	Last sex	All	25-49	36.0%
	Last sex	All	50+	13.8%

DHS = Demographic and Health Survey. HSRC = Human Sciences Research Council. NHCS = National HIV Communication Survey.

For the purpose of fitting the model to the data, we defined a simple binomial likelihood to represent the probability of generating the survey data given the model estimate of the 'true' rate of condom use. However, because the sample sizes were not published in many cases, and because most of the published rates of condom use did not include 95% confidence intervals, it was necessary to approximate the likelihood by assuming an effective sample size of 50 for each year in the age group (for example, an effective sample size of 250 for a 5-year age group). This is based roughly on the sample size in the DHSs and a design effect of 1.63 (i.e. taking into account that due to variation across clusters, the effective sample size is smaller than the actual sample size). The likelihood was maximized using the Nelder-Mead simplex method [16].

The resulting estimates of the model parameters are summarized in Table S3. Although previous versions of Thembisa made provision for significant 'risk compensation' in recent years, this updated analysis suggests that in fact there has been no reduction in condom use in recent years ($k_2 = 0.016$).

Table S3: Maximum likelihood estimates of condom use parameters

Parameter	Symbol	Value
Self-reported condom use at last sex in unmarried women aged 20		
Initial rate in 1985	k_0	0.039
Increase in rate due to BCC and condom distribution	k_1	0.597
Change in condom use in recent years	k_2	0.016
Relative rate of condom use per year increase in age	ν	0.980
Relative rate of condom use in marital relationships	β_1	0.391
Relative rate of reporting for contraceptive purposes	θ_1	0.343
Median time to behaviour change (in years after 1985)	m_1	15.9
Shape parameter for time to behaviour change	ϕ_1	6.26

BCC = behaviour change communication.

Figure S1 shows the extent of the consistency between the model predictions and the survey estimates of condom use. As an example of model calibration in a specific sub-population, Figure S2 further shows the time trend in condom use, for women aged 15-24, and the difference in condom usage when comparing reporting of condom use at last sex with reporting of condom use for contraceptive purposes. (We focus on this age group as it is relatively homogeneous, with relatively few women married and relatively few women diagnosed positive.) The model suggests a substantial increase in condom use in the late 1990s and early 2000s, consistent with the introduction of major HIV communication programmes in South Africa [17] and increases in numbers of male condoms distributed [18]. The trend is also consistent with reporting of condom use at sexual debut, which increased from around 10% in those reporting sexual debut before 1995 to around 60-70% in those reporting sexual debut after 2005 [13].

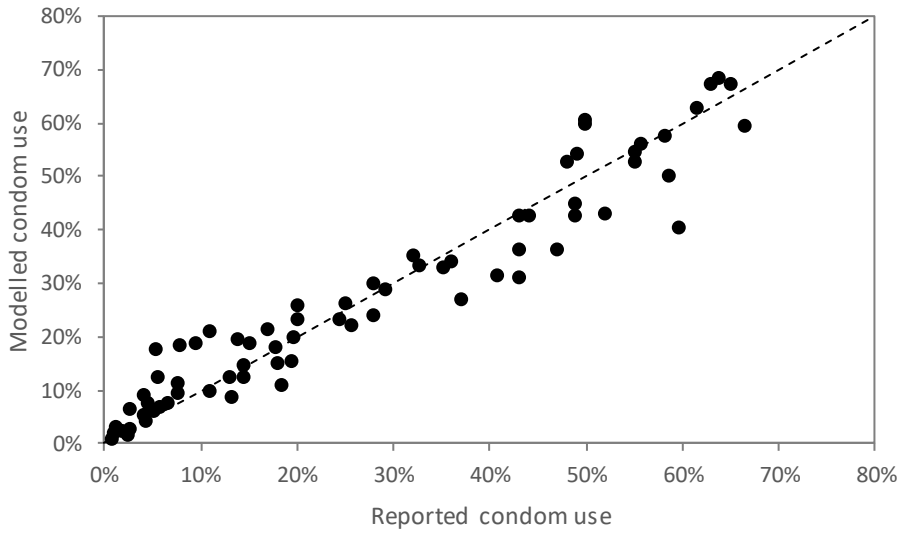

Figure S1: Comparison of model and survey estimates of condom use

Each dot represents one of the 71 data points used in model calibration. The dashed line represents the line of equality between the model and survey estimates.

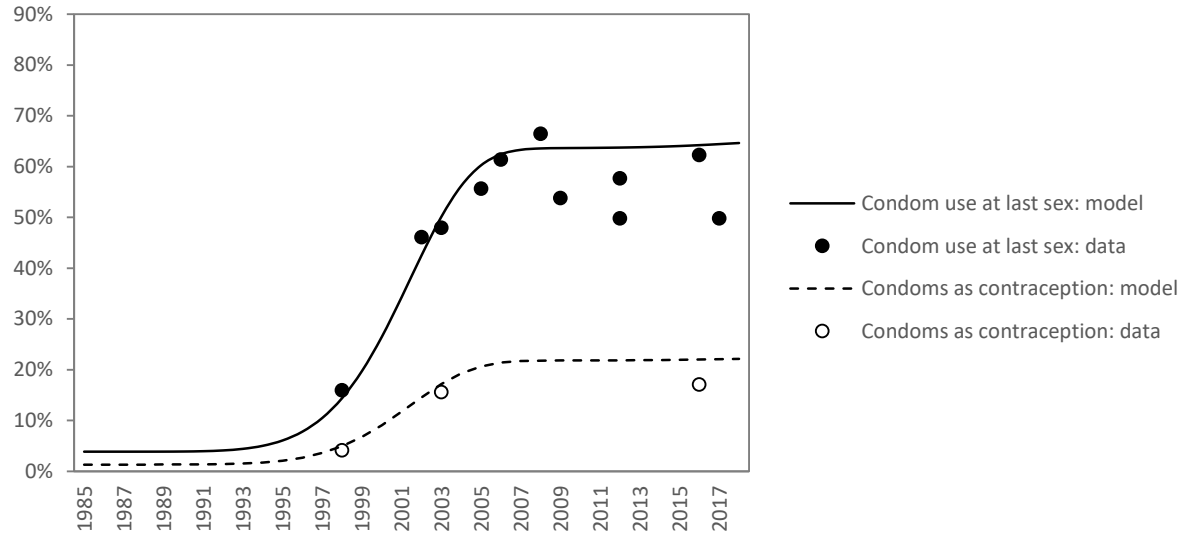

Figure S2: Condom use in women aged 15-24

For the sake of comparison, model estimates are shown for women aged 20 who are unmarried and not diagnosed positive (at this age relatively few women are married and few have been diagnosed HIV-positive). Survey estimates combine data for the 15-19 and 20-24 age groups, although these are in many cases entered as separate data points for calibration purposes.

When calibrating the Thembisa model to adult HIV prevalence data and mortality data, we allow for uncertainty regarding the extent of the bias in the self-reported condom use data. We assume that the true rate of condom use is somewhere between the reported rate of condom use at last sex (θ_0) and reported rate of condom use for contraceptive purposes (θ_1). If r represents the extent of the bias in the self-reported condom use at last sex, then the 'true' condom adjustment factor is $\theta = \theta_0(1 - r) + \theta_1 r$, where r lies in the range (0, 1). We assign a uniform (0,1) distribution to represent the uncertainty in r.

2.2.2 Condom use in men (excluding commercial sex)

To ensure that male and female assumptions are consistent, the probability that an HIV-negative man uses a condom in a marital or non-marital relationship is calculated as

$$\gamma_{1,l}(x,t) = \sum_{y} f_{1,l}(y \mid x)\gamma_{2,l}(y,t), \qquad (4)$$

where $f_{1,l}(y \mid x)$ is the probability that a female partner is aged y, if the male partner is aged x. It is assumed that the rate of condom use in same-sex relationships is the same as that in heterosexual relationships [19-21]. The effect of HIV diagnosis and ART initiation on condom use is the same as assumed in women.

2.2.3 Condom use in sex worker-client relationships

We define $\gamma_{2,2}(x,t)$ as the probability that an HIV-negative sex worker aged x uses a condom in an act of sex with a client at time t (time is measured in years since 1985). This is modelled as

$$\log\left(\frac{\gamma_{2,2}(x,t)}{1-\gamma_{2,2}(x,t)}\right)=\log\left(\frac{\gamma_{2,0}(20,t)}{1-\gamma_{2,0}(20,t)}\right)+\log(\beta_2), \quad (5)$$

where β_2 is the ratio comparing the odds of condom use in HIV-negative sex workers to that in HIV-negative women aged 20 in non-marital relationships. (We choose to work on an odds ratio scale rather than a relative risk scale to avoid possible condom usage in excess of 100%.) Note that there is no dependence on x in the right-hand side of the equation, i.e. we are assuming the rate of condom use in sex workers is the same at all ages, due to lack of age-specific data on condom use in sex worker-client interactions. The effects of HIV diagnosis and ART initiation on condom use are the same as assumed previously (on a relative risk scale).

A challenge in estimating β_2 is that no nationally representative sex worker data are available. However, by comparing sex workers' reporting of condom use at last sex in different settings with that reported by women in the general population, we can approximate the average odds by which condom use increases in the context of commercial sex. Table S4 summarizes the available data on sex workers' self-reported condom use at last client contact (we have not included data in which the type of relationship is unspecified, as a substantial proportion of sex workers have regular partners). These rates have been adjusted (based on equation 3) to represent the rates that would be expected in HIV-negative sex workers, based on Thembisa estimates of the fraction of sex workers who are HIV-diagnosed and on ART (fourth column). The final column shows the study-specific odds ratio relating the adjusted condom use in HIV-negative sex workers to $\zeta(t)$. These odds ratios are highly variable between studies (range 1.5-50.7), reflecting heterogeneity across samples within South Africa. We have set β_2 to the median of these values, 7.9.

Table S4: Condom use by sex workers in contacts with clients

Study	Year	Reported condom use	HIV-negative condom use*	Condom use with short-term partners ($\zeta(t)$)	Odds ratio (β_2)
Peltzer *et al* [22]	2002†	85.7%	85.4%	42.5%	7.9
Richter *et al* [23]	2010	94.5%	93.9%	63.7%	8.8
SWEAT [24]	2012	95%	94.2%	63.7%	9.3
Delva *et al* [25]	2010	99%	98.9%	63.7%	50.7
UCSF, Anova, WRHI [26]	2013	76.4%	72.4%	63.8%	1.5
	2013	89.4%	87.6%	63.8%	4.0
	2013	84.5%	81.9%	63.8%	2.6
Median					7.9

* Corresponding to $\gamma_{2,2}(x,t)$, estimated from the reported rates using a formula similar to that in equation 3. † Date not specified – a date two years prior to publication has been assumed.

2.2.4 Effect of HIV diagnosis on condom use

Most evidence suggests that HIV testing does not significantly affect sexual behaviour or HIV incidence in individuals who receive negative test results [27-31], and our model therefore assumes no change in behaviour following an HIV-negative test result. However, studies from developing countries show that HIV-positive diagnoses usually lead to significant declines in unprotected sex. A meta-analysis of data from resource-limited settings, over the 1990-2010

period, estimated a significant increase in the odds of condom use after diagnosis (OR 3.24, 95% CI: 2.29-4.58) [31]. A more recent meta-analysis by Tiwari *et al* [32], which synthesized data from the 2010-2019 period, estimated a slightly more modest increase in condom use after diagnosis (OR 1.65, 95% CI: 1.36-1.99). Since the two meta-analyses cover separate studies, it is reasonable to pool the two odds ratios: using a random effects meta-analysis to combine these two results gives an odds ratio of 2.28 (95% CI: 1.17-4.41). This can alternatively be expressed as a reduction in the odds of unprotected sex after HIV diagnoses (OR 0.44, where 0.44 = 1/2.28), although in reality the relationship is not exactly inverse because some individuals may abstain from sex (in which cases they are counted as having reduced unprotected sex but not as having increased condom use).

A challenge is that our model is parameterized in terms of a percentage reduction in unprotected sex after HIV diagnosis. This is effectively a relative risk (RR) measure rather than an odds ratio (OR) measure. RRs will generally be closer to 1 than ORs, especially when the outcome of interest is highly prevalent. For example, if 75% of sex acts in undiagnosed HIV-positive women are unprotected (the current Thembisa estimate), the OR of 0.44 is equivalent to an RR of 0.76 ($(0.75 + (1 – 0.75)/0.44)^{-1}$), i.e. a 24% reduction in unprotected sex. This means that the 0.44 can be considered a lower bound on the RR parameter in our model.

Another reason why the OR of 0.44 might exaggerate the true effect of HIV diagnosis is that changes in risk behaviour soon after diagnosis might not be sustained over the longer term. Tiwari *et al* note that their meta-analysis relies mainly on short-term changes [32], but cite several examples of studies that have found some degree of increase in HIV risk behaviour over longer follow-up. As one example, a study in Tanzania found that the proportion of newly diagnosed individuals who reported recent unprotected sex dropped from around 45% prior to diagnosis to around 10% by 6 months after diagnosis, but at longer durations increased to around 15-20% [33]. Thus the proportionate reduction in unprotected sex at longer durations ($1 – 0.18/0.45 = 60\%$) was substantially less than that at early durations ($1 – 0.10/0.45 = 78\%$).

To represent the uncertainty around the reduction in unprotected sex after diagnosis, we assign a beta prior with a mean of 0.18 and a standard deviation of 0.15. This is equivalent to assuming an average relative rate of unprotected sex after HIV diagnosis of 0.82, with 95% confidence interval from 0.45-0.99, i.e. roughly consistent with the OR of 0.44 as the likely lower bound on the RR. The mean of 0.18 is consistent with the 24% relative risk reduction noted previously, adjusted by a multiple of 0.60/0.78 to take into account the partial reversion towards previous risk levels, as observed in the Tanzanian study [33].

2.2.5 Effect of ART on condom use

The *h* parameter has been set to 0.18. This is based on a meta-analysis [34], which found that in high-quality studies receipt of ART was associated with a significant reduction in unprotected sex (OR 0.68, 95% CI: 0.58-0.79). (Low-quality studies were excluded, as these tend not to control for time since diagnosis and thus tend to conflate the effects of HIV diagnosis and ART on levels of condom usage.) As in the previous section, it is important to consider that the OR is likely to be different from the RR, which is what we require to parameterize Thembisa. If the prevalence of unprotected sex is 45% in South African ART patients [35], then the OR of 0.68 implies an RR of 0.82 ($0.45 \times (1 + 0.68(1/0.45 – 1))$). We have therefore set the *h* parameter to 0.18 ($1 – 0.82$) rather than 0.32 ($1 – 0.68$).

2.3 Model of trends in marriage and divorce

In previous versions of Thembisa, marriage rates were specified by age and sex, and were fixed over time. The rates were the same as those estimated previously in the STI-HIV Interaction model, which were set such that the modelled proportion of the population married, by sex and 5-year age group, was similar to that in the 1996 and 2001 censuses and the 2007 Community Survey [36]. The rates were also constrained such that the number of new marriages in each year had to be the same for males and females. Rates of divorce were set to be two times the age-specific divorce rates estimated in 2004 [37], with the multiple of two being assumed because our definition of marriage includes cohabiting partnerships (which dissolve at a higher rate than formal marriages [38], but which are not reflected in official divorce statistics) and because the reporting of divorce is incomplete [39]. Individuals who were widowed or divorced were assumed to have the same rate of (re)marriage as individuals of the same age who had never been married.

This previous modelling approach has a number of obvious limitations. It does not take into account that there have been major declines in marriage rates in South Africa in recent decades [40-42]. It also does not account for the possibility that divorce rates may be changing, although evidence of such changes is inconsistent [43], and the assumption of a 2-fold difference between the true rates of union dissolution and those reported by Statistics South Africa is arbitrary. Rates of remarriage following divorce/widowhood are also high in many African settings, particularly in the first year or two after union dissolution [44], and it may therefore be unrealistic to assume that widowed/divorced individuals have the same rate of entry into marriage as people of the same age and sex who have never been married. Finally, the constraint that the number of men entering marriage must equal the number of women entering marriage was imposed without regard to polygyny. Although polygyny is uncommon in South Africa [45], it could account for the finding that there are more women than men who report being in marital/cohabiting relationships, both in the 2011 census and the 2016 Community Survey.

Here we attempt to address these limitations by developing a more flexible parametric model of marriage and divorce rates, and fitting the model to South African marriage data, using a Bayesian approach. In the sections that follow we first describe the parametric model, then describe the prior distributions that are assigned to represent the uncertainty in the key parameters, then describe the data to which the model is fitted and the model fitting procedure, and finally present the posterior estimates.

2.3.1 Model of divorce and marriage

We model the time to first marriage using a log-logistic distribution, which has the advantage that it allows a non-monotone hazard function [46], consistent with patterns of marriage rates in many settings [47]. It also has the advantage that the hazard rates in different birth cohorts differ more substantially at younger ages than at older ages, again consistent with empirical observations [47]. This is a common property of accelerated failure time models, which differ from proportional hazards models that assume hazard rates in different cohorts differ by a constant proportion.

For an individual of sex g who was born at time t (in years after 1985), the probability that they have never been married at exact age x is

$$S_g(x,t) = \frac{1}{1+\left(\left(x-a_g\right)\exp\left(-C_g - B_g t\right)\right)^{1/\gamma_g}}, \qquad (6)$$

for $x > a_g$. Here we use the same log-logistic parameterization as in STATA, with γ_g representing the shape parameter and C_g representing the scale parameter. The a_g parameter has been included to prevent marriage from occurring at very young ages, i.e. we set $S_g(x, t) = 1$ for $x \leq a_g$. The β_g parameter represents the effect of the individual's birth cohort on their rate of entry into marriage; positive values imply a trend towards later marriage in more recent birth cohorts.

The probability that an individual of sex g, currently aged x and born in year t, who has never been married, enters into marriage in the next 12 months is

$$p_g(x,t) = 1 - \frac{S_g(x+1,t)}{S_g(x,t)}.$$

The probability that a married individual, of sex g and age x in year τ, gets divorced in the next year is

$$D_g(x,t) = 1 - \exp\left(-Kd_g(x)G^{\tau-2004}\right),$$

where $d_g(x)$ is the empirically-estimated rate of divorce in 2004, K is a constant that represents the ratio of the true rate of union dissolution to the recorded rate of divorce in 2004, and G is the factor by which rates of union dissolution decrease per year.

In the Thembisa model married individuals are stratified according to both their own risk group (high/low) and their partner's risk group, which is important when calculating widowhood due to AIDS mortality. For a married individual of sex g, aged x and in risk group i, with a spouse in risk group j, the probability of widowhood due to AIDS in year τ is

$$\sum_y f_g(y \mid x) A_{g',j,i}(y,\tau)$$

where $f_g(y \mid x)$ is the assumed probability that the spouse of an individual of sex g aged x is aged y, and $A_{g',j,i}(y, \tau)$ is the probability of AIDS mortality in year τ for an individual aged y and in risk group j, who is married to a partner of sex g in risk group i (g' represents the sex opposite to g). The proportions of married partners in different age groups are estimated from the 1998 DHS [5], and rates of AIDS mortality in married partners are estimated directly in the Thembisa model. Similarly the probability of widowhood due to non-AIDS mortality is calculated as

$$\sum_y f_g(y \mid x) q_{g'}(y,\tau)$$

where $q_{g'}(y, \tau)$ is the assumed probability of non-AIDS mortality in year τ for an individual aged y and of sex g'. The net probability of divorce or widowhood in year τ is then calculated as

$$W_{g,i,j}(x,\tau) = 1 - (1 - D_g(x,\tau))(1 - \sum_y f_g(y \mid x) A_{g',j,i}(y,\tau))(1 - \sum_y f_g(y \mid x) q_{g'}(y,\tau)).$$

We assume that the age-specific rates of remarriage in divorced/widowed individuals, in the year *after* divorce/widowhood, are the same as those in never-married individuals, but we allow for a different probability in the year of divorce/widowhood, on the assumption that any excess rate of marriage in widowed/divorced individuals will be concentrated in the period soon after divorce/widowhood [44]. We define R_g to be the ratio of the odds of remarriage in the year of divorce/widowhood to the odds of getting married in individuals of the same age who have never been married, for sex g. Then the probability that an individual who was married at the start of year τ remains married 12 months later, after taking into account the possibility of remarriage, is

$$1 - W_{g,i,j}(x,\tau) + W_{g,i,j}(x,\tau) \frac{R_g p_g(x,t)}{R_g p_g(x,t) + 1 - p_g(x,t)}.$$

2.3.2 Prior distributions

For the purpose of setting prior distributions for the parameters that determine the rate of first marriage, we fit log-logistic survival models to 2016 DHS data on age at first entry into a union [14]. We censor individuals who have never married at their current age, and exclude individuals who report an age at first marriage younger than 15, or who report an age at first marriage younger than their reported age at sexual debut (on the assumption that such cases reflect reporting errors). The model fitted is of the same form as in equation (6), with a_g fixed to 15 years. The model is fitted separately for males and females, using the 'streg' command for parametric survival modelling in STATA 15.0.

Table S5 summarizes the results of these regression models. The male analysis was based on 1273 reported ages at marriage among 3379 men, after excluding 104 men who reported an age at marriage before their age at sexual debut, and a further 4 men who reported their age at marriage was younger than 15. The female analysis was based on 2893 reported ages at marriage among 7656 women, after excluding 535 women who reported an age at marriage younger than their age at sexual debut and a further 19 women who reported their age at first marriage was before 15. In both men and women there is strong evidence of a trend towards later marriage in more recent birth cohorts.

Table S5: Log-logistic model fits to age at first marriage

	Males	Females
Constant scale parameter (C_g)	3.01 (2.96-3.06)	2.90 (2.87-2.94)
Effect of birth cohort (β_g)	0.007 (0.004-0.011)	0.005 (0.001-0.009)
Shape parameter (γ_g)	0.46 (0.44-0.48)	0.59 (0.58-0.61)

95% confidence intervals around model parameters are shown in brackets.

The 95% confidence intervals around the scale and shape parameters are narrow, and one might be tempted to fix these parameters for the purpose of our model calibration. However, retrospective reporting on age at marriage is generally considered to be unreliable, with potential for significant recall bias and a tendency (especially in older women) not to report on

earlier unsuccessful unions [44, 47], which makes it important to allow for uncertainty in these parameters. In setting prior distributions for our model parameters we therefore use the same means as in Table S5 but assign larger standard deviations: 0.3 for the constant scale parameter, 0.005 for the effect of birth cohort and 0.1 for the shape parameter. We use normal distributions for the scale parameter and effect of birth cohort, and use gamma priors for the shape parameter (since the log-logistic shape parameter has to be positive).

Although the a_g parameter was fixed at 15 for the purpose of fitting the log-logistic model to the DHS data, this parameter is fixed at 16 in the Thembisa model.

The empirically-estimated rates of divorce were previously estimated by dividing the reported numbers of divorces at each age in 2004 [37] by the geometric average of the corresponding number of formally married individuals in the same age cohort in the 2001 census and 2007 Community Survey. This estimate of the divorce rate, $\delta_g(x)$, is shown in Table S6. However, we would expect the rate of union dissolution to be substantially higher in unmarried cohabiting partnerships than in marital unions; for example, Porter *et al* [38] found that Ugandan women who were in consensual unions (i.e. living with their partner but not formally married) had a rate of union dissolution 5.4 times that in married women. We therefore approximate the average rate of union dissolution at age x, in individuals of sex g, as

$$d_g(x) = \delta_g(x)(H_g(x)V + (1 - H_g(x))),$$

where $H_g(x)$ is the proportion of unions that are not formal marriages and V is the relative rate of union dissolution in individuals who are not formally married. We calculate $H_g(x)$ from the 2001 census and 2007 Community Survey (again averaging over the results to obtain an approximation for 2004), and set $V = 5$ [38]. The resulting estimates of $d_g(x)$ are shown in Table S6.

Table S6: Empirically estimated rates of union dissolution in 2004

	Divorce rates, $\delta_g(x)$		% of unions that are not formal marriages, $H_g(x)$		Rates of union dissolution, $d_g(x)$	
Age	Male	Female	Male	Female	Male	Female
15-19	0.0002	0.0034	32.9%	52.7%	0.0004	0.0104
20-24	0.0081	0.0098	51.8%	47.8%	0.0250	0.0287
25-29	0.0126	0.0120	41.9%	33.8%	0.0337	0.0282
30-34	0.0125	0.0118	30.1%	23.7%	0.0276	0.0229
35-39	0.0109	0.0093	22.3%	17.8%	0.0206	0.0159
40-44	0.0091	0.0080	16.9%	14.4%	0.0152	0.0126
45-49	0.0073	0.0057	13.4%	11.3%	0.0112	0.0083
50-54	0.0055	0.0039	11.4%	8.5%	0.0079	0.0052
55-59	0.0036	0.0025	8.9%	6.5%	0.0048	0.0032
60-64	0.0023	0.0014	7.6%	4.9%	0.0030	0.0017
65-69	0.0018	0.0009	6.0%	4.8%	0.0022	0.0011
70-74	0.0010	0.0003	4.8%	3.6%	0.0012	0.0004
75+	0.0008	0.0003	4.7%	3.2%	0.0009	0.0003

The K parameter represents the ratio of the true rate of union dissolution to the empirically-estimated rate in Table S6. To the extent that there is uncertainty around V, and to the extent that there is uncertainty around the proportion of divorces that are recorded, K may differ from

1. There are few other sources against which we can compare our $d_g(x)$ estimates. Clark and Brauner-Otto [43] estimated that the cumulative probability of divorce, by 15-19 years after entry into first marriage, was 0.202 in South African women, based on data from the 1998 DHS. Using our estimates of $d_g(x)$ in Table S6, the cumulative probability of divorce for a woman who marries at age 30 is 0.23 by 15 years and 0.25 by 19 years, which is only slightly higher than the 0.202 proportion estimated by Clark and Brauner-Otto. To represent the uncertainty around the K parameter, we assign a gamma prior distribution with a mean of 1 and standard deviation of 0.3.

It is difficult to directly estimate trends in rates of divorce from South African data sources. Recorded numbers of divorces have not been published for the period before 2004, and in all of the household surveys and censuses after 2004, the question about marital status does not distinguish between traditional/customary marriages and civil/religious marriages. The distinction is important because traditional/customary marriages are unlikely to be registered and therefore should not be included in the denominator when calculating the divorce rate from civil registration. In the absence of comparable estimates of rates of union dissolution after 2004, it is difficult to assess temporal trends in divorce rates. Although there has been a slight decline in the annual numbers of divorces recorded over the 2004-2016 period, this has been accompanied by an increasing proportion of marital/cohabiting relationships that are not formal marriages – an increase that we might expect to be associated with rising average rates of union dissolution. Analyses of divorce trends in other African countries, based on DHS data, have produced inconsistent results; although trends towards declining divorce rates were observed in a number of countries, these analyses did not control for changes in the age at which marriage occurred, and thus the apparent declines in divorce rates could potentially be due to shifts towards later age at marriage [43]. In the absence of reliable empirical evidence, we represent the uncertainty around the G parameter by assigning a gamma prior with a mean of 1 and a standard deviation of 0.025, i.e. assuming that over the long term the average divorce rate is unlikely to increase or decrease by more than 5% per year on average.

The parameter R_g, the ratio of the odds of remarriage in the year of divorce/widowhood to the odds of getting married in individuals of the same age who have never been married, is also difficult to estimate empirically. However, we might reasonably expect that this ratio should be greater than 1. We therefore assign a uniform (0, 1) prior distribution to represent the uncertainty around the ratio $1/R_g$, i.e. the ratio of the annual odds of marriage in never-married individuals of sex g to the annual odds of marriage in recently divorced or widowed individuals. It is likely that the odds ratio differs for men and women, with widowed or divorced men having relatively more opportunities for remarriage, and we therefore set the prior separately for men and women.

Table S7 summarizes the prior distributions.

Table S7: Prior distributions for marriage and divorce parameters

Parameter	Symbol	Prior	Mean	Std dev
Log-logistic parameters for marriage				
Constant scale parameter: male	C_1	Normal (3.01, 0.30)	3.01	0.30
Constant scale parameter: female	C_2	Normal (2.90, 0.30)	2.90	0.30
Birth cohort effect: male	β_1	Normal (0.007, 0.005)	0.007	0.003
Birth cohort effect: female	β_2	Normal (0.005, 0.005)	0.005	0.003
Shape parameter: male	γ_1	Gamma (21.1, 46.0)	0.46	0.10
Shape parameter: female	γ_2	Gamma (34.8, 59.0)	0.59	0.10
Union dissolution parameters				
Adjustment to empirical estimates	K	Gamma (4.0, 4.0)	1.00	0.50
Annual change in divorce rates	G	Gamma (1600, 1600)	1.00	0.025
Remarriage parameters				
Ratio: male odds of first marriage to odds of remarriage, per year	$1/R_0$	Uniform (0, 1)	0.50	0.29
Ratio: female odds of first marriage to odds of remarriage, per year	$1/R_1$	Uniform (0, 1)	0.50	0.29

2.3.3 Likelihood function

We calibrate the model to data on the proportion of adults who are married in four national censuses/community surveys (the community surveys are less complete versions of the census, but are substantially larger than most national household surveys):

- The 1996 census
- The 2001 census
- The 2007 community survey
- The 2016 community survey

Although it would have been desirable to include the 2011 census, there appear to be problems with the reporting of marriage in the 2011 census, with the reporting of marriage by young adults being substantially higher than in previous censuses/surveys, and out of line with general trends.

Let $M_g(x, t)$ be the model estimate of the fraction of the population of sex g, aged x to $x + 4$ in year t, who are married, and let $y_g(x, t)$ be the corresponding census/survey estimate. For the purpose of defining the likelihood function, we assume that the difference between $M_g(x, t)$ and $y_g(x, t)$ is normally distributed with zero mean and variance σ^2. This then means that the log likelihood is calculated as

$$l = \sum_g \sum_x \sum_t -0.5\left[\log\left(2\pi\sigma^2\right) + \left(\frac{M_g(x,t) - y_g(x,t)}{\sigma}\right)^2\right].$$

The σ^2 parameter has been set to 0.0015, the average of the squared difference obtained when we previously fitted the STI-HIV Interaction model to the 1996-2007 data sets [36] (equivalently, $\sigma = 0.038$). Although a logit or probit transformation of the $M_g(x, t)$ and $y_g(x, t)$ variables might be considered preferable in defining the likelihood, this would make the calibration very sensitive to the measured proportion married in the 15-19 age group, where

the proportion married is low, and this is likely to be inappropriate given the uncertain reliability of reporting of marital status in this age group.

2.3.4 Posterior estimates

We obtain posterior estimates of the model parameters numerically, using Incremental Mixture Importance Sampling (IMIS) [48]. Table S8 compares the prior and posterior distributions for the 10 parameters. The most striking difference is in the effect of birth cohort, which is much greater in the posterior analysis than in the analysis of the 2016 DHS data (which informed the prior means), despite the high degree of precision with which the birth cohort effect was estimated in the DHS analysis. The constant scale parameters and shape parameters, however, are not substantially different from the values estimated in the DHS analysis. The posterior analysis suggests rates of union dissolution are slightly higher than estimated in Table S6, although the difference is not statistically significant, and there is a significant trend towards reducing rates of union dissolution, counteracting the effect of reducing marriage rates. The posterior ratio of first marriage to remarriage, when controlling for age, is substantially lower in men than in women, confirming that men have a much higher rate of remarriage after a union dissolution than women do.

Table S8: Comparison of prior and posterior distributions

Parameter	Prior (mean, 95% CI)	Posterior (mean, 95% CI)
Log-logistic parameters for marriage		
Constant scale parameter: male	3.01 (2.42-3.60)	2.98 (2.89-3.07)
Constant scale parameter: female	2.90 (2.31-3.49)	2.63 (2.52-2.72)
Birth cohort effect: male	0.007 (-0.003-0.017)	0.017 (0.012-0.021)
Birth cohort effect: female	0.005 (-0.005-0.015)	0.020 (0.015-0.025)
Shape parameter: male	0.46 (0.29-0.68)	0.50 (0.44-0.57)
Shape parameter: female	0.59 (0.41-0.80)	0.66 (0.60-0.72)
Union dissolution parameters		
Adjustment to empirical estimates	1.00 (0.27-2.19)	1.39 (0.91-1.96)
Annual change in divorce rates	1.000 (0.952-1.050)	0.989 (0.979-0.999)
Remarriage parameters		
Ratio: male odds of first marriage to odds of remarriage, per year	0.500 (0.025-0.975)	0.039 (0.025-0.057)
Ratio: female odds of first marriage to odds of remarriage, per year	0.500 (0.025-0.975)	0.742 (0.419-0.971)

Figure S3 shows the model fit to the data. Although the model fits the data well in some years, there are some years in which the model fails to fit the data well in certain age groups. In men, the model slightly under-estimates the married proportions at ages 75 and older in 1996, but the model slightly over-estimates the married proportions at ages 50-74 in 2016. In women, the model over-estimates the married proportion at ages 60 and older in both 2001 and 2007, but under-estimates the married proportion at ages 80 and older in 2016. It would be difficult for any model to provide a substantially better fit to the data, as the data are in some cases quite anomalous. For example, the data suggest the married proportions in women aged 60 and older are substantially higher in 1996 and 2016 than in 2001 and 2007, and there is no clear explanation for these inconsistent trends (decreasing between 1996 and 2001 then increasing between 2007 and 2016). It is likely that this reflects data quality problems rather than real

changes in union formation/dissolution in older women. The standard deviation of the differences between the model estimates and the census/survey estimates is 0.039, close to the value of 0.038 specified in the calculation of the likelihood. The 0.038 standard deviation is that obtained previously when manually fitting a model with many more degrees of freedom than the one considered here, to data from the 1996-2007 datasets [36].

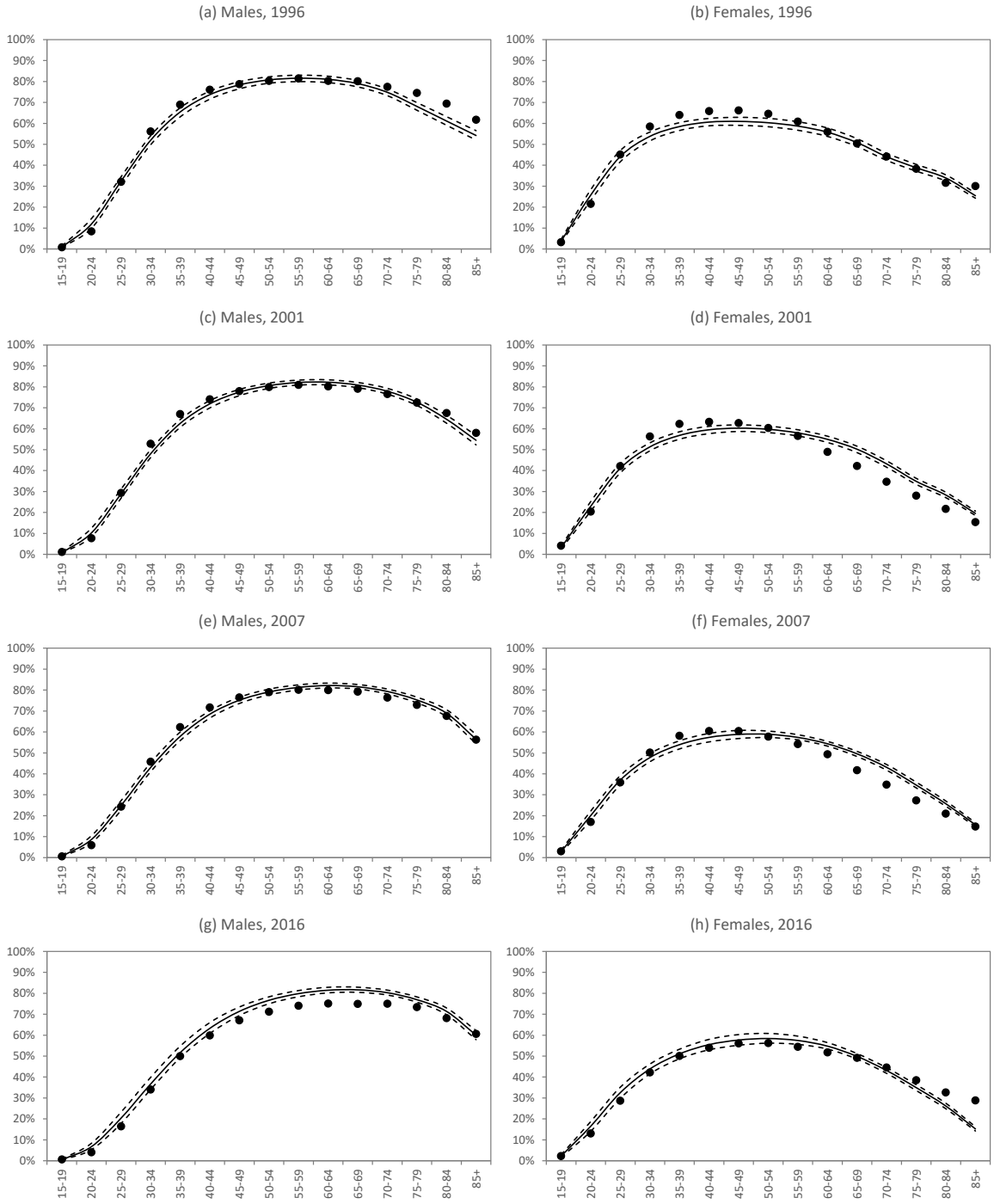

Figure S3: Proportion of adults who are married or in cohabiting relationships

Dots represent data from the censuses and community surveys. Solid lines represent model estimates (means of the posterior distributions) and dashed lines represent 95% credible intervals (2.5 and 97.5 percentiles of the posterior distributions).

In subsequent sections we fix the marriage and divorce parameters at the posterior means shown in Table S8, i.e. we ignore the uncertainty around the marriage and divorce parameters for the purpose of estimating trends in HIV incidence.

2.4 Prior distributions

Table S9 summarizes the prior distributions for the parameters that were allowed to vary in the model calibration process. The table also includes references to the section of the supplementary material that provide a more detailed explanation of the parameter and the data sources on which the prior distribution is based. We have chosen gamma prior distributions to represent the uncertainty around the parameters that are defined on the range $[0, \infty)$ and beta or uniform prior distributions for parameters that are defined on the range $[0, 1]$.

Table S9: Prior distributions for model parameters

Parameter	Prior distribution	Prior mean, std deviation	Ref.
RR of ST partner acquisition in low-risk single males*	Uniform (0, 1)	0.50, 0.29	2.4.1
RR of ST partner acquisition in low-risk single females*	Uniform (0, 1)	0.50, 0.29	2.4.1
RR of ST partner acquisition in high-risk married males*	Beta (4.44, 13.31)	0.25, 0.10	2.4.1
RR of ST partner acquisition in high-risk married females*	Beta (4.44, 13.31)	0.25, 0.10	2.4.1
Gamma density of relative rates of ST partnership formation by age, in unmarried females			
Mean	Gamma (89.1, 2.30)	38.7, 4.1	2.4.1
Standard deviation	Gamma (47.5, 2.46)	19.3, 2.8	2.4.1
Sexual mixing parameter	Beta (8.64, 7.66)	0.53, 0.12	2.4.1
Bias in reported condom use at last sex	Uniform (0, 1)	0.50, 0.29	2.2.1
Reduction in unprotected sex after HIV diagnosis	Beta (1.00, 4.56)	0.18, 0.15	2.2.4
Average survival in absence of ART (years)	Gamma (144, 12.0)	12, 1	2.4.2
RR of HIV disease progression in women	Gamma (369, 384)	0.96, 0.05	2.4.2
Increase in HIV disease progression per 10-year increase in age	Gamma (9.00, 50.0)	0.18, 0.06	2.4.2
Reduction in mortality† per unit increase in rate of ART initiation (at CD4<200) over last 3 years	Gamma (4.59, 0.612)	7.5, 3.5	2.4.3
Female-to-male transmission probability in short-term/ non-spousal partnerships	Beta (7.05, 874)	0.008, 0.003	2.4.4
Male-to-female transmission probability in short-term/ non-spousal partnerships	Beta (5.68, 468)	0.012, 0.005	2.4.4
Male-to-male transmission probability in short-term/ non-spousal partnerships	Beta (15.66, 767.3)	0.020, 0.005	2.4.4
Client-to-female sex worker transmission probability	Beta (4.00, 3991)	0.001, 0.0005	2.4.4
Relative risk of transmission per sex act in long-term partnerships (relative to short-term partnerships)	Beta (3.00, 12.0)	0.20, 0.10	2.4.4
Odds of viral suppression relative to that in IeDEA-SA	Gamma (109.6, 133.7)	0.819, 0.078	2.4.5
RR HIV+ fertility before diagnosis/immune decline	Gamma (100, 76.9)	1.30, 0.13	2.4.6
Initial HIV prevalence in high-risk women, ages 15-49	Uniform (0, 0.002)	0.001, 0.00058	2.4.7

* Relative to high-risk unmarried individuals of the same sex. † On a natural log scale. IeDEA-SA = International epidemiology Databases to Evaluate AIDS, Southern Africa. RR = relative rate. ST = short-term.

2.4.1 Rates of short-term partnership formation

We define $c_{g,i,l}(x)$ to be the annual rate of short-term (non-marital) partnership formation in individuals aged *x*, of sex *g* and marital status *l*, who are in risk group *i*. The female rates of partnership formation at different ages are modelled using a scaled gamma density of the form

$$c_{2,i,l}(x) = c_{2,i,l}(20)\frac{\lambda^{\alpha}(x-10)^{\alpha-1}\exp(-\lambda(x-10))}{\lambda^{\alpha}10^{\alpha-1}\exp(-10\lambda)},$$

where the λ and α parameters determine the mean and variance of the gamma distribution, and the offset of 10 years is included to prevent sexual activity below age 10. The $c_{2,i,l}(20)$ value is 3.3 for women in the high risk group (i = 1) who are unmarried (l = 0), based on previous modelling of rates of partnership formation in South Africa [36]. The mean and standard deviation of the gamma density are uncertain; in Thembisa version 4.2, different posterior estimates were obtained for each of the 9 provinces. The average of the gamma means was 38.7 years (standard deviation 4.1 years), and the average of the gamma standard deviations was 19.3 years (standard deviation 2.8 years) [49]. We have therefore represented the uncertainty regarding the gamma mean and standard deviation using gamma prior distributions, with means and standard deviations equal to those estimated from the previous provincial fits. For each sampled value of the gamma mean and standard deviation, λ and α parameters are calculated to be consistent with these values.

For single (unmarried) individuals in the low risk group, the rate of non-marital partnership is assumed to be

$$c_{g,2,0}(x) = L_g c_{g,1,0}(x),$$

where L_g is the ratio of the rate of non-marital partnership formation in the low risk group to that in the high-risk group. Because the low risk group is defined to consist of individuals who do not engage in concurrent partnerships, it might be expected that the rate of partnership formation would be lower in the low risk group than in the high-risk group. To represent the uncertainty in L_1 and L_2 we therefore assign uniform (0, 1) prior distributions for both parameters.

For married individuals in the high-risk group, of sex g, the rate of non-marital partnership formation is assumed to be

$$c_{g,1,1}(x) = R_g c_{g,1,0}(x),$$

where R_g is the ratio of the rate of non-marital partnership formation in married high-risk individuals to that in unmarried high-risk individuals. Values of R_g have previously been estimated as 0.33 (95% CI: 0.10-0.70) for males and 0.14 (95% CI: 0.03-0.33) for females, based on fitting the STI-HIV Interaction model to South African sexual behaviour data and HIV prevalence data [50]. We have chosen a beta prior distribution, with a mean of 0.25 and a standard deviation of 0.10 to represent the uncertainty in both R_1 and R_2. This prior distribution has 2.5 and 97.5 percentiles of 0.08 and 0.47 respectively, thus including most of the posterior uncertainty that was previously estimated for these two parameters.

No non-marital partnership formation is modelled in married low-risk individuals, as the low-risk group would (by definition) not engage in concurrent partnerships. Male rates of non-marital relationship formation are calculated to be consistent with the assumed rates at which females form new non-marital partnerships. Further mathematical details are provided in Appendix A of the Thembisa report [1].

Mixing between the high- and low-risk groups is determined by a sexual mixing parameter, ε. This parameter takes on values between 0 and 1, 0 implying completely assortative sexual mixing (i.e. individuals only choose sexual partners from their own risk group), and 1 implying random sexual mixing (i.e. individuals have no preferences regarding the risk group of their partners and choose partners in proportion to their availability) [51]. The ε parameter is difficult to determine from empirical data, and we have therefore assigned a beta prior distribution to represent the uncertainty around this parameter. The mean and standard deviation of this prior distribution are 0.53 and 0.12 respectively, based on the distribution of values estimated when the model was previously fitted for each of the 9 provinces [49].

2.4.2 Disease progression and mortality in untreated HIV-positive adults

In untreated individuals, we define the symbol $\lambda_{g,s}(x)$ to be the annual rate of transition from HIV state *s* to state (*s* + 1) in untreated HIV-positive individuals of sex *g* (1 for males, 2 for females) who are aged *x*. This is calculated as

$$\lambda_{g,s}(x) = \lambda_s \varpi^{g-1} (1+k)^{(x-30)/10} E^{t-1999},$$

where λ_s is the rate that applies in men aged 30 in 1999, ϖ is the factor by which HIV disease progression is adjusted in women, *k* is the proportional increase in the rate of disease progression per 10-year increase in age, and *E* is the factor by which the rate is adjusted per year as a result of changes in HIV virulence. Similarly, we define the symbol $\mu_{g,s}(x)$ to be the annual HIV-related mortality rate in HIV state *s* in untreated individuals of sex *g* who are aged *x*. This is calculated as

$$\mu_{g,s}(x) = \mu_s \varpi^{g-1} (1+k)^{(x-30)/10},$$

where μ_s is the HIV mortality rate that applies in men aged 30. The adjustment factors for the effects of age and sex on HIV disease progression are thus the same as the adjustment factors for the corresponding effects on HIV-related mortality (except in respect of the HIV evolution parameter). HIV-positive women tend to have lower viral loads [52-54] and lower rates of CD4 decline [55] than HIV-positive men, and studies suggest a lower mortality rate in HIV-positive women than in HIV-positive men in the pre-ART era [54, 56-58]. To represent the uncertainty regarding the ϖ parameter, a gamma prior distribution has been assigned, with a mean of 0.96 and standard deviation of 0.05 [59].

Evidence suggests that increasing age is associated with both increasing rates of CD4 decline [60, 61] and increasing mortality in HIV-positive adults [62-65]. To represent the uncertainty around the *k* parameter, a gamma prior with a mean of 0.18 and standard deviation of 0.06 has been assigned [59]. A gamma prior has also been assigned to represent the uncertainty regarding the overall mean HIV survival time (mean 12 years, standard deviation 1 year), and this is used to determine λ_s and μ_s parameters (corresponding prior means are shown in Table S10) [59]. Assumptions about the relative lengths of time spent in different CD4 stages were determined by calibrating the model to cross-sectional surveys of CD4 distributions in HIV-positive adults [66-73], and assumptions about relative rates of mortality by CD4 stage were

based on the assumption of negligible HIV-specific mortality at CD4 counts >350 cells/μl and a mortality hazard ratio of 0.13 for individuals with CD4 counts of 200-349, when compared to individuals with CD4 counts <200 cells/μl [74].

HIV virulence may be changing as a result of HIV evolution. Although our original analysis estimated the value of E to be significantly less than one [59], a subsequent analysis found that after allowing more realistically for the effect of ART interruptions in the model, the E estimate was not significantly different from one [75]. We have therefore fixed $E = 1$ for the purpose of this analysis.

Table S10: Parameters by HIV disease stage

Parameter	Acute HIV	CD4 range 500+	350-499	200-349	<200	Source
Average time (in years) to next stage, in absence of ART* ($1/\lambda_s$)	0.25	3.16†	2.13†	3.20†	-	Calibrated
Annual HIV mortality rate, in absence of ART* (μ_s)	0.00	0.00	0.00	0.033†	0.254†	Calibrated
Relative infectiousness if untreated (I_s)	10	1	1	2	7	[76-78]
Annual male HIV mortality after ART initiation, by baseline CD4‡						
1st 6 months of ART	-	0.0002	0.0016	0.0146	0.2554	[79]
Months 7-18	-	0.0009	0.0050	0.0132	0.0613	
Months 19-30	-	0.0027	0.0085	0.0116	0.0306	
Months 31-42	-	0.0042	0.0076	0.0076	0.0202	
Months 43+	-	0.0049	0.0063	0.0063	0.0166	
Annual female HIV mortality after ART initiation, by baseline CD4‡						
1st 6 months of ART	-	0.0001	0.0016	0.0159	0.2072	[79]
Months 7-18	-	0.0008	0.0045	0.0101	0.0490	
Months 19-30	-	0.0020	0.0057	0.0057	0.0235	
Months 31-42	-	0.0027	0.0034	0.0034	0.0141	
Months 43+	-	0.0025	0.0025	0.0025	0.0103	

* Parameters are specified for 30-year old males, and adjustments for age and sex are made in the process of calibrating the model to reported death data. † Prior means corresponding to average untreated survival of 12 years. ‡ Parameters are adjusted to take into account age effects, and effects of increasing baseline CD4 counts over time.

2.4.3 ART mortality and treatment interruptions

HIV-related mortality after ART initiation is assumed to depend on age, sex, baseline CD4 category and time since ART initiation. The mortality rates specified in Table S10 relate to individuals who are aged 35, and these mortality rates are assumed to increase by factors of 1.12 and 1.09 per 10-year increase in age, in men and women respectively. For the most part these parameters have been determined from a model fitted to data from the IeDEA Southern Africa collaboration [79].

Within the group of patients starting ART at CD4 counts <200 cells/μl there is substantial heterogeneity in mortality depending on the exact baseline CD4 value. Although the model does not explicitly model variation in mortality rates by CD4 count below the 200 cells/μl cut-off, mortality rates are adjusted to take into account the rate of ART initiation, since high rates of ART initiation would imply that (a) most individuals starting ART at CD4 <200 cells/μl do so soon after their CD4 count falls below 200, and (b) most untreated individuals with CD4

<200 cells/μl have CD4 counts close to 200. We therefore calculate the theoretical minimum mortality rates that would be expected (both in untreated individuals with CD4 <200 and in treated individuals starting ART with CD4 <200) if ART was started soon after the CD4 count dropped below the 200 threshold. The difference between the mortality rate in Table S10 and the theoretical minimum is reduced by a factor of $\exp\left(-m\rho_g(t^-)\right)$ in year *t*, where $\rho_g(t^-)$ is the average rate of ART initiation in the 3 years prior to year *t*, in adults of sex *g* with CD4 <200 cells/μl, and *m* is a scaling factor. This scaled difference is added to the minimum mortality rate to determine the modelled mortality rate in year *t*. To represent the uncertainty regarding the *m* scaling parameter, a gamma prior has been assigned, with a mean of 7.5 and standard deviation of 3.5 [59]. The adjustments are made only to those ART-naïve adults with CD4 counts <200 cells/μl and those treated adults with baseline CD4 counts <200 cells/μl.

Individuals are assumed to interrupt ART and resume ART at a constant rate that is independent of their ART duration or baseline CD4 count. Based on an analysis of three South African studies of treatment interrupters [80-82], we estimate the average rate of treatment resumption after an interruption to be around 0.90 per year, with reasonable consistency across studies. However, there is considerable uncertainty around estimates of the annual rate of ART interruption in these studies (for more discussion see Appendix G of the Thembisa report [1]). We therefore allowed for uncertainty in this parameter when calibrating the Thembisa model to province-specific ART data, and obtained posterior estimates of the annual ART interruption rate between 0.12 (95% CI: 0.11-0.13) in Mpumalanga and 0.31 (95% CI: 0.27-0.34) in Gauteng [83]. The weighted average of the annual ART interruption rate (using as weights the total number of ART patients in each province) was 0.20. We have therefore fixed the annual rate of ART interruption in the national version of Thembisa at 0.20. The assumptions about ART interruption and resumption are used for the purpose of calculating the numbers of people currently on ART, by time since first ART initiation, but do not influence the calculation of mortality rates after ART initiation.

2.4.4 HIV transmission probabilities per sex act

The symbol $\beta_{g,l}$ represents the average HIV transmission probability, in a single act of unprotected sex, from an untreated HIV-positive individual of sex *g*, to an HIV-negative partner in relationship type *l*. (In the case of female-to-male transmission, the probability applies to uncircumcised men, and the transmission rate for circumcised men is assumed to be 60% lower [84].)

In the case of male-to-female transmission in non-marital relationships, studies in South Africa suggest extremely high transmission probabilities. Two studies have estimated transmission probabilities based on HIV prevalence in young women and young men, using women's self-reported number of past partners to determine what the transmission probability must have been in order to be consistent with observed prevalence levels. Pettifor *et al* [85] estimated that if the HIV prevalence among male partners was at the upper end of the confidence interval around male HIV prevalence among South African youth, the male-to-female transmission probability per sex act was between 0.02 and 0.06. However, this estimate did not take account of young women's likely under-reporting of the number of partners. Auvert *et al* [86] estimated that if young women under-reported their lifetime number of partners by 50% on average, the male-to-female transmission probability per partnership was 0.49. Applying the same method as Pettifor *et al* to convert this per-partnership transmission probability into a per-sex act

probability yields estimates of $\beta_{2,0}$ in the range 0.008-0.030. The assumption of 50% under-reporting is somewhat arbitrary and in our previous analysis of South African sexual behaviour data we estimated that unmarried women's odds of *reporting* multiple partners were only 16% (95% CI: 12-26%) of their true odds of having multiple partners [36]. We therefore consider the previously-published estimates of male-to-female transmission probabilities in young South African women to be likely over-estimates of the true transmission risk. To represent the uncertainty around the $\beta_{2,0}$ parameter, we assign a beta prior distribution with a mean of 0.012 and a standard deviation of 0.005, which has 2.5 and 97.5 percentiles of 0.004 and 0.024 respectively (i.e. slightly lower than the corresponding upper and lower limits estimated from Auvert *et al*).

In the case of female-to-male transmission in non-marital relationships, studies in Africa have suggested probabilities of 0.0128 [87] and 0.016 [88] per sex act. However, these are likely to be over-estimates, as they may be inflated by male acquisition of HIV infection through sex worker contact, which is often substantially under-reported [89]. To represent the uncertainty around the $\beta_{1,0}$ parameter, we assign a beta prior distribution with a mean of 0.008 and a standard deviation of 0.003. The mean of 0.008 is chosen to be below the empirical estimates because of the probable bias, but the standard deviation is chosen such that the 97.5 percentile of the distribution (0.015) is close to the empirical estimates.

Estimates of transmission probabilities in long-term relationships are typically substantially lower than those in short-term relationships. Gray *et al* [90] estimated that in cohabiting Ugandan couples the transmission probability per sex act was 0.0009 for male-to-female transmission and 0.0013 for female-to-male transmission. Allen *et al* [91] found higher transmission rates among cohabiting couples in Zambia: 0.0029 per sex act in the case of male-to-female transmission and 0.0035 per sex act in the case of female-to-male transmission. Thus estimates of transmission probabilities per sex act in cohabiting/marital relationships are typically around 0.002, substantially lower than our prior means for the transmission probabilities per sex act in short-term relationships (which are around 0.01). Rather than specify separate prior distributions for the $\beta_{1,1}$ and $\beta_{2,1}$ parameters, we assign a single prior to the parameter Ω, which represents the ratio of $\beta_{g,1}$ to $\beta_{g,0}$. Based on the previously reviewed estimates we assign a beta prior with a mean of 0.2 and a standard deviation of 0.1 to represent the uncertainty around Ω.

Estimates of transmission probabilities from clients to female sex workers are also relatively low when compared to those in short-term relationships, although there are relatively few estimates of client-to-sex worker transmission probabilities in African populations. In a study of Senegalese sex workers, Gilbert *et al* estimated that the average probability of HIV-1 transmission per act of sex with an infected client was between 0.00031 and 0.00056, depending on the approach to dealing with missing data on numbers of clients [92]. A similarly low probability of transmission per unprotected sex act with an infected client, 0.00063, was estimated in a cohort of Kenyan sex workers [93]. Data from a South African study of sex workers in KwaZulu-Natal (KZN) can also be used to estimate the probability of transmission per sex act. In this study, an HIV incidence rate of 14.7 per 100 person years was observed [94] in sex workers who reported an average of 23.3 sex acts with clients per week, of which 20.3 were protected [95]. HIV prevalence in truck driver clients was estimated to be 56% [96]. If β is the probability of transmission per act of unprotected sex, and condoms are assumed to reduce this transmission probability by 90% [97], we can crudely estimate the average weekly rate of HIV acquisition as

$$0.56 \times \beta \times (20.3 \times (1 - 0.9) + 3.0).$$

Setting this expression to 0.147/52 and solving for β yields a β estimate of 0.00100. However, the true HIV prevalence in clients is unknown, as truck driver clients might not be typical of clients generally. In a systematic review of HIV risk factors in sub-Saharan Africa, Chen *et al* [98] estimated an average HIV prevalence in sex worker clients of 35%. If the true prevalence in KZN sex worker clients were closer to this average, the estimate of β would be higher. To represent the uncertainty regarding β, we assign a beta prior with a mean of 0.001 (the same as the value from the estimated from the KZN study) and a standard deviation of 0.0005. This prior distribution has a 2.5 percentile of 0.0003 (consistent with the lowest estimate of Gilbert *et al*) and a 97.5 percentile of 0.0022 (a likely upper bound around the transmission probability in the KZN sex worker study).

The only published estimates of male-to-male transmission probabilities are from high-income settings [99-101], and as heterosexual transmission probabilities in developing countries tend to be higher than those in high-income settings [78], we have chosen a prior distribution for the South African setting with a mean higher than that observed (mean 0.020, standard deviation 0.005). The model does not distinguish transmission probabilities according to the type of sex act.

2.4.5 Effect of HIV disease stage and ART on transmission

Table S10 shows how relative levels of HIV infectiousness are assumed to differ by CD4 count in untreated adults. Although we do not express these assumptions in terms of differences in viral load between CD4 stages, we do make assumptions about viral load distributions and HIV infectiousness as a function of viral load for the purpose of calculating average levels of infectiousness after ART initiation. Suppose that random variable $X_{a,s}$ is the difference between the maximum viral load and the actual viral load, on the logarithmic scale, in individuals with ART status a (0 = untreated, 1 = treated) and CD4 stage s (in untreated individuals, s refers to the current CD4 stage, while in treated individuals s refers to the CD4 stage at the time of ART initiation). The maximum viral load is set to 6 on the $\log_{10}$ scale (although higher values are possible, these have little effect on the HIV transmission dynamics in which we are interested). Variable $X_{a,s}$ is assumed to be Weibull-distributed, with parameters $\omega_{a,s}$ and ϕ. The probability of viral suppression (a viral load of less than 400 copies/ml) in treated individuals is thus

$$\exp\left(-\omega_{1,s}(6 - \log 400)^{\phi}\right),$$

from which it follows that if $V_s(t)$ is the probability of viral suppression in year t, at a threshold of <400 copies/ml, then

$$\omega_{1,s} = \frac{-\ln(V_s(t))}{(6 - \log 400)^{\phi}}. \qquad (7)$$

In fitting Weibull distributions to viral load data from both treated [69, 72] and ART-naïve South Africans [102], we have found that a ϕ parameter of 1.5 produces reasonable fits. For a given level of viral suppression, $V_5(t)$, it is then possible to calculate $\omega_{1,5}$. For example, if the rate of viral suppression in patients starting ART with CD4 <200 cells/μl is set to 0.77,

substituting $V_5(t) = 0.77$ into equation (7) yields a $\omega_{1,5}$ estimate of 0.042. For ART-naïve patients, a different approach is adopted in estimating $\omega_{a,s}$. Based on fitting the Weibull model to the median and inter-quartile range of viral loads prior to ART initiation in South Africans who almost all had CD4 counts of <200 cells/μl [102], we estimate the $\omega_{0,5}$ parameter to be 0.635.

The $V_5(t)$ parameters have been estimated from reported levels of viral suppression, allowing for a change in the rate of viral suppression over time; a more detailed explanation of the data sources and assumptions is provided in Appendix F of the Thembisa report [1]. Very briefly, estimates of viral suppression are derived from IeDEA-SA data over 2005-2019 [103], allowing for uncertainty in the representativeness of the IeDEA-SA data and the extent of the bias due to missing viral load data. For the purpose of the calibration of Thembisa, we specify a parameter to represent the ratio of the 'true' (unobserved) odds of viral suppression nationally to the odds of viral suppression measured in IeDEA-SA cohorts (the model input up to 2019). To represent the uncertainty around this odds ratio we assign a gamma prior with a mean of 0.819 and standard deviation 0.078 (the 2.5 and 97.5 percentiles of this distribution are 0.67 and 0.98 respectively, i.e. we allow for substantial uncertainty regarding the bias in the IeDEA-SA data).

We assume that if x is the difference between the maximum viral load and the actual viral load (on the logarithmic scale), the HIV transmission risk per act of sex is

$$c\exp\left(-\theta x^{\phi}\right),$$

where c is the maximum HIV transmission risk (when $x = 0$) and parameter θ determines the extent of the association between viral load and HIV transmission risk. Including $\phi > 1$ in the above equation ensures that the effect of viral load is less substantial at higher viral load levels than at lower viral load levels [104]. For reasons of mathematical convenience, explained below, we use the same value of $\phi = 1.5$ as estimated in the model of viral load distributions. The θ parameter is estimated by noting that if the factor by which infectiousness increases, per unit increase in viral load, is of the order of 2.5 [53, 105, 106], this implies that

$$\frac{-\frac{d}{dx}\left[c\exp\left(-\theta x^{\phi}\right)\right]}{c\exp\left(-\theta x^{\phi}\right)} = \ln(2.5).$$

From this it follows that $\theta\phi x^{\phi-1} = \ln(2.5)$. Substituting $\phi = 1.5$ and $x = 2$ [53, 105] yields $\theta = 0.432$. The average HIV transmission probability, for patients with ART status a and CD4 stage s, is then

$$\int_0^{\infty} \omega_{a,s}\phi x^{\phi-1}\exp\left(-\omega_{a,s}x^{\phi}\right)c\exp\left(-\theta x^{\phi}\right)dx = c\int_0^{\infty}\omega_{a,s}\phi x^{\phi-1}\exp\left(-\left(\theta+\omega_{a,s}\right)x^{\phi}\right)dx$$
$$= \frac{c\omega_{a,s}}{\omega_{a,s}+\theta}. \qquad (8)$$

The advantage of using the same value of $\phi = 1.5$ in the modelled relationship between viral load and HIV transmission risk is thus that it ensures a simple mathematical expression for the

average probability of HIV transmission. From equation (8), the ratio of the infectiousness after ART initiation to that prior to ART initiation is

$$R_s = \frac{\omega_{1,s}}{\omega_{1,s} + \theta} \Big/ \frac{\omega_{0,s}}{\omega_{0,s} + \theta} . \qquad (9)$$

Substituting the values of $\omega_{1,5} = 0.042$ and $\omega_{0,5} = 0.635$ into this equation, for example, yields an R_5 estimate of 0.149. This is somewhat higher than the relative risk estimates of 0.04-0.08 estimated from randomized controlled trials [77, 107], but lower than the relative risk of 0.36 estimated in a meta-analysis of observational studies [108]. It is important to note, however, that the value of R_s changes over time, as the $\omega_{1,s}$ parameter in the numerator changes as the rate of viral suppression changes.

Patients who start ART at higher CD4 counts (>200 cells/μl) have lower rates of virological failure after ART initiation [109]. Based on IeDEA-SA data [110], we assume that the odds of viral suppression in the CD4 200-349, 350-499 and ≥500 categories are 1.49, 1.73 and 1.92 times those in the <200 category respectively; these assumptions determine the $\omega_{1,s}$ values, for given values of $V_5(t)$. In untreated patients with CD4 >200 cells/μl, we assume average viral load levels decrease by 0.16 for each 100-cell increase in the CD4 cell count [66] (which determines the $\omega_{0,s}$ values). Reductions in infectivity in patients who start ART at CD4 counts >200 cells/μl are then calculated from equation (9).

Individuals who have interrupted ART are assumed to be as infectious as individuals with the same CD4 count who are ART-naïve, as viral loads return to pre-treatment levels fairly rapidly after people interrupt treatment.

2.4.6 Relative rates of fertility in HIV-positive women

Assumptions about differences in fertility by HIV disease stage are important because they determine the model calibration to antenatal HIV prevalence data. Fertility rates in HIV-positive women are specified as multiples of corresponding fertility rates in HIV-negative women of the same age. Mathematically, the fertility rate in HIV-positive women aged x in year t, in CD4 stage s, with HIV testing history v, ART status a and ART duration d, is calculated as

$$F(x, t)\ \Gamma(s, v, a, d)\ L_v(x, t),$$

where $F(x, t)$ is the fertility rate in HIV-negative women, $\Gamma(s, v, a, d)$ is the HIV-positive multiplier, and $L_v(x, t)$ is a further adjustment to take account of differences in lactation between HIV-diagnosed mothers and other mothers (since differences in breastfeeding determine the extent of lactational amenorrhoea).

The $\Gamma(s, v, a, d)$ multiplier is calculated as the product of a number of adjustment factors:

$$\Gamma(s, v, a, d) = B_0\ B_1(s)\ B_2(v)\ B_3(a).$$

The $B_1(s)$ adjustment factor represents the relative fertility rate in HIV-positive women in CD4 compartment s to that in HIV-positive women with CD4 counts of 500 cells/μl or higher (by

definition, $B_1(2)$ is 1). Based on a recent analysis of pregnancy incidence rates in HIV-positive women in the Western Cape province of South Africa [111], we set these ratios to 0.99 in the CD4 350-499 category, 0.90 in the CD4 200-349 category, and 0.66 in the CD4 <200 category. These rate ratios are consistent with CD4 effects observed in other African cohorts [112-114]. The $B_1(1)$ parameter (corresponding to the first 3 months of HIV infection) is more difficult to estimate directly, but our previous works suggests that there is a strong association between recent HIV infection and pregnancy, largely because both are determined by recent unprotected sexual activity [115]. We set $B_1(1) = 1.91$, based on attempts to find the model parameters that provide the best fits to antenatal HIV prevalence data (a more detailed explanation is given in Appendix I of the full Thembisa report [1]).

The $B_2(2)$ adjustment factor represents the relative fertility rate in HIV-diagnosed women compared to undiagnosed HIV-positive women (by definition, $B_2(0)$ and $B_2(1)$ are both 1). Based on attempts to find the parameter combinations most consistent with South African antenatal HIV prevalence data (described in Appendix I of the full Thembisa report [1]), we set $B_2(2)$ to 0.77, consistent with previous studies showing that HIV diagnosis is associated with increases in condom use [29, 116, 117] and lower childbearing intentions [118-121].

The $B_3(1)$ adjustment factor represents the relative rate of fertility in women on ART when compared to women who are untreated (by definition, $B_3(0)$ is 1). Based on the previously-mentioned analysis of Western Cape data [111], the $B_3(1)$ parameter has been set to 1.35. This higher rate of pregnancy incidence in women on ART, after controlling for recent CD4 count, is consistent with the findings of some studies [112, 122], although results from other studies have been inconsistent [123, 124].

The B_0 adjustment factor represents the relative rate of fertility in undiagnosed HIV-positive women in the early stages of HIV infection (CD4 ≥500 cells/μl), when compared to fertility in sexually experienced HIV-negative women of the same age. This parameter is difficult to estimate directly, as most studies do not report fertility rates in undiagnosed HIV-positive women, or do not include comparisons with HIV-negative women. However, one might expect B_0 to be greater than 1 if women who have recently acquired HIV are more sexually active and therefore more likely to become pregnant. In a sensitivity analysis of the Western Cape data, it was found that pregnancy incidence rates in women on ART with CD4 counts above 500 cells/μl were 1.42 (95% CI: 1.38-1.45) times those in HIV-negative women [111]. Substituting this and the other previously-assumed values into the equation for $\Gamma(s, v, a, d)$ gives $1.42 = B_0 \times B_2(2) \times 1.35$. Equivalently, $B_0 = (1.42/1.35)/B_2(2)$. In our previous fitting of the Thembisa model we estimated a $B_2(2)$ value of 0.939 [125]; substituting this into the equation for B_0 gives $B_0 = 1.12$. However, if we instead set $B_2(2)$ to 0.77 (as described above), the estimated value of B_0 is 1.37. To reflect the uncertainty around B_0 is, we assign a gamma prior distribution with a mean of 1.30 and a standard deviation of 0.13.

The lactation adjustment for HIV-negative women and undiagnosed HIV-positive women is set to 1 (i.e. $L_0(x, t) = L_1(x, t) = 1$). To estimate the lactation adjustment for HIV-diagnosed women, $L_2(x, t)$, we first define $l_v(x, t)$ as the proportion of women aged x in year t, with HIV testing history v, who are breastfeeding. The breastfeeding proportion is assumed to be the same for HIV-negative women ($v = 0$) and HIV-positive women who are undiagnosed ($v = 1$), but lower for HIV-diagnosed women ($v = 2$) because of the effects of PMTCT programmes. Suppose $F^*(x, t)$ is the fertility rate in sexually-experienced HIV-negative women who are not breastfeeding. Then if we assume breastfeeding women do not fall pregnant,

$$F(x, t) = F^*(x, t) \times (1 - l_0(x, t)).$$

The fertility rate in HIV-diagnosed women aged x in year t (ignoring the $\Gamma(s, v, a, d)$ adjustment specified previously) is then

$$\begin{aligned} & F^*(x, t) \times (1 - l_2(x, t)) \\ &= F(x,t)\frac{1-l_2(x,t)}{1-l_0(x,t)} \\ &= F(x, t)\, L_2(x, t) \end{aligned}$$

where $L_2(x, t) \equiv (1 - l_2(x, t))/(1 - l_0(x, t))$. We further define $S_v(d, t)$ to be the proportion of mothers who are still breastfeeding d years after birth, if birth occurred in year t. For HIV-negative women and undiagnosed HIV-positive women

$$\begin{aligned} l_0(x,t) = l_1(x,t) &= \int_0^x F(x-u,t-u)S_0(u,t-u)du \\ &\approx F(x-1,t-1)\int_0^x S_0(u,t-u)du \\ &\approx F(x-1,t-1)\mu_0(t-1) \end{aligned}$$

where $\mu_0(t)$ is the average duration of breastfeeding by HIV-negative mothers who give birth in year t ($\int_0^\infty S_0(u,t)du$). For HIV-diagnosed women, we use a similar approximation:

$$l_2(x,t) \approx F^+(x-1,t-1)\mu_2(t-1),$$

where $F^+(x, t)$ is the average fertility rate in HIV-diagnosed women aged x in year t, and $\mu_2(t)$ is the average duration of breastfeeding by HIV-diagnosed women who give birth in year t. The latter is calculated from the assumed proportions of HIV-diagnosed mothers who choose to breastfeed, the proportion who breastfeed exclusively, the average durations of exclusive and mixed breastfeeding and the proportion of who discontinue breastfeeding completely after stopping exclusive breastfeeding (see section 5.2 of the Thembisa report [1]). The proportions of women who choose to breastfeed change over time, with increases after the phasing out of free formula milk in 2011 [126].

2.4.7 Initial HIV prevalence

The initial HIV prevalence in women in the high-risk group 'seeds' the HIV epidemic. Considering that the HIV prevalence in the first national antenatal clinic survey in 1990 was 0.76% and this grew by a multiple of 1.8 in each of the next two years [127], it is unlikely that HIV prevalence in women aged 15-49 in 1985 would have been more than 0.04% (i.e. 0.0076×1.8^{-5}), since antenatal HIV prevalence tends to exceed prevalence in the general female population [128]. Since we assume that 25% of women are in the high-risk group, this suggests an upper limit of 0.16% on the initial HIV prevalence in the high risk group (0.0004/0.25). The initial HIV prevalence in 15-49 year old females in the high risk group has therefore been assigned a uniform (0, 0.002) prior. The initial ratio of male prevalence to female

prevalence, as well as the initial age distribution of HIV, is set to be consistent with patterns of infection observed in the early stages of the epidemic in KwaZulu-Natal in 1991 [129].

2.5 Likelihood function

The model is calibrated to four HIV prevalence data sources: antenatal clinic survey data, household survey data, female sex worker survey data and data from surveys in men who have sex with men (MSM). In addition, the model is calibrated to recorded death data and antiretroviral metabolite data. The likelihood for all six data sources is simply the product of the likelihood calculated for each individual data source, as detailed below.

2.5.1 Likelihood function for antenatal survey data

The model is fitted to antenatal HIV prevalence data from national surveys that have been conducted every year from 1994 to 2015, and in 2017 and 2019 (surveys were not conducted in 2016 or 2018). Survey data collected prior to 1994 have not been included, as these early antenatal surveys were based on convenience samples and are unlikely to be representative. We include HIV prevalence estimates for 5 age groups (15-19, 20-24, 25-29, 30-34 and 35-39).

We define $H_1(x, t)$ to be the HIV prevalence at delivery in women aged x to $x + 4$ in year t (excluding women who experience miscarriage/stillbirth). This is calculated as

$$H_1(x,t) = 1 - \frac{\sum_{j=x}^{x+4} F(j,t) \sum_{v} N^1_{v,0,0,0}(j,t)}{\sum_{j=x}^{x+4} \bar{F}(j,t) \sum_{i,v,a,s,d} N^i_{v,a,s,d}(j,t)},$$

where $N^i_{v,a,s,d}(x,t)$ is the total number of women aged x with sexual experience indicator i (0 for virgins, 1 for sexually-experienced women), HIV testing history v, ART status a, CD4 stage s, and ART duration d years. $F(x, t)$ is the fertility rate in HIV-negative sexually experienced women aged x in year t, and $\bar{F}(x, t)$ is the average fertility rate in all women aged x in year t (including women who are not sexually experienced).

Section 2.4.6 described the approach to estimating the numbers of live births to HIV-positive mothers. For the purpose of model calibration we wish to estimate HIV prevalence in pregnant women at the time of their first antenatal visit, which may differ from the HIV prevalence in women having live births (a) because HIV causes higher rates of miscarriage and stillbirth [130], and (b) because some women who are HIV-negative at the time of their first antenatal visit could acquire HIV by the time they deliver. Suppose $H_0(x, t)$ is the HIV prevalence at the time of the first antenatal visit. Let m_0 and m_1 be the probabilities of miscarriage/stillbirth in HIV-negative and HIV-positive women respectively, and let $I(x, t)$ be the HIV incidence rate in women aged x to $x + 4$. Then

$$H_1(x,t) = \frac{H_0(x,t)(1-m_1) + (1-H_0(x,t))(1-m_0)I(x,t)\Delta}{H_0(x,t)(1-m_1) + (1-H_0(x,t))(1-m_0)},$$

where Δ is the average time between first antenatal visit and delivery. Based on unpublished data from the Western Cape public sector, we assume that in HIV-negative women, there is a 3% risk of a miscarriage (after her first antenatal visit) or stillbirth, and that this increases by a factor of 1.3 (to 3.9%) if the woman is HIV-positive. To be consistent with the assumptions in Thembisa, we assume an average interval of 16 weeks between the first antenatal visit and delivery ($\Delta = 16/52 = 0.31$). Rearranging the terms in the previous equation gives

$$H_0(x,t) = \frac{(1-m_0)(H_1(x,t) - I(x,t)\Delta)}{(1-m_1) - H_1(x,t)(m_0 - m_1) - (1-m_0)I(x,t)\Delta}.$$

We use this equation to determine the HIV prevalence in pregnant women from the HIV prevalence in women at delivery.

Accounting for differences in HIV prevalence between public and private sectors

We define $G_0(x, t)$ as the HIV prevalence in pregnant women attending public antenatal clinics and $G_1(x, t)$ as the HIV prevalence in pregnant women attending private antenatal clinics. We assume that the HIV prevalence in women attending private antenatal facilities is Y times that in women attending public antenatal facilities, i.e. $G_1(x, t) = Y \times G_0(x, t)$. We set Y to 0.35, based on an analysis of the antenatal bias parameters that provide the best model fits to South African antenatal survey data (see Appendix I of the full Thembisa report [1]).

We further define $\varphi(x)$ as the proportion of pregnant women aged x to $x + 4$ who use private antenatal facilities. The HIV prevalence in all pregnant women is then

$$H_0(x, t) = G_0(x, t)(\varphi(x)Y + (1 - \varphi(x))).$$

The proportions of pregnant women who use private antenatal facilities are estimated from the 1998 and 2016 DHSs [5, 14]; the results are summarized in Table S11. The results of the 2016 DHS suggest a lower private sector proportion at the younger ages when compared against the 1998 DHS, but at the older ages (35+) there is greater similarity between the two surveys. As the samples sizes at each age are relatively small and there are thus wide uncertainty ranges, we take the average of the two surveys when setting the assumed values of $\varphi(x)$, as shown in the last row.

Table S11: Proportions of pregnant women using private antenatal facilities

Age group	15-19	20-24	25-29	30-34	35-39	40-49	15-49
1998 DHS	8.2%	13.5%	20.9%	28.5%	19.1%	13.9%	18.4%
2016 DHS	1.0%	4.3%	7.9%	13.2%	15.7%	15.8%	9.4%
Average, $\varphi(x)$	4.6%	8.9%	14.4%	20.9%	17.4%	14.9%	13.9%

Correcting for HIV test specificity

In the public sector antenatal surveys that were conducted between 1997 and 2015, a single ELISA was used to test for HIV. This could lead to some over-estimation of HIV prevalence due to false-positive reactions. It is therefore important to know the specificity of the ELISA used in the antenatal clinic surveys, but there have been no local studies published on the specificity of the Abbott Axsym ELISA, the assay used in the surveys. We define $Sp(t)$ as the

specificity of the HIV testing algorithm in year *t*. For the years 1997-2015, this is set to 0.99, based on analyses of the parameter combinations that provide the best fit to antenatal survey data (see Appendix I of the full Thembisa report [1]). In the other years (1990-1996, 2017 and 2019), there was confirmatory testing of all initially positive specimens, which would have excluded all (or almost all) false-positive reactions. We therefore set $Sp(t)$ to 1 in these years.

Suppose that $G'_0(x, t)$ is the HIV prevalence that we would expect to observe in the antenatal clinic survey, after taking into account the specificity of the ELISA. This expected prevalence is

$$G'_0(x, t) = G_0(x, t) + (1 - G_0(x, t))(1 - Sp(t))$$
$$= 1 - Sp(t) + \frac{Sp(t)H_0(x,t)}{\varphi(x)(Y-1)+1}$$

This is the equation that we use in our model to adjust the estimated HIV prevalence in pregnant women ($H_0(x, t)$) to be comparable to the results from the antenatal survey.

The corresponding prevalence of HIV actually measured in the antenatal survey is represented by $y_{x,t}$. It is assumed that the difference between the logit-transformed model estimate and the logit-transformed observed prevalence is normally distributed with zero mean. The variance of the distribution is assumed to be composed of a 'survey error' term (representing the uncertainty around the survey estimate due to binomial variation and cluster variation in the survey) and a 'model error' term (representing the error that may arise due to the sources of antenatal bias not described previously). More formally, it is assumed that

$$\log\left(\frac{y_{x,t}}{1-y_{x,t}}\right) = \log\left(\frac{G'_0(x,t)}{1-G'_0(x,t)}\right) + m_{x,t} + \varepsilon_{x,t},$$

where $m_{x,t} \sim N\left(0, \sigma_m^2\right)$ and $\varepsilon_{x,t} \sim N\left(0, \sigma_{x,t}^2\right)$. 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. The $\sigma_{x,t}^2$ values are estimated from the 95% confidence intervals that have been published for the various survey estimates. The σ_m^2 parameter has been set to 0.4^2, to achieve acceptably wide confidence intervals around the model estimates. The value of 0.4 was chosen such that when the model was fitted after omitting the 20% of the most recent antenatal survey data (from 2013-2017), the 95% prediction intervals around $G'_0(x, t)$ included 95% of the omitted $y_{x,t}$ values.

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

$$L(\mathbf{y} \mid \boldsymbol{\varphi}) = \prod_x \prod_t \frac{\exp\left(-\frac{\left(\text{logit}\left(y_{x,t}\right) - \text{logit}\left(H_{x,t}(\boldsymbol{\varphi})\lambda_{x,t}(\boldsymbol{\varphi})^{\theta}\right) - \hat{b}\right)^2}{2\left(\hat{\sigma}_m^2 + \sigma_{x,t}^2\right)}\right)}{\sqrt{2\pi\left(\hat{\sigma}_m^2 + \sigma_{x,t}^2\right)}},$$

where **y** represents the matrix of $y_{x,t}$ values, across age bands 15-19 to 35-39, and across calendar years 1994-2015, 2017 and 2019, and **φ** represents the vector of model inputs.

2.5.2 Likelihood function for household survey HIV prevalence data

The model is calibrated to HIV prevalence data from four nationally-representative household surveys conducted by the Human Sciences Research Council (HSRC) in 2005 [9], 2008 [10], 2012 [12] and 2017 [15], as well as HIV prevalence data from the 2016 Demographic and Health Survey (DHS) [14]. HIV prevalence levels in each survey are estimated by 5-year age group (from 15-19 up to 55-59) and by sex. The approach adopted in defining the likelihood function in respect of the HSRC and DHS HIV prevalence data is the same as that for the antenatal data, except that the model error term (m) is omitted. Although an initial attempt was made to include the model error term, and to estimate its variance using the same out-of-sample approach described previously (after omitting the 2017 data from the calibration procedure), the 95% prediction intervals included all of the omitted 2017 data points, even when the variance of the model error term was set to zero. This suggests that it is not necessary to allow for model error when defining the likelihood for the HSRC/DHS survey data; the confidence intervals around the survey estimates are wide enough that it is possible to achieve a reasonable degree of consistency between the model and all of the 2017 data points.

2.5.3 Likelihood definition for antiretroviral metabolite data

We calculate a likelihood to represent the goodness of model fit to 2012 and 2017 household survey estimates of the proportions of HIV-positive adults who are on ART. In both household surveys, the proportion of HIV-positive adults on ART was estimated based on testing for antiretroviral metabolites (efavirenz, nevirapine, lopinavir and other less commonly used drugs, i.e. accounting for most first- and second-line ART regimens) [12, 15]. Although the survey also collected self-reported data on ART use, we have not used these data in calibration, in part to be consistent with the methods used in the HSRC survey reports, and in part because there were high levels of non-response to questions about ART use (Jeffrey Eaton, personal communication). Estimates of coverage were also obtained separately for men and women, so that the model was calibrated to a total of 4 data points (Table S12). We calculated the likelihood on the assumption that the difference between the survey estimate of ART coverage and the modelled ART coverage, on a logit scale, was normally distributed with zero mean and variance calculated from the 95% confidence interval around the survey estimate.

Table S12: Survey estimates of the proportion of HIV-positive adults (15+) on ART

Sex	2012	2017
Male	24.2% (19.3-29.2%)	58.0% (53.7-62.3%)
Female	34.2% (30.8-37.6%)	66.7% (64.2-69.1%)

2.5.4 Likelihood definition for recorded death data

To calculate the likelihood in respect of the reported death data, we restrict this analysis to deaths occurring over the period from the start of 1997 to the end of 2016 [131]. (Death data

have also been published for 2017 but are not included due to concerns that they may be biased by missing deaths yet to be reported.) Because certain causes of death are often misclassified, the reported AIDS deaths are likely to be only a fraction of the actual HIV-related deaths [132]. We therefore compare model estimates of all-cause mortality with reported levels of all-cause mortality. However, for the purpose of calculating the variance of the model estimates, it is necessary to consider the model estimate of the fraction of deaths that are AIDS-related (as explained below). The comparison of modelled and recorded deaths is only likely to be meaningful in those age groups in which a substantial proportion of deaths are HIV-related, and this analysis is therefore restricted to deaths occurring from ages 20 to 59. Mortality data are grouped in 5-year age bands for calibration purposes, and estimates are considered separately for males and females.

We define $N_g(x, t)$ to be the model estimate of the total number of deaths in year t, in adults in age group x, of sex g. Similarly, we define $R_g(x, t)$ to be the recorded number of deaths in year t, in adults in age group x, of sex g. In order to specify a likelihood function for the reported death data, it must be assumed that a certain proportion of adult deaths, $\gamma_{g,x,t}$, is reported. It is assumed that the difference between the log-transformed model estimate of the number of reported deaths ($N_g(x, t)\ \gamma_{g,x,t}$) and the log-transformed actual number of reported deaths is normally distributed with zero mean. More formally, the likelihood is calculated on the assumption that

$$\log\left(R_g(x,t)\right) = \log\left(N_g(x,t)\gamma_{g,x,t}\right) + \varepsilon_{g,x,t},$$

where $\varepsilon_{g,x,t} \sim N\left(0, \sigma_d^2\right)$. The parameter $\varepsilon_{g,x,t}$ can be regarded as comprising both a 'model error' and 'random binomial error' component, but because the population numbers are very large, the random binomial component of the error is relatively small on the log scale. It is therefore reasonable to assume that the variance of the error term is independent of the population size in the relevant sex and age group.

The $\gamma_{g,x,t}$ parameters have been estimated from a variety of sources. Over the period from October 1996 to October 2001, Dorrington *et al* [133] estimate that the fraction of adult deaths recorded was 84%, based on Death Distribution Methods (i.e. based on comparing the recorded numbers of adult deaths to the changes in the population sizes (after accounting for migration) in each age cohort over the inter-census period). The authors also estimate that the annual increase in the proportion of deaths recorded, over this 5-year period, was 1.7% in men and 2.1% in women, based on an assumption of stable mortality rates at ages 65 and older (where AIDS would be expected to have relatively little impact on mortality). In the period after 2001, estimates of the completeness of adult death recording have been around 93%, based on similar methods [134-136]. Based on these estimates, we set initial completeness assumptions – independent of age and sex – that increase linearly from 80.2% in 1997 to 87.8% in 2001 (an increase of 1.9% per annum, with 84% completeness in 1999) and 93% in 2004, after which completeness is assumed to remain constant (Table S13). The assumption of constant completeness after 2004 is supported by an analysis of factors affecting the recording of deaths in ART patients, which showed no significant change in the completeness of vital registration over the 2004-2014 period [137].

In the final set of completeness assumptions, we use the completeness estimates by age and sex, as estimated in the analysis of factors affecting the recording of deaths in ART patients over the 2004-2014 period [137], and scale these down by the ratio of initial completeness

assumptions to 0.93 in the period prior to 2004. The completeness assumptions are shown in Table S13.

Table S13: Completeness assumptions (fraction of deaths that are recorded)

Year	1997	1998	1999	2000	2001	2002	2003	2004+
Initial completeness assumptions								
	0.802	0.821	0.84	0.859	0.878	0.897	0.914	0.930
Final completeness assumptions								
Women aged								
20-24	0.798	0.817	0.836	0.855	0.874	0.892	0.909	0.925
25-29	0.809	0.828	0.847	0.866	0.886	0.905	0.922	0.938
30-34	0.817	0.836	0.855	0.875	0.894	0.913	0.931	0.947
35-39	0.823	0.842	0.862	0.881	0.901	0.920	0.937	0.954
40-44	0.827	0.847	0.866	0.886	0.905	0.925	0.943	0.959
45-49	0.831	0.850	0.870	0.890	0.909	0.929	0.947	0.963
50-54	0.834	0.853	0.873	0.893	0.913	0.932	0.950	0.967
55-59	0.836	0.856	0.876	0.895	0.915	0.935	0.953	0.969
Men aged								
20-24	0.756	0.774	0.792	0.810	0.828	0.846	0.862	0.877
25-29	0.772	0.791	0.809	0.827	0.845	0.864	0.880	0.896
30-34	0.789	0.807	0.826	0.845	0.863	0.882	0.899	0.914
35-39	0.802	0.821	0.840	0.859	0.878	0.897	0.914	0.930
40-44	0.813	0.832	0.852	0.871	0.890	0.909	0.927	0.943
45-49	0.821	0.841	0.860	0.880	0.899	0.918	0.936	0.952
50-54	0.827	0.847	0.866	0.886	0.906	0.925	0.943	0.959
55-59	0.832	0.851	0.871	0.891	0.910	0.930	0.948	0.964

The variance term σ_d^2 is estimated by considering separately the variance in the AIDS deaths and the variance in the non-AIDS deaths. Suppose $A_g(x, t)$ represents the model estimate of AIDS deaths in individuals of sex g and age group x, in year t, and that $B_g(x, t)$ represents the model estimate of non-AIDS deaths (due to 'background' mortality), i.e. $A_g(x, t) + B_g(x, t) = N_g(x, t)$. The variance is assumed to be of the form

$$\begin{aligned}\sigma_d^2 &= \text{Var}[\ln(N_g(x, t))] \\ &\approx \text{Var}[N_g(x, t)] / N_g(x, t)^2 \\ &= \text{Var}[\ln(A_g(x, t))] \, (A_g(x, t) / N_g(x, t))^2 + \text{Var}[\ln(B_g(x, t))] \, (B_g(x, t) / N_g(x, t))^2\end{aligned}$$

The variance of the non-AIDS mortality, $\sigma_b^2 \equiv \text{Var}[\ln(B_g(x, t))]$, has been estimated from the difference between the model predictions of mortality and the recorded levels of mortality at ages 60 and older (after adjusting for completeness), since the contribution of AIDS mortality to total mortality is expected to be small at these older ages.

$$\sigma_b^2 = \frac{1}{240} \sum_{x=60} \sum_{g} \sum_{t} \left(R_g(x,t) - N_g(x,t) c_g(x,t) \right)^2 ,$$

where 240 is the number of squared differences across which we are averaging (20 years, 2 sexes and 6 five-year age groups). Using the mortality estimates from Thembisa version 4.3 in this formula yields a σ_b^2 estimate of 0.141^2.

We have set the variance of the AIDS mortality term, Var[ln($A_g(x, t)$)], to 0.3^2, based on the same out-of-sample approach described previously (omitting the 2013-2016 data from the calibration and finding the Var[ln($A_g(x, t)$)] value that ensures the 95% prediction intervals around the model estimates include 95% of the recorded deaths over 2013-2016).

The likelihood in respect of the reported death data is then calculated based on the assumed normality of the error terms:

$$L(\mathbf{R} \mid \boldsymbol{\varphi}) = \prod_g \prod_x \prod_{t=1997}^{2016} \left(2\pi\hat{\sigma}_d^2\right)^{-0.5} \exp\left(- \frac{\left(\log\left(R_g(x,t)\right) - \log\left(N_g(x,t)\gamma_{g,x,t}\right)\right)^2}{2\hat{\sigma}_d^2} \right),$$

where **R** represents the matrix of reported death data.

2.5.5 Likelihood definition for female sex worker prevalence data

Table S14 summarizes the HIV prevalence data from surveys of sex workers, which have been used in model calibration. We have also included unpublished data from a large survey conducted in 12 South African centres in 2019 (Jenny Coetzee, personal communication), but these data are not shown as they have not yet been released. We have excluded studies in which HIV status was based on self-report [138, 139], as this has been shown to have low sensitivity in the South African setting [140]. The surveys of commercial sex workers have been conducted in specific communities, and cannot be considered representative of sex workers nationally. It is therefore necessary to allow for potential heterogeneity in HIV prevalence between commercial sex workers surveyed in different communities, using different sampling techniques. We use the notation t_i, n_i and p_i to represent the time of the i^{th} survey, the sample size of the i^{th} survey and the HIV prevalence measured in the i^{th} survey respectively.

Table S14: Studies of HIV prevalence in South African sex workers

Study	Location	Year (t_i)	Sample size (n_i)	Prevalence of HIV (p_i)
Ramjee *et al* [94]	Truck stops between Durban and Johannesburg	1996	416	50%
Dunkle *et al* [141]	Johannesburg	1996	295	46.4%
Leggett *et al* [142]	Johannesburg, Durban, Cape Town	1998*	249	42.6%
Williams *et al* [143]	Carletonville	1998	121	68.6%
Ndhlovu *et al* [144]	Carletonville	2001	101	78%
van Loggerenberg *et al* [145]	Durban	2004	775	59.6%
Luseno & Wechsberg [146]	Pretoria	2005	276	59.1%
Greener *et al* [147]	Durban	2012	349	66.9%
USCF [26]	Johannesburg	2013	764	71.8%
	Cape Town	2013	650	39.7%
	Durban	2013	766	53.5%
Schwartz *et al* [148]	Port Elizabeth	2014	410	61.5%
Black *et al* [149]	Johannesburg	2014	249	75.1%
Coetzee *et al* [150]	Johannesburg	2016	508	53.6%
University of California	Johannesburg	2018	546	58.3%
San Francisco	Cape Town	2018	781	42.5%
(unpublished)	Durban	2018	600	77.7%

* The study date was not stated, and has been assumed to be three years prior to the date of publication.

For the purpose of defining the likelihood function, suppose that $C(t_i, \boldsymbol{\varphi})$ represents the model estimate of HIV prevalence in sex workers in the year of the i^{th} study, where the vector $\boldsymbol{\varphi}$ represents the values of the model input parameters. The difference between the logit-transformed model estimate of HIV prevalence and the logit-transformed observed prevalence is assumed to be composed of a 'random effect' (representing the true difference in HIV prevalence between the HIV prevalence in sex workers nationally and the prevalence in sex workers in the community being studied) and a 'random error' term (representing the binomial sampling variation due to the limited sample size). More formally, it is assumed that

$$\log\left(\frac{p_i}{1-p_i}\right) = \log\left(\frac{C(t_i,\boldsymbol{\varphi})}{1-C(t_i,\boldsymbol{\varphi})}\right) + r_i + \varepsilon_i,$$

where $r_i \sim N\left(0,\sigma_r^2\right)$ and $\varepsilon_i \sim N\left(0,\sigma_i^2\right)$. The variance of the random error term, σ_i^2, is estimated by noting that the sample variance of p_i is $p_i(1-p_i)/n_i$, and after logit-transformation, the Taylor approximation to the value of the sample variance of logit(p_i) is

$$\hat{\sigma}_i^2 = \frac{1}{n_i p_i (1-p_i)}.$$

The variance of the random effects is set to 0.63, based on previous attempts to quantify the variation in prevalence measurements that was not attributable to binomial sampling variation [1]. The likelihood function in respect of the commercial sex worker prevalence data is then

$$L(\mathbf{p} \mid \boldsymbol{\varphi}) = \prod_{i=1}^{29} \left(2\pi\left(\hat{\sigma}_r^2 + \hat{\sigma}_i^2\right)\right)^{-0.5} \exp\left[-\frac{\left(\text{logit}(p_i) - \text{logit}(C(t_i,\boldsymbol{\varphi}))\right)^2}{2\left(\hat{\sigma}_r^2 + \hat{\sigma}_i^2\right)}\right],$$

where $\mathbf{p}$ is the vector of p_i values.

2.5.6 Likelihood definition for MSM prevalence data

Table S15 summarizes the HIV prevalence data from surveys of men who have sex with men (MSM), which have been used in model calibration. Only studies that used respondent-driven sampling (RDS) have been used for calibration (i.e. excluding venue-based sampling studies, which tend to be biased towards recruitment of higher-risk MSM). Since none of the surveys are nationally representative, the approach used in defining the likelihood function is the same as for sex worker HIV prevalence data, i.e. based on a random effects model to represent heterogeneity between studies. The only difference is that the model estimates of HIV prevalence have been adjusted so that each model estimate of HIV prevalence in MSM is age-standardized to correspond to the age profile in the survey of MSM (as represented by the fraction of sampled MSM who are aged 18-24, shown in the last column of Table S15). This age standardization is necessary because South African surveys of MSM appear to be biased toward younger MSM, and without appropriate age adjustment, this may lead to the model under-estimating HIV prevalence in MSM [151]. The variance of the random effects is set to 0.59, based on previous attempts to quantify the variation in prevalence measurements that was not attributable to binomial sampling variation [1].

Table S15: Studies of HIV prevalence in South African MSM

Study	Location	Year (t_i)	Sample size (n_i)	Prevalence of HIV (p_i)	% aged 18-24
Cloete *et al* [152]	Cape Town	2012	286	22.3%	67.3%
	Durban	2012	290	48.2%	27.0%
	Johannesburg	2012	349	26.8%	52.1%
Lane *et al* [153]	Gert Sibande district	2012	307	29.4%	29.6%
	Ehlanzeni district	2012	298	15.9%	28.0%
Lane *et al* [154]	Soweto	2008	363	13.6%	31.0%
Rispel *et al* [155]	Johannesburg	2008	202	49.5%	33.3%
	Durban	2008	69	27.5%	33.3%
Tucker *et al* [156]	Cape Town	2010	171	34.5%	42.9%
Sandfort *et al* [157]	Pretoria	2011	480	30.1%	41.0%
Kufa *et al* [158]	Johannesburg	2015	546	43.4%*	45.2%*
	Bloemfontein	2015	525	17.3%*	71.6%*
	Mafikeng	2015	474	14.6%*	71.2%*
	Polokwane	2015	358	22.4%*	59.7%*
Sandfort *et al* [159]	Cape Town	2015	139	31.7%	74.1%
	Johannesburg	2015	171	49.1%	67.8%
Fearon *et al* [160]	Johannesburg	2017	300	37.5%	48%

* Unpublished data. RDS-weighted estimates are not yet available (although an RDS design was used), so only the unweighted estimates are used. Variance estimates were calculated using the RDS design effects described previously.

3. Additional results

3.1 Comparison of prior and posterior distributions

Table S16 compares the prior and posterior distributions for the parameters that were included in the uncertainty analysis. Posterior estimates of the relative rates of partnership formation in low-risk and married individuals are low, indicating that there are relatively high levels of heterogeneity in rates of short-term partnership formation. The condom bias parameter has a

posterior mean of 0.713, which indicates that there is substantial over-reporting of condom use at last sex, consistent with our previous findings [50]. The posterior estimate of the reduction in unprotected sex after diagnosis (mean 0.307) is greater than the prior mean (0.180). Most of the other posterior estimates are reasonably close to the prior means.

Table S16: Comparison of prior and posterior distributions

	Prior distribution (mean, 95% CI)	Posterior distribution (mean, 95% CI)
RR of ST partner acquisition in		
low-risk single males*	0.500 (0.025-0.975)	0.170 (0.114-0.227)
low-risk single females*	0.500 (0.025-0.975)	0.303 (0.226-0.378)
high-risk married males*	0.250 (0.084-0.469)	0.275 (0.219-0.334)
high-risk married females*	0.250 (0.084-0.469)	0.167 (0.126-0.201)
Gamma density of relative rates of short-term partnership formation by age, in unmarried females		
Mean	38.7 (31.1-47.1)	34.9 (33.9-35.7)
Standard deviation	19.3 (14.2-25.2)	19.8 (18.7-21.2)
Sexual mixing parameter	0.530 (0.295-0.758)	0.503 (0.428-0.600)
Bias in reported condom use at last sex	0.500 (0.025-0.975)	0.713 (0.608-0.804)
Reduction in unprotected sex after HIV diagnosis	0.180 (0.006-0.555)	0.307 (0.146-0.451)
Average survival in absence of ART (years)	12.00 (10.12-14.04)	11.94 (11.42-12.52)
RR of HIV disease progression in women	0.960 (0.864-1.060)	0.936 (0.920-0.955)
Increase in HIV disease progression per 10-year increase in age	0.180 (0.082-0.315)	0.166 (0.141-0.191)
Reduction in mortality† per unit increase in rate of ART initiation (at CD4<200) over last 3 years	7.50 (2.29-15.76)	8.36 (6.80-10.53)
Female-to-male transmission probability in short-term/ non-spousal partnerships	0.0080 (0.0032-0.0149)	0.0063 (0.0059-0.0067)
Male-to-female transmission probability in short-term/ non-spousal partnerships	0.0120 (0.0043-0.0236)	0.0126 (0.0111-0.0139)
Male-to-male transmission probability in short-term/ non-spousal partnerships	0.0200 (0.0114-0.0309)	0.0209 (0.0184-0.0242)
Client-to-female sex worker transmission probability	0.0010 (0.0003-0.0022)	0.0008 (0.0007-0.0011)
Relative risk of transmission per sex act in long-term partnerships (relative to short-term partnerships)	0.200 (0.047-0.428)	0.233 (0.186-0.274)
Odds of viral suppression relative to that in IeDEA-SA	0.819 (0.673-0.979)	0.884 (0.848-0.919)
RR HIV+ fertility before diagnosis/immune decline	1.30 (1.06-1.57)	1.30 (1.23-1.36)
Initial HIV prevalence in high risk women, ages 15-49	0.10% (0.01-0.20%)	0.05% (0.03-0.08%)

* Relative to high-risk unmarried individuals of the same sex. † On a natural log scale. IeDEA-SA = International epidemiology Databases to Evaluate AIDS, Southern Africa. RR = relative rate. ST = short-term.

3.2 Additional calibration plots

Figure S4 shows the model calibration to the age-specific antenatal HIV prevalence data. Although the model is consistent with the age-specific HIV prevalence data in most years and most age groups, the model estimates of HIV prevalence tend to be too high in the period before 1994, when compared against the survey data. (The early survey data were not included in the calibration due to concerns regarding the representativeness of the early surveys.) The model estimates of prevalence in the 20-24 age group appear slightly too high over the 1997-2008 period. In the 30-34 age group the model estimates appear slightly too low in the 2002-2008 period but slightly too high in the 2012-2019 period. Finally, in the 35-39 age group the model estimates appear slightly too high in 2017 and 2019.

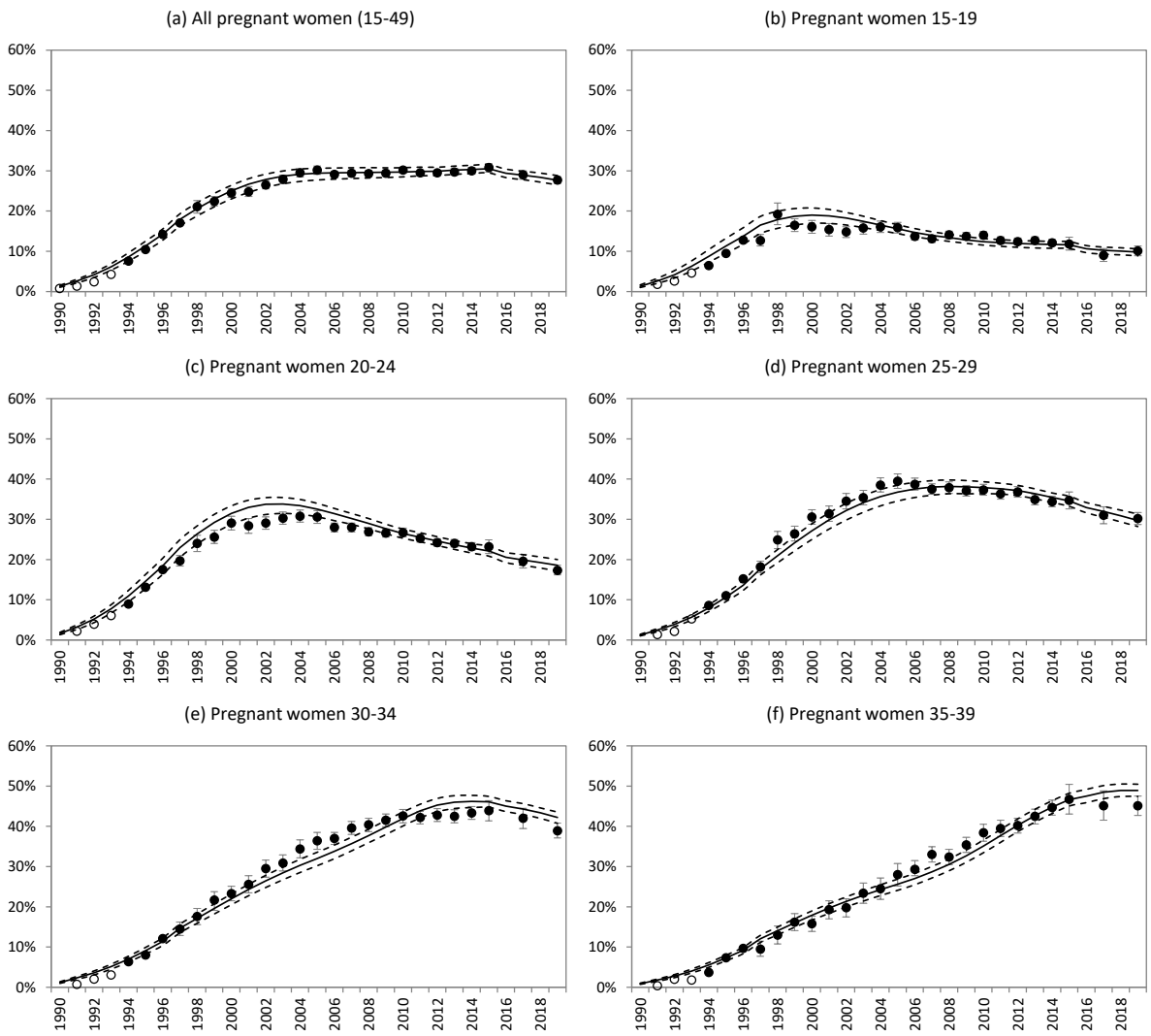

Figure S4: HIV prevalence levels in pregnant women attending public antenatal clinics
Dots represent HIV prevalence levels reported in surveys conducted from 1990-2015, 2017 and 2019 (the 1998 data were adjusted to correct an error in the provincial weights in that year). Solid lines represent the posterior mean model estimates of HIV prevalence in pregnant women, and dashed lines represent 2.5 and 97.5 percentiles of the posterior distributions. Survey data in the pre-1994 period (open circles) are included in the graphs even though they were not used in defining the likelihood function.

Figure S5 shows the calibration to the age-specific data from the Human Sciences Research Council (HSRC) household surveys. The model fits the survey data reasonably well, although the confidence intervals around the age-specific survey estimates tend to be wide.

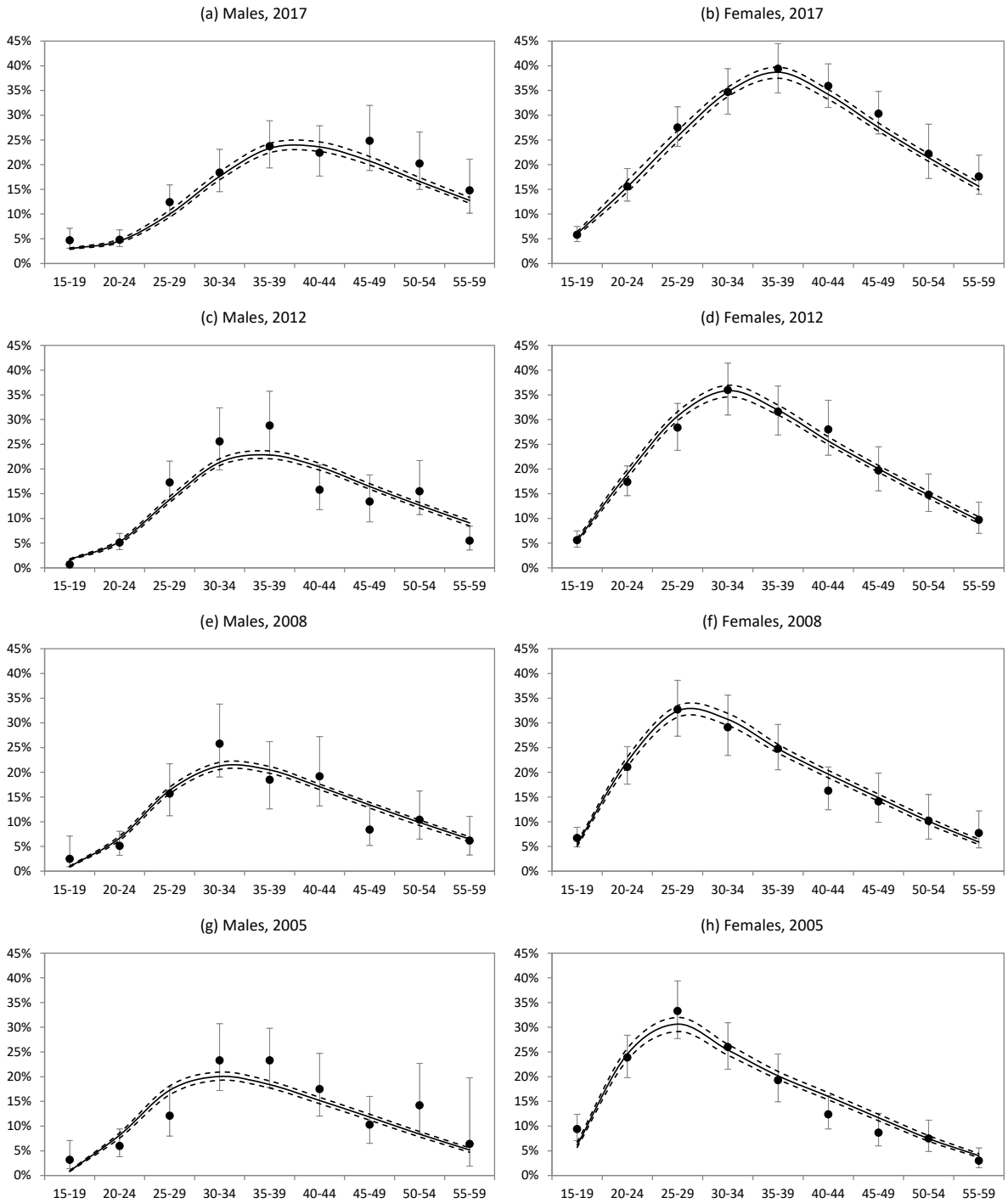

Figure S5: HIV prevalence levels in the general population

Dots represent HSRC survey prevalence estimates, together with 95% confidence intervals. Solid lines represent the posterior mean model estimates of HIV prevalence, and dashed lines represent the 95% confidence intervals around these estimates.

Figure S6 shows the model fits to the data from the 2016 Demographic and Health Survey (DHS). Although there is not as much consistency between the model and the survey data as in the previous figure, the age pattern of HIV prevalence in the 2016 DHS data appears relatively erratic, again with fairly wide confidence intervals.

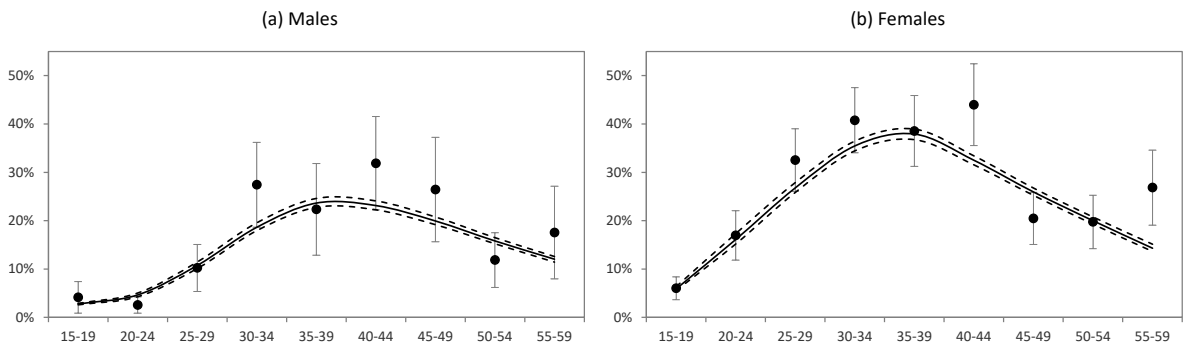

Figure S6: HIV prevalence levels in the general population in 2016
Dots represent DHS prevalence estimates, together with 95% confidence intervals. Solid lines represent the posterior mean model estimates of HIV prevalence, and dashed lines represent the 95% confidence intervals around these estimates.

Figure S7 shows the model fit to the survey estimates of the fraction of HIV-positive adults on ART (i.e. having detectable antiretroviral metabolites). The model appears to significantly under-estimate the male ART coverage in 2017, suggesting that either (a) the model is under-estimating the number of men on ART, (b) the model is over-estimating HIV prevalence in men, or (c) there is a non-response bias (with HIV-positive men who are untreated being less likely to agree to HIV testing than those on ART). Explanation (a) seems unlikely as the model is in good agreement with the reported total numbers of ART patients stratified by sex. Explanation (b) also seems unlikely, given that the model appears to be slightly under-estimating male HIV prevalence in recent surveys (Figures S5 and S6).

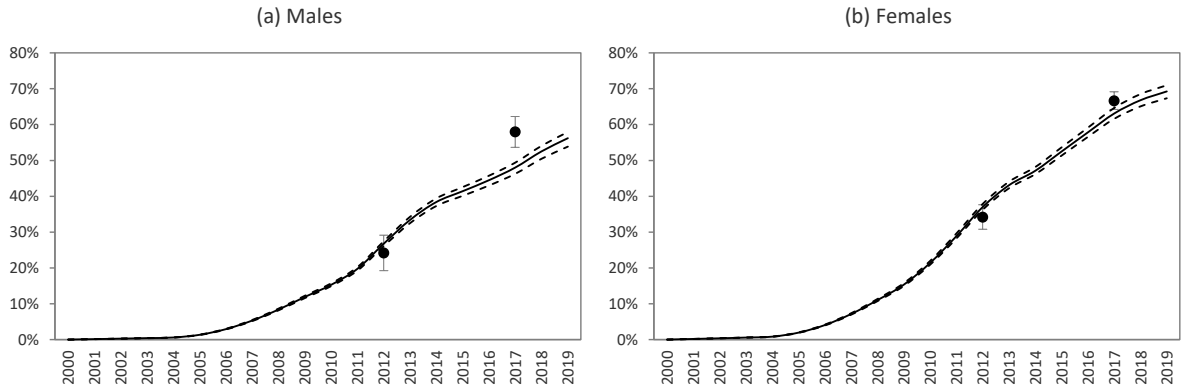

Figure S7: ART coverage in the adult population (15 years and older)
Dots represent HSRC survey prevalence estimates, together with 95% confidence intervals. Solid lines represent the posterior mean model estimates of ART coverage, and dashed lines represent the 95% confidence intervals around these estimates.

Figure S8 shows the model fit to the recorded death data (after adjusting the recorded deaths for incomplete reporting, as described previously). The model estimates and the data represent mortality due to all causes. In most years and in most age groups the model is in good agreement with the recorded numbers of deaths. However, the model does not fit the recorded numbers of male deaths in the 55-59 age group well, which could be an indication of problems with the non-HIV mortality assumptions.

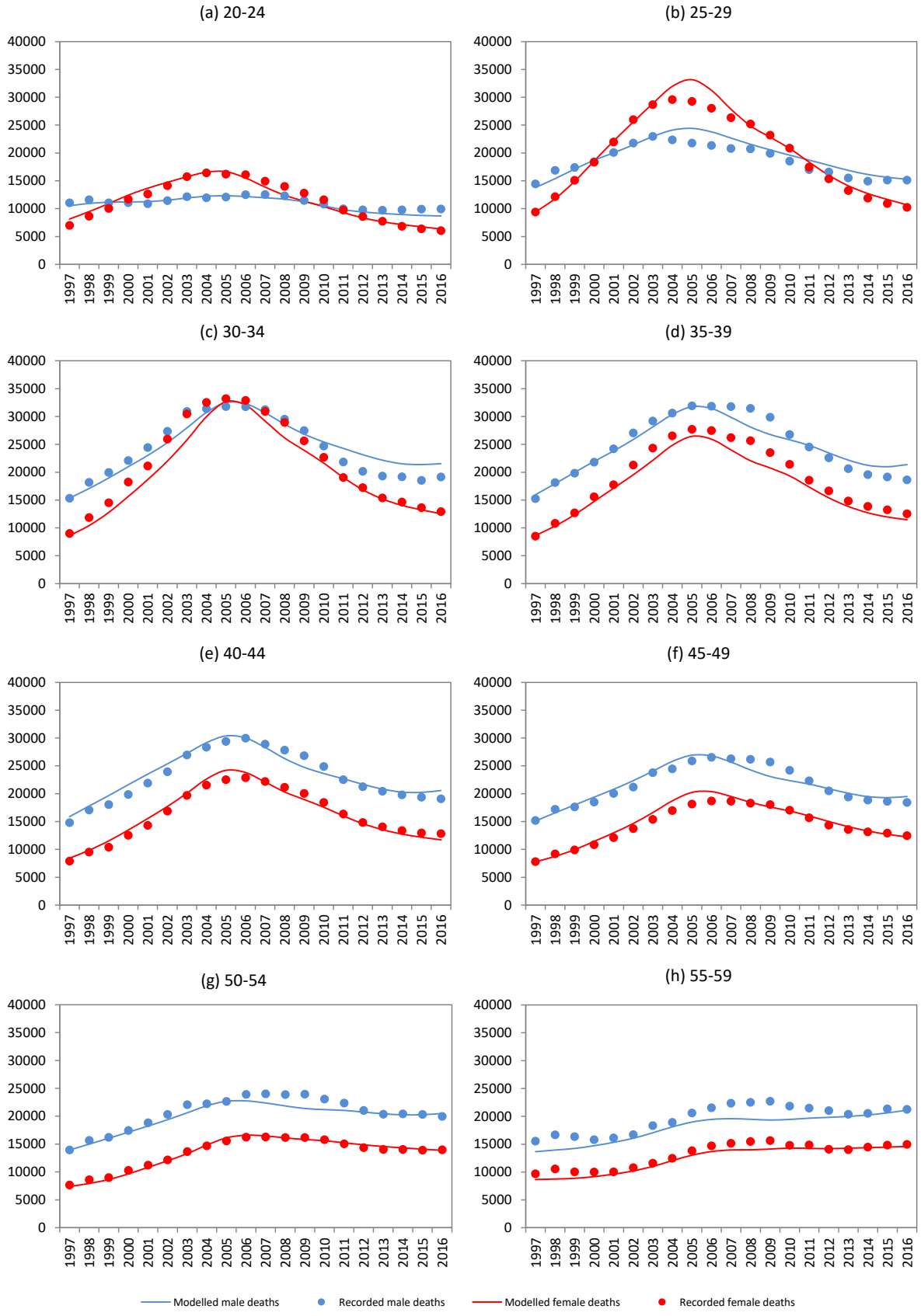

Figure S8: Numbers of deaths in adults, by five-year age group

Dots represent recorded numbers of deaths, after adjusting for incomplete registration. Solid lines represent the posterior mean model estimates.

Figure S9 shows the model calibration to the HIV prevalence data from surveys of sex workers and MSM. As none of the key population surveys is nationally representative, some degree of divergence between model estimates and survey estimates is to be expected. Survey estimates of HIV prevalence are highly variable, reflecting variation in geographic locations and sampled populations. Due to the absence of any HIV prevalence surveys amongst MSM in the early stages of South Africa's HIV epidemic, confidence intervals around the model estimates of HIV prevalence in MSM during the 1990s are very wide.

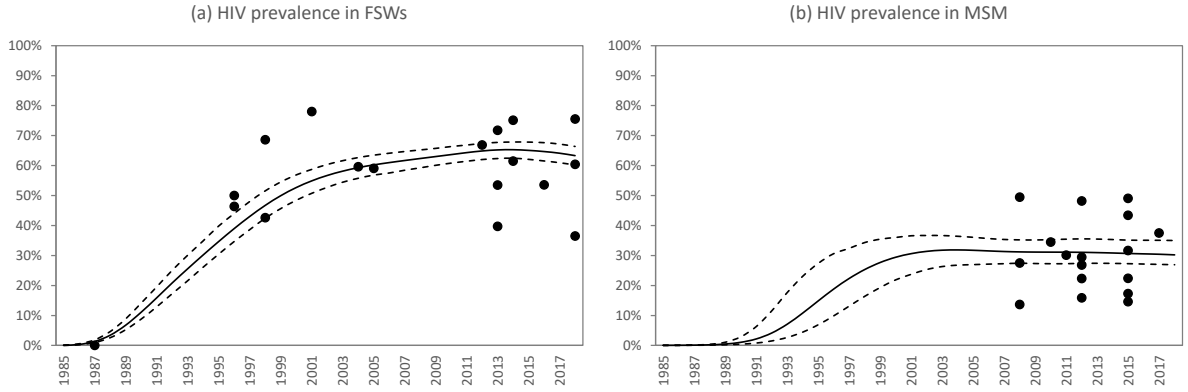

Figure S9: HIV prevalence in key populations

Dots represent survey prevalence estimates (the 1987 data point shown in panel (a) was not included in the definition of the likelihood as the survey found no HIV in sex workers [161], and the likelihood for this observation was thus undefined). Solid lines represent the posterior mean model estimates of HIV prevalence, and dashed lines represent the 95% confidence intervals around these estimates.

3.3 Trends in HIV incidence by age and sex

Figure S10 shows the model estimates of HIV incidence trends by age and sex. HIV incidence rates have consistently been highest among females aged 15-24, and roughly 60% lower among males aged 15-24. Incidence rates are lowest in adults aged 50 and older, with greater similarity in male and female incidence rates at older ages. Incidence rates in the 15-24 and 25-49 age groups are estimated to have peaked around 2000, while incidence rates in the 50+ age group peaked later.

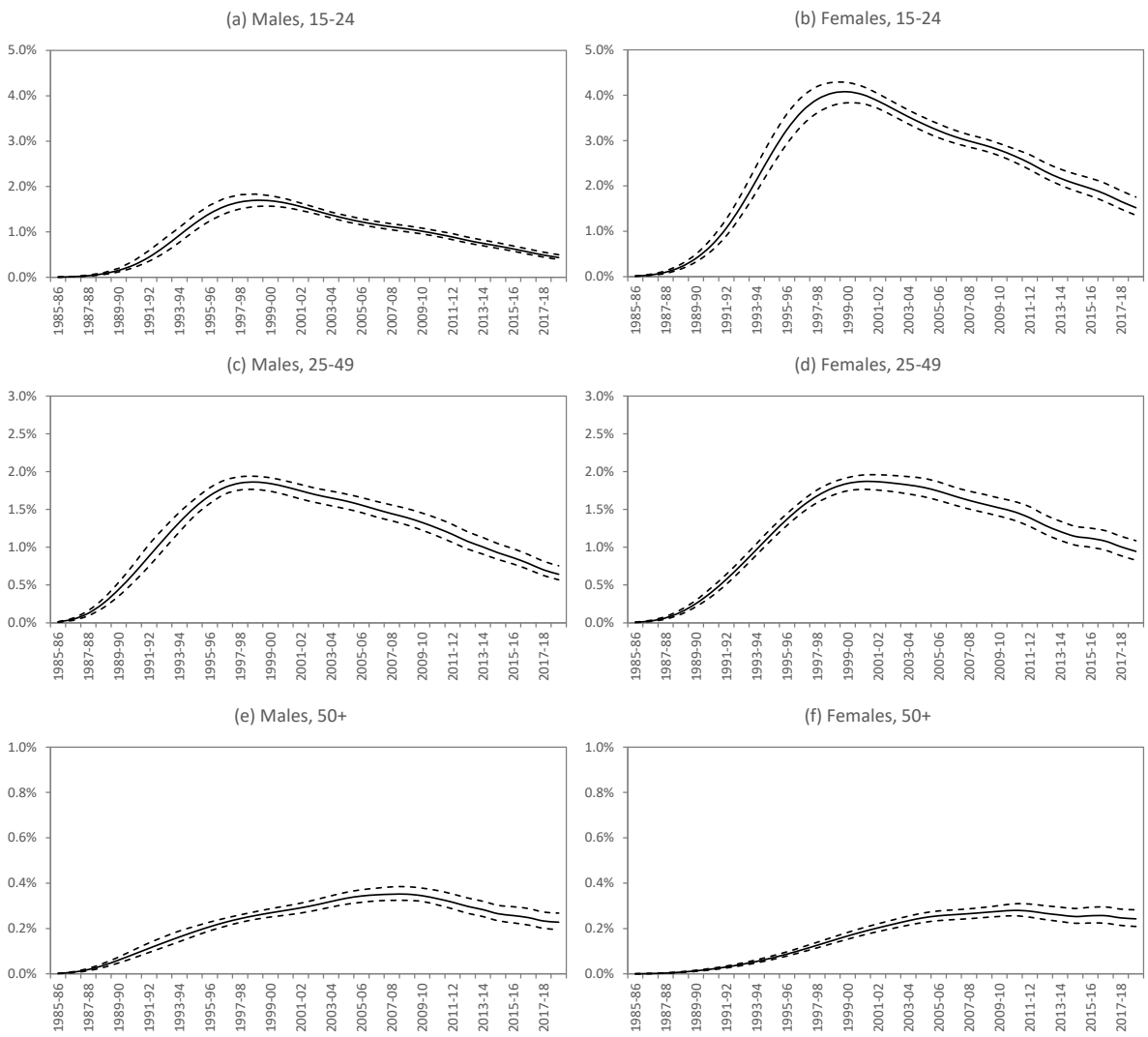

Figure S10: Trends in HIV incidence, by age and sex

Solid lines represent the posterior mean model estimates of HIV incidence, and dashed lines represent the 95% confidence intervals around these estimates.

Figure S11 compares the proportionate reductions in HIV incidence by age and sex, over two time periods: from the start of 2000 to the start of 2019 and from the start of 2010 to the start of 2019. In all age groups, and over both periods, male incidence reductions are estimated to be greater than female HIV incidence reductions. The only group in which HIV incidence is estimated to have increased is older women (aged 50+), which represents a natural 'aging' of the HIV epidemic rather than a change in HIV risk behaviour. HIV incidence declines are estimated to have been greatest in the youngest (15-24) age group.

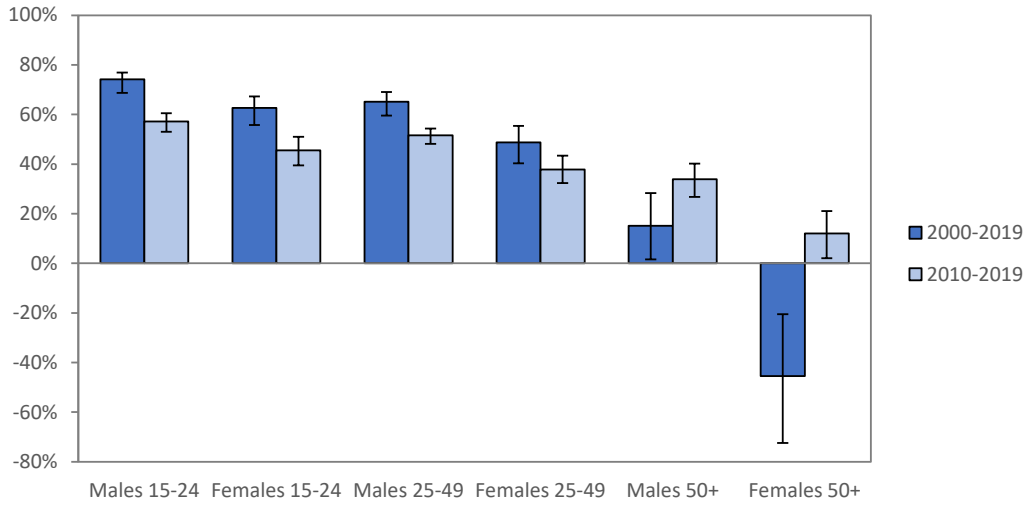

Figure S11: Reductions in HIV incidence, 2000-2019
Bars represent posterior means and error bars represent 95% confidence intervals around the posterior means.

Figure S12 shows the change over time in the age distribution of new HIV infections in adults. In both sexes there has been a steady shift in the distribution of new HIV infections over the last two decades, with relatively more new HIV infections occurring at the older ages.

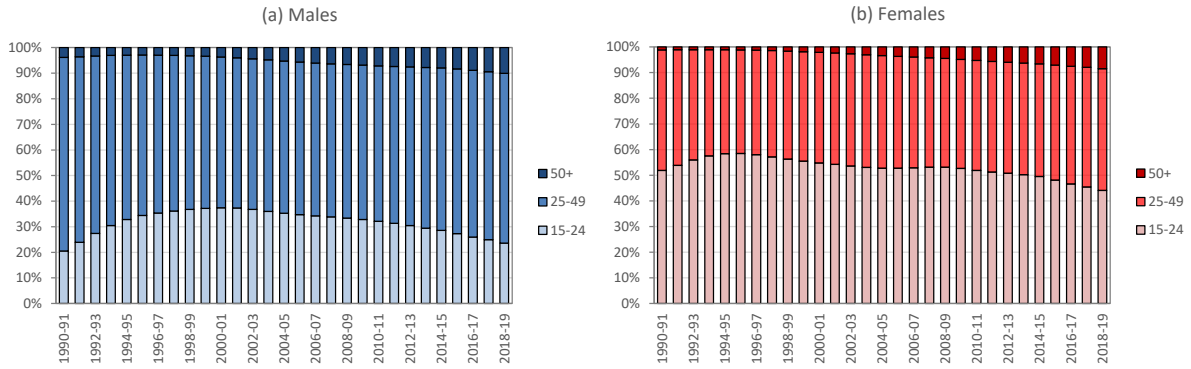

Figure S12: Age distribution of new HIV infections

3.4 Trends in HIV incidence in key populations

Figure S13 shows the estimates of HIV incidence in sex workers and MSM. HIV incidence in sex workers in 2018-19 is estimated to be 5.5% (95% CI: 4.3-7.5%). This is roughly consistent with the results of a national survey conducted in 2019, which estimated HIV incidence in sex workers to be around 5%, based on different methods (Reshma Kassanjee, personal communication). Although there are no other nationally-representative estimates, a study in sex workers in KwaZulu-Natal estimated the HIV incidence rate to be 14.7 per 100 person years over the 1996-2000 period, which is roughly consistent with our model estimates (e.g. an HIV incidence over 1997-98 of 15.6% (95% CI: 12.8-20.5%)). The overall reduction in HIV incidence in sex workers, between the start of 2010 and the start of 2019 is 39%, similar to the overall HIV incidence reduction in women over this period.

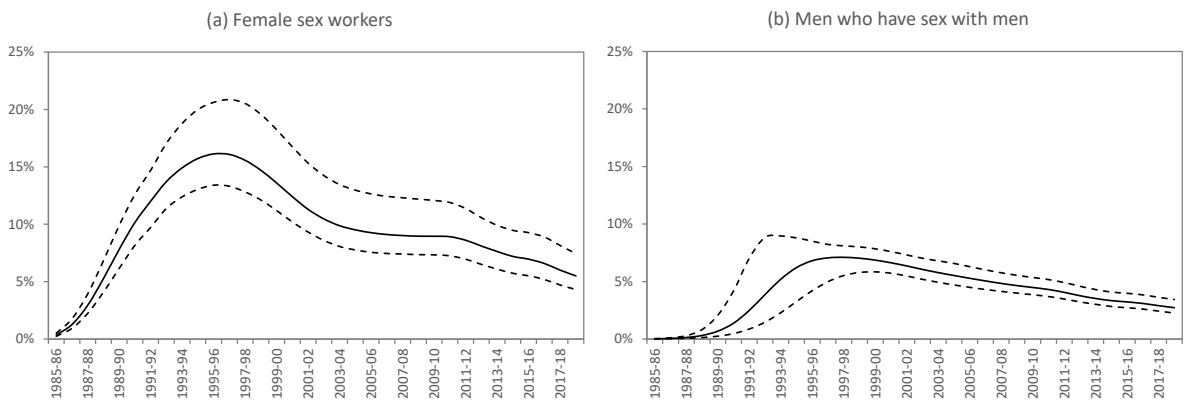

Figure S13: HIV incidence trends in key populations
Solid lines represent the posterior mean model estimates of HIV incidence, and dashed lines represent the 95% confidence intervals around these estimates.

HIV incidence in MSM at the start of 2019 is estimated to be 2.73% (95% CI: 2.26-3.44%). This is a 39% reduction relative to the HIV incidence rate at the start of 2010. HIV incidence trends prior to 2010 are highly uncertain, due to the lack of rigorous HIV prevalence surveys in MSM prior to 2008.

3.5 Comparison with MicroCOSM

In this section we validate the Thembisa model estimates of HIV incidence and HIV programmes impacts by comparing the key model results with the estimates from another South African HIV model, MicroCOSM. MicroCOSM (Microsimulation for the Control of South African Morbidity and Mortality) is an agent-based model that was originally developed to simulate HIV and sexually transmitted infections (STIs) in South Africa [162-164]. The model has been extended to include a number of the socio-economic and structural determinants of HIV in South Africa [115, 165-167]. MicroCOSM is calibrated to most of the data sources that are used in calibrating the Thembisa model, and relies on the same routine programme data. However, MicroCOSM differs from Thembisa in several respects that are likely to influence estimates of HIV incidence:

- MicroCOSM is a network model, whereas Thembisa is a frequency-dependent model. We previously showed that the frequency-dependent assumption is likely to exaggerate the importance of behaviour change in the 'general population', while understating the importance of behaviour change in high-risk groups (e.g. sex workers and people with concurrent partners) in driving reductions in the incidence of HIV and other STIs [162].
- MicroCOSM links fertility in women to their sexual behaviour and contraceptive practices, while Thembisa does not model contraception (other than condom use) or directly link sexual behaviour assumptions to fertility assumptions. This means that in MicroCOSM the difference between HIV prevalence in pregnant women and HIV prevalence in the general population ('antenatal bias') is directly determined by the assumptions about sexual behaviour and contraception [115]. In contrast, the Thembisa model requires additional assumptions about antenatal bias for the purpose of calibrating the model to antenatal HIV prevalence data (as described in sections 2.4.6 and 2.5.1). These assumptions about antenatal bias can be influential in determining model estimates of HIV incidence trends [115].

- Thembisa assumes an average probability of condom use per sex act, which applies to all individuals of the same age, sex and relationship type. MicroCOSM allows for individual-level heterogeneity in condom use, with people either using condoms consistently with a given partner or not using condoms at all with that partner (though consistency of condom use in a relationship can change over the course of the relationship). There is thus greater heterogeneity in HIV acquisition risks per sex act in MicroCOSM.
- MicroCOSM allows for substantial individual-level variation in HIV viral loads, which determines HIV infectiousness. In Thembisa the infectiousness of an HIV-positive individual depends only on their CD4 stage and receipt of ART (with high infectiousness during acute HIV infection) and the effect of viral load is not modelled explicitly. This also leads to substantially greater heterogeneity in HIV transmission risks per sex act in MicroCOSM than in Thembisa.
- MicroCOSM simulates the process of behaviour change after HIV diagnosis in more detail than Thembisa, modelling the effect of disclosure of HIV status to partners on condom use and partner HIV testing [166]. MicroCOSM also allows for the possibility that disclosure of HIV status to a sexual partner may lead to relationship dissolution [168]. We might therefore expect the effect of increased HIV testing on HIV incidence to be simulated more realistically in MicroCOSM than in Thembisa.
- MicroCOSM simulates the transmission of other STIs and assumes that these other STIs increase HIV transmission probabilities. Improvements in STI treatment in South Africa in the late 1990s are believed to have caused a modest reduction in HIV incidence [169], and this dynamic is captured in MicroCOSM but not in Thembisa.

In the most recent MicroCOSM publication, estimates of HIV prevalence were shown to be consistent with antenatal and household survey data collected up to 2017 [115]. However, MicroCOSM has not been recalibrated to the latest HIV prevalence data from the 2019 antenatal clinic survey. In the comparisons that follow we therefore focus only on the period up to 2017. MicroCOSM is calibrated by identifying the 100 parameter combinations that yield the best fit to the available HIV prevalence data. For the purpose of the comparisons that follow we summarize the MicroCOSM estimates in term of a mean and interquartile range (IQR), calculated from these 100 best-fitting parameter combinations. The IQR is not directly comparable to the 95% confidence interval from the Thembisa model, but is included to give a sense of the uncertainty around the model estimates. (It should be noted that because MicroCOSM is an individual-based stochastic model, much of the uncertainty represented by the IQR is in fact due to stochastic variation.)

Figure S14 compares the estimates of HIV incidence trends, in the same scenarios as described in the main text, for the two models. Estimates of HIV incidence in recent years tend to be slightly higher in MicroCOSM than in Thembisa. In this 'no intervention' counterfactual scenario, incidence rates level off at around 3% per annum in Thembisa, but continue to increase in MicroCOSM. This could be due to higher levels of heterogeneity in HIV acquisition risk in Thembisa than in MicroCOSM. In the absence of interventions, HIV incidence rates eventually level off (and can even decline) because once most of the high-risk individuals are infected there are relatively few high-risk individuals left in the HIV-negative population, and hence the rate of HIV acquisition in the HIV-negative population slows down. More heterogeneity in HIV acquisition risk therefore implies an earlier peak in HIV incidence in the 'no intervention' counterfactual [50]. Although it may seem paradoxical that heterogeneity in HIV acquisition risk might be greater in Thembisa than in MicroCOSM, given the previously noted differences in the modelling of condoms and viral load, there is in fact more

heterogeneity in rates of short-term partner turnover in the Thembisa model than in MicroCOSM.

The estimates of HIV incidence in the baseline scenario follow a more similar trend, peaking around the start of 2000 (at 2.2% in Thembisa and 2.3% in MicroCOSM) and declining to relatively low levels by 2016-17 (1.0% in Thembisa and 1.3% in MicroCOSM). The higher HIV incidence estimates in MicroCOSM may be because MicroCOSM is not calibrated to mortality data; we have previously shown that when Thembisa is not calibrated to mortality data, it produces higher estimates of HIV prevalence and substantially higher estimates of AIDS mortality [59], both of which would imply an over-estimation of HIV incidence. The impact of HIV testing services appears to be substantially greater in Thembisa than in MicroCOSM, which may be because of the previously-noted differences in the modelling of behaviour change after HIV diagnosis. In Thembisa the absolute difference in HIV incidence between the 'no ART' and 'no ART or HTS' scenarios in 2016-17 is 0.46%, with a wide 95% confidence interval (0.20-0.72%), which reflects the wide range of uncertainty around the proportionate reduction in unprotected sex after diagnosis (Table S16). The lower limit of this confidence interval is consistent with the 0.2% absolute difference between the 'no ART' and 'no ART or HTS' scenarios in MicroCOSM.

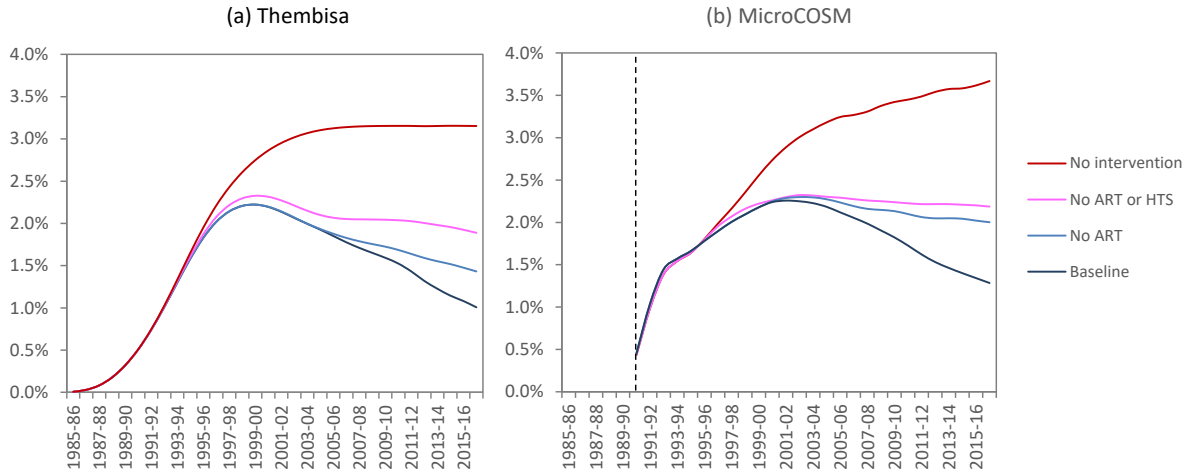

Figure S14: HIV incidence trends in 15-49 year olds, under different scenarios
In MicroCOSM, HIV is only introduced into the population in 1990, hence HIV incidence rates are not shown prior to 1990 (dashed line in panel b). Because of stochastic variation in MicroCOSM, the estimates of HIV incidence in the counterfactual scenarios are sometimes slightly lower than those in the baseline scenario. ART = antiretroviral treatment, HTS = HIV testing services.

Table S17 compares key indicators calculated from the two models. The HIV incidence decline over the 2000-2017 period is estimated to be greater in Thembisa than in MicroCOSM (55% versus 41%). The two models produce similar estimates of the HIV incidence reduction in 2017 that is attributable to interventions (68% in Thembisa versus 65% in MicroCOSM). However, the relative significance of different interventions is different: Thembisa estimates a greater reduction in incidence due to condoms and HIV testing (compared to MicroCOSM), and a slightly smaller reduction in incidence due to ART. These differences may be due to the previously mentioned greater heterogeneity in condom use in MicroCOSM. When we considered an alternative MicroCOSM specification in which the probability of condom use was the same in all individuals (after controlling for age, sex and relationship, as in Thembisa), the MicroCOSM estimates of the impact of condom use increased substantially (to 63%), while

the modelled impact of ART on HIV incidence reduced slightly (to 34%) and the combined effect of ART and HIV testing increased to 46%. The difference between the 46% and the 34%, which represents the impact of HIV testing, is more consistent with Thembisa. The default MicroCOSM assumption is that the standard deviation in condom preferences, across individuals, is 1.4 time the mean condom preference, which implies quite extreme variation in condom preferences. Although based on local evidence regarding consistency of condom use across different relationships [170, 171], the assumption needs to be treated with caution, as self-reporting of consistency in condom use across relationships may well be affected by social desirability bias and recall bias.

Table S17: Comparison of estimates of HIV incidence in 15-49 year olds

	Thembisa (mean, 95% CI)	MicroCOSM (mean, IQR)
HIV incidence, start of 2000	2.22% (2.15-2.29%)	2.18% (2.03-2.33%)
HIV incidence, start of 2010	1.59% (1.52-1.69%)	1.82% (1.68-2.00%)
HIV incidence, start of 2017	1.01% (0.91-1.13%)	1.28% (1.15-1.42%)
Reduction in incidence, 2000-2017	55% (47-59%)	41% (34-48%)
Reduction in incidence, 2010-2017	37% (32-41%)	29% (25-35%)
Reduction in incidence at start of 2017		
Due to increased condom use	48% (45-53%)	42% (39-46%)
Due to VMMC	6% (6-6%)	6% (-1-13%)
Due to ART	30% (28-31%)	36% (32-40%)
Due to ART and HTS	46% (37-54%)	41% (37-46%)
Due to all interventions	68% (62-72%)	65% (63-67%)
Reduction in incidence at start of 2008		
Due to increased condom use	38% (35-42%)	36% (33-39%)
Due to ART	4% (4-5%)	8% (4-12%)
Due to ART and HTS	16% (11-22%)	10% (6-18%)
Due to all interventions	46% (42-48%)	40% (37-43%)

In the interests of comparison with our previous estimates of HIV incidence declines over the period up to the start of 2008 [50], we also compare in Table S17 the model estimates of HIV incidence reductions due to interventions at the start of 2008. (VMMC is not included here as it was only introduced in 2008.) Both models suggest a 36-38% reduction in incidence rates at the start of 2008 due to increased condom use, consistent with our previous estimates of 23-37%, based on two earlier models, the STI-HIV Interaction model and the ASSA2003 model. These two models also estimated that by the start of 2008 HIV incidence rates had reduced by 1-8% as a result of ART, again consistent with the results of the MicroCOSM and Thembisa models in Table S17.

3.6 Comparison with condom distribution data

Data on total numbers of male condoms distributed by the Department of South Africa have been regularly published [18, 172-178]. For the sake of simplicity we do not include data on female condom distribution, which are less complete, and which account for only a small fraction of total condom distribution. It is also not possible to obtain data on private purchase of condoms. Figure S15a shows the total numbers of male condoms distributed: these have increased from very low levels in the mid-1990s to around 800 million condoms per annum in the 5 most recent years.

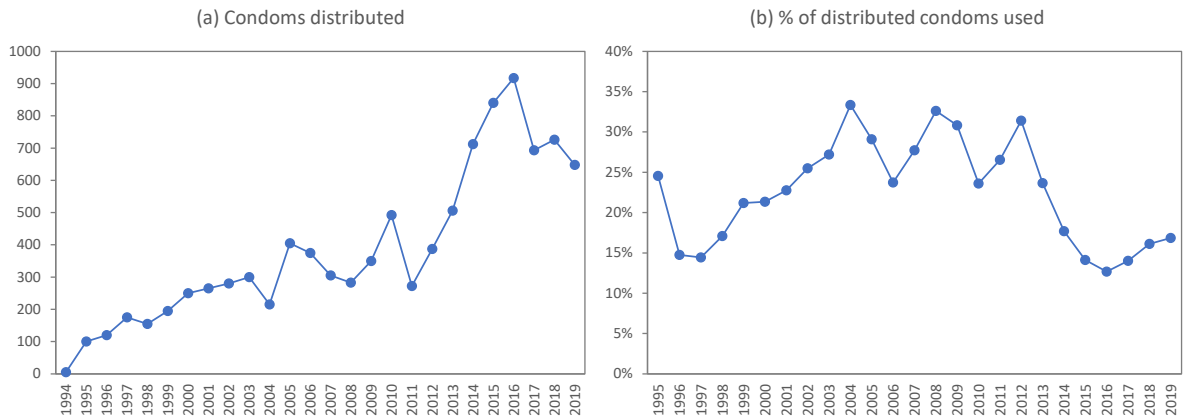

Figure S15: Male condom distribution in South Africa
In panel b the proportion of condoms used is calculated as the ratio of the modelled number of protected sex acts in a year to the average annual number of male condoms distributed in that year and the previous year (to account for delays between condom distribution and use).

These distributed numbers of condoms can be compared to our model estimates of the numbers of sex acts in which condoms are used. Figure S15b shows the ratio of the number of protected sex acts to the number of male condoms distributed, which might be crudely interpreted as the fraction of condoms distributed that are actually used. This proportion has been 30% on average, ranging from 18% to 44%. These proportions may appear too low, particularly when compared against a 1998-99 survey, which found the proportion of condoms used to be 44% [179]. However, this survey was based on interviewing individuals who had been given condoms, and may therefore have suffered from the same social desirability biases described earlier. It is also possible that many condoms 'distributed' (i.e. placed in facilities) might never be taken, and hence interviewing individuals who have taken condoms may give a biased indication of the proportion of condoms that are used. Our results are more consistent with studies conducted in other African countries, in which condom distribution figures have been compared against self-reported data on frequency of protected sex. In these surveys the reported numbers of protected sex acts have typically been only a small fraction of the numbers of condoms distributed [180].

The proportion of condoms used (Figure S15b) does not appear to follow a clear trend over time. However, there appears to have been a substantial drop in this ratio since 2011-12, coinciding with substantial increases in condom distribution. This drop could be interpreted as condom distribution having reached a 'saturation point', i.e. it is possible that there are diminishing marginal returns as condom distribution is scaled up. Alternatively, it is possible that the model is understating the rate of growth in condom use in recent years, despite being calibrated to recent condom use data from the 2016 DHS and 2017 HSRC survey (see section 2.2.1). If this were the case, the actual proportion of condoms used over the 2013-2019 period might be higher than shown in Figure S15b.

It is also possible that the decline in the proportion of condoms used may reflect a decline in HIV communication programmes. Although it is true that expenditure on social and behaviour change communication has reduced in the three most recent years, this happened well after the declines in the proportion of condoms used (Table S18). This suggests that declines in funding for social marketing around condoms are unlikely to be the primary reason for the relatively low proportion of condoms used in recent years.

Table S18: Nominal annual expenditure on social and behaviour change communication programmes, from all funding sources, in South African rands

2009/10	2011/12	2012/13	2013/14	2016/17	2017/18	2018/19	2019/20
83 005 764	247 211 514	262 726 025	319 492 166	302 768 785	176 050 103	127 732 781	162 200 773

Sources: National AIDS Spending Assessments, Investment Case expenditure tracking [181, 182]. Amounts are not adjusted for inflation.

4. Trends in other sexual risk behaviours: a review

Although there is strong evidence of increases in condom use in South Africa, since the mid-1990s, evidence of other forms of behaviour change is conflicting. In this section we review the data on other risk behaviours and consider whether there is evidence of behaviour change. For the sake of consistency with the analysis of the condom data, we focus mainly on nationally-representative household-based surveys.

4.1 Age at sexual debut

Previous reviews of South African data have concluded that evidence of recent changes in age at sexual debut is conflicting [183, 184]. However, over longer time scales there appears to be a trend toward earlier sexual debut when comparing those born before 1990, with a possible reversal of this trend in the 1990-1994 birth cohort [183]. These previous reviews did not consider more recent survey data, after 2009, and thus do not reflect the possible impact of the rollout of ART and other changes to HIV programmes in recent years. Different national surveys have assessed age at sexual debut in different ways, and it is therefore difficult to compare the results of all the surveys using the same metric. Here we consider five different approaches to assess trends in the age at sexual debut.

The first is to consider the data from the five national households conducted by the Human Sciences Research Council (HSRC). The five surveys have been compared in terms of the fraction of 15-24 year olds who report ‘early sexual debut’ (sex before age 15) [15]. The surveys suggests that in males this proportion remained stable over the 2002-2008 period, but then increased substantially in the 2012 and 2017 surveys, while in women there was only a modest increase in this proportion in the most recent survey (Figure S16a).

The second approach is to compare the three DHSs, which all asked women aged 25-49 at which age they had begun sexual activity. Figure S16b shows the cumulative proportion sexually experienced by each age, as reported in the three DHSs. The results from the first two DHSs (in 1998 and 2003) were similar, but the most recent DHS suggests that there has been a shift toward earlier sexual debut in recent years.

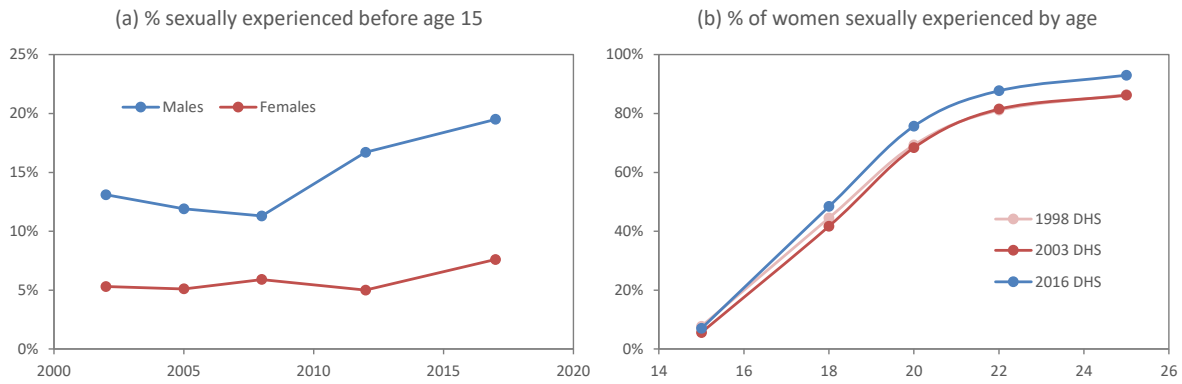

Figure S16: Trends in sexual debut
Data in panel a are from the HSRC household surveys [15].

A third approach is to conduct a survival analysis of the time to sexual debut, and to assess whether there is a difference in rates of sexual debut across birth cohorts. We apply a Cox regression model to the 2016 DHS data, censoring individuals at their current age if they are not yet sexually experienced, and treating age as a continuous variable. In this analysis, the rate of sexual debut was found to be significantly lower in men in recent birth cohorts (HR 0.92 per 10-year increase in age, 95% CI: 0.89-0.95). In women there was no significant effect of birth cohort in a simple linear model (HR 1.02 per 10-year increase in age, 95% CI 0.99-1.04), but when considering a quadratic model the effect of birth cohort became significant (in women aged 25-44 there has been a trend towards earlier sexual debut over time, but in women aged 15-24 the trend has been in the opposite direction).

A fourth approach is to assess the changes between the 2002 and 2008 Youth Risk Behaviour Surveys [185, 186]. Both surveys were conducted among high school students, and in both cases questionnaires were self-administered. This is in contrast to most other surveys, which rely on face-to-face interviews, an important distinction in view of the concern that face-to-face interviews are more susceptible to social desirability bias [187, 188]. Between 2002 and 2008 there appeared to be a slight reduction in the proportion of males and females reporting sexual experience, at almost all ages (Figure S17). It is worth noting here that the proportions sexually experienced at age 15 (an age at which almost all South African youth are at school) are substantially higher than those in Figure S16, which confirms that there is likely to be substantial social desirability bias in the context of face-to-face interviews. (After age 15 school dropout becomes increasingly common, and the survey respondents thus become less representative of the general population at each age.)

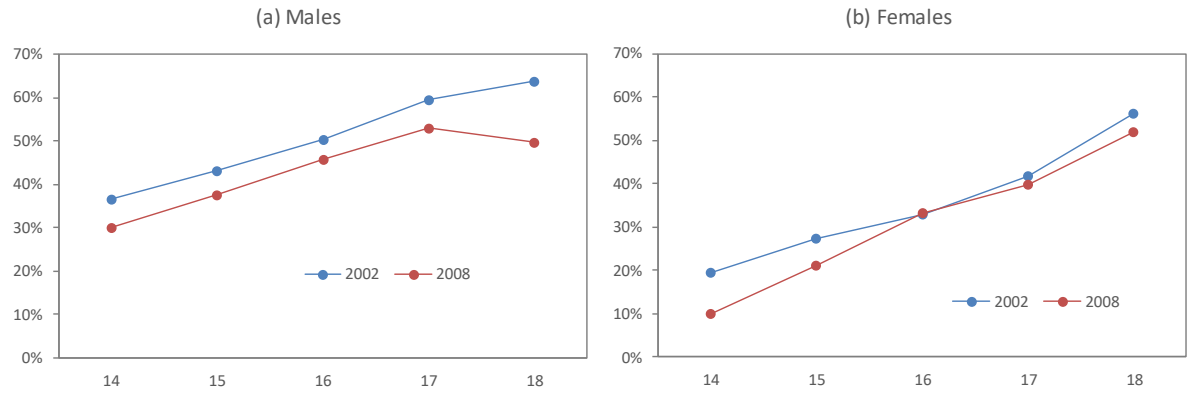

Figure S17: Proportion of youth who are sexually experienced, in the National Youth Risk Behaviour Surveys

Finally we compare the proportion of youth who report previous sexual experience in the 2006 and 2009 National HIV Communication Surveys [11, 189]. On the whole there appears to have been little change in sexual experience between the two surveys (Figure S18).

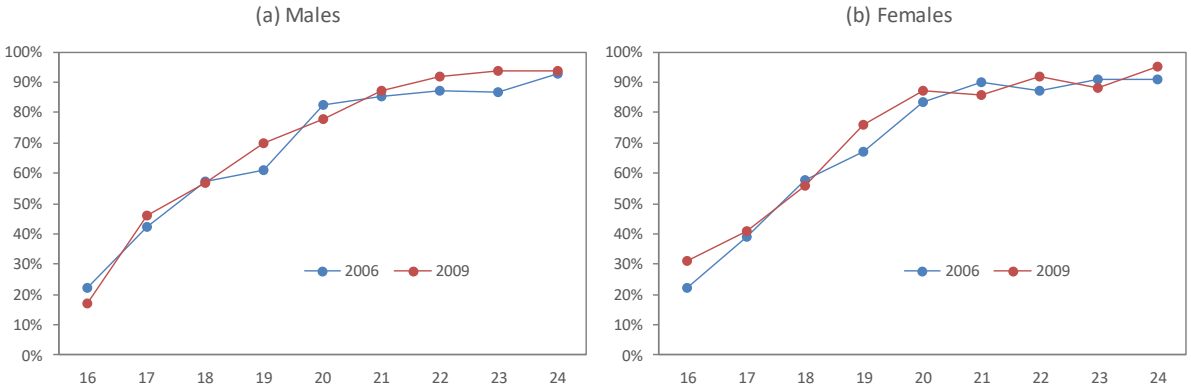

Figure S18: Proportion of youth who are sexually experienced, in the National HIV Communication Surveys

In summary, the evidence from these five different data sources and analytic approaches do not appear to tell a consistent story. In males there appears to have been little change in sexual debut in the period before 2008 (and there may even have been a decline), but the 2016 DHS and HSRC data suggest that there may have been a shift towards earlier male sexual debut in the period after 2008. In women, the 2016 DHS finding of a trend towards earlier sexual debut in women aged 25-44 (who would have mostly begun sexual activity between 1990 and 2010) is inconsistent with the other data sources (most notably the HSRC and Youth Risk Behaviour surveys, which found either no clear trend or a trend towards later sexual debut in the period up to 2010). Similarly, the 2016 DHS finding of a shift towards later sexual debut in the youngest birth cohort appears inconsistent with the findings of the HSRC surveys, in which the proportion of young women reporting early sexual debut increased in 2017.

4.2 Secondary abstinence

Secondary abstinence is defined as no sexual activity in the last 12 months, among individuals who are sexually experienced. This is a less frequently reported indicator, and hence it is difficult to assess whether this has changed over time. A previous review combined the data from five national surveys over the 2002-2009 period [183]; to these we have added the data from the 2016 DHS (Figure S19a). The data collected before 2009 suggest a possible trend towards increasing secondary abstinence, both in males and females. However, the levels of secondary abstinence reported in the 2016 DHS are substantially lower than those reported in the 2002-2009 surveys.

A limitation of this analysis is that it considers a broad age grouping (ages 16-55) and it is not clear how much of the change over time might be due to changes in age and/or marriage. We therefore consider an alternative analysis in which we focus only on youth aged 15-24, drawing on data from the 1998 and 2016 DHSs, the 2002 and 2005 HSRC surveys and a 2003 national youth survey [8]. In this analysis, trends are similar to those noted previously: over the 1998-2005 period there appears to have been a trend towards increasing secondary abstinence, but the levels of secondary abstinence reported in the 2016 DHS are substantially lower than those reported up to 2005 (Figure S19b).

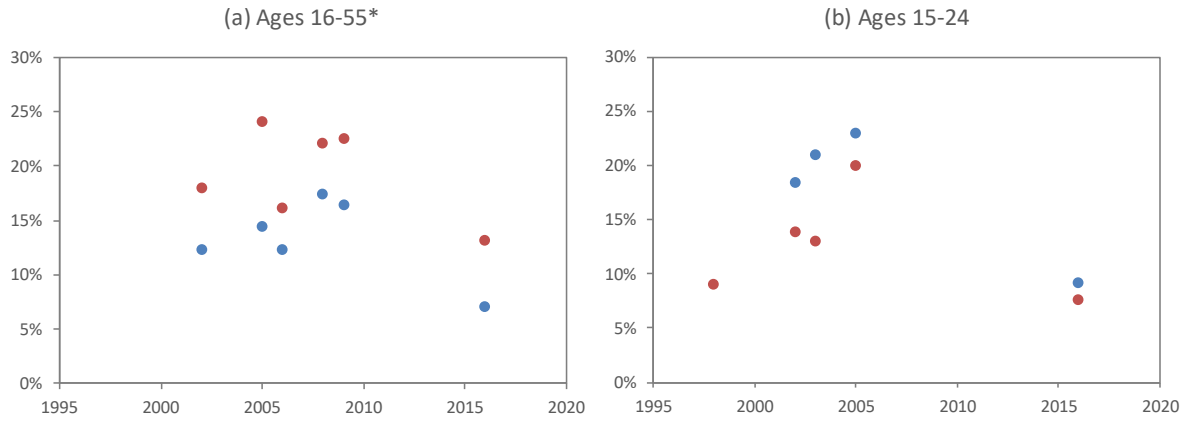

Figure S19: Proportions of sexually experienced individuals who report no sexual activity in the last 12 months (secondary abstinence)
Results for males are in blue and results for females are in red. * Results from the 2016 DHS are for the 15-49 age group, not the 16-55 age group.

Taken together, these results suggest a trend towards increased secondary abstinence in South Africa, over the period in which AIDS mortality was rapidly increasing (1998-2006), but possibly a decline in secondary abstinence thereafter. It is difficult to be confident about the latter decline, as the 2016 DHS is the only recent survey that has reported secondary abstinence.

4.3 Multiple sexual partners

Several surveys have included questions about numbers of sexual partners in the last year. Here we consider the proportion of sexually active adults (i.e. sexually active in the last year) who report more than one partner in the last year. Figure S20 shows the results stratified by sex and age group. In youth (ages 15-24) there is no strong evidence of a change in reporting of multiple partnerships over time. In adults aged 15-49 there are fewer data points, and the proportions

reporting multiple partnerships are substantially lower than in youth, for both sexes. Although there appears to have been a slight trend towards increased reporting of multiple partnerships in both sexes, this might not be due to behaviour change at the individual level. Mathematical models predict that even in the absence of behaviour change at the individual level, average rates of partner change would drop in the early stages of the HIV epidemic (before the introduction of ART), because individuals with higher rates of partner change are more likely to acquire HIV and die from AIDS [36, 190]. Conversely, models predict that after the rollout of ART, even in the absence of behavioural disinhibition, increases in average rates of partner change would be observed due to the longer survival of individuals with higher rates of partner change [190]. One would expect these changes to be more significant in older adults (in whom the cumulative impact of AIDS mortality is greatest) than in younger adults, which might explain the lack of any increase in numbers of partners in younger adults.

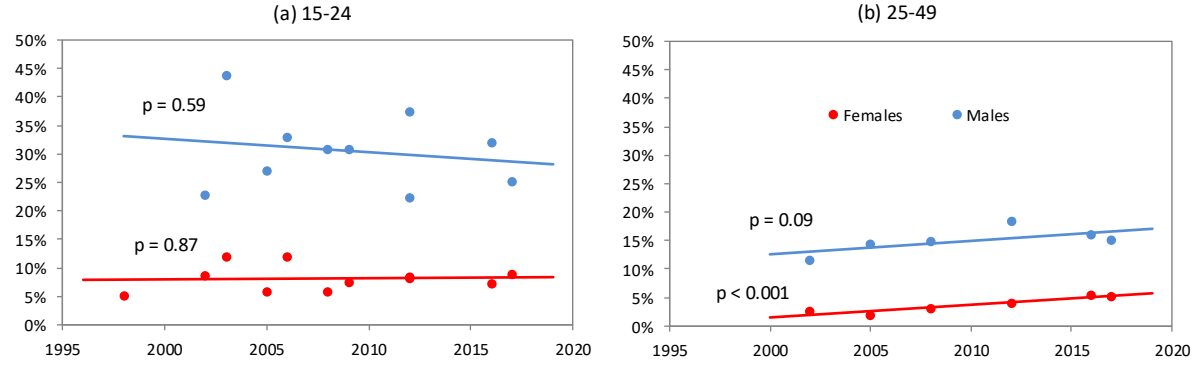

Figure S20: Proportion of sexually active individuals reporting multiple partners in the last 12 months

Dots represent estimates from nationally representative surveys (men in blue, women in red). Solid lines represent simple linear regression models fitted to the data points, with the p values representing the significance of the gradient in each case (a $p < 0.05$ indicates the gradient is significantly different from zero).

It is also possible that the increase in the proportion of individuals who report multiple partners might be due to long-term declines in rates of marriage in South Africa [40, 41], since married individuals are less likely to report multiple partners. A previous review of trends in sexual risk behaviour in South Africa found that although there was some evidence of a trend towards more reporting of multiple partners over time in men, this ceased to be significant after controlling for age and marital status [183], suggesting that declining rates of marriage might be part of the explanation for the changes in the reporting of multiple partnerships. Our model estimates that over the 1990-2015 period there is little change in the proportion of sexually-experienced 15-24 year olds who have more than one new partner in a year: a 7% decline in males and a 7% increase in females (Figure S21, solid lines). However in adults aged 25-49 there is a clearer increase in the proportion with more than one new partner in a year: an 11% increase in males and a 13% increase in females. The fact that we see this increase in older adults but not in younger adults is probably because rates of marriage in 1995 were low in youth (especially male youth) but higher at older ages, and thus any reduction in marriage rates after 1995 would have had negligible impact on average rates of partner acquisition at younger ages. This is confirmed when we consider a counterfactual analysis in which marriage rates are assumed to remain constant over time: in this scenario, the proportions with multiple partners would have been expected to decline by 14% and 4% in male and female youth respectively, and by 9% and 8% in males and females aged 25-49 (i.e. the relative change in multiple partnerships due to changing marriage rates is greater in the 25-49 age group than in the 15-24

age group). The model trends in Figure S21 are roughly consistent with the empirical trends in Figure S20.

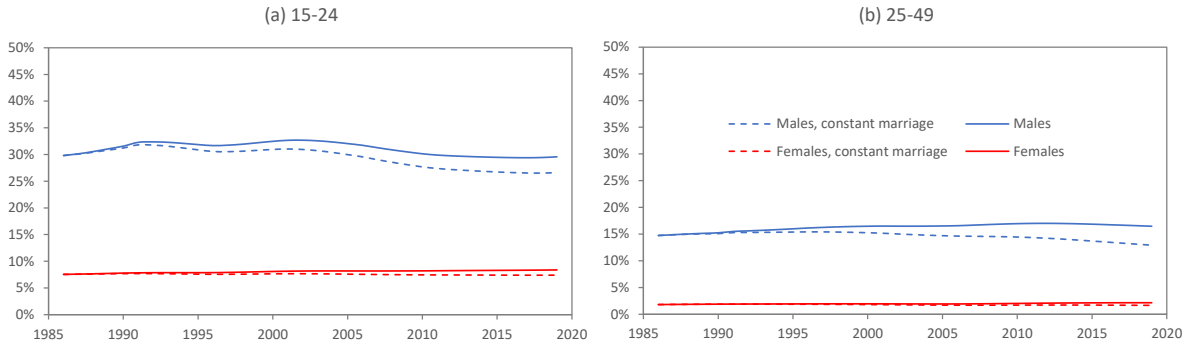

Figure S21: Model estimates of the proportion of sexually-experienced individuals who have more than one new partner in a year

Solid lines represent the main scenario, and dashed lines represent the counterfactual scenario in which marriage rates are assumed to remain constant over time. Model estimates are calculated on the assumption than in each age/sex/marital status/risk group compartment the number of new partners in a year is Poisson-distributed, with the mean of the Poisson distribution equal to the average annual rate of partner acquisition in that compartment.

4.4 Age-disparate partnerships

Age-disparate relationships are usually defined as relationships with partners who are 5 or more years younger (or older). Figure S22a shows the trend in the proportion of sexually active women aged 15-19 who report having an age-disparate partner, and Figure S22b shows the same trend in women aged 15-24 (different surveys report on different indicators, but these are the two most commonly compared indicators). In both cases there appears to be some evidence of an increase in age-disparate relationships after 2006, although this conclusion depends very much on the 2005 HSRC survey, which found the proportion of young women reporting age-disparate relationships to be much lower than in older women, in contrast to other surveys [9], which have found female reporting of age-disparate relationships to be more uniform across age groups [11]. Although the results of the 2006 National Communication Survey (Figure S22b) appear to confirm the relatively low levels of age-disparate partnerships around 2005, the results of this survey were reported inconsistently: at 25% in one publication [11] and at 38% in another [189].

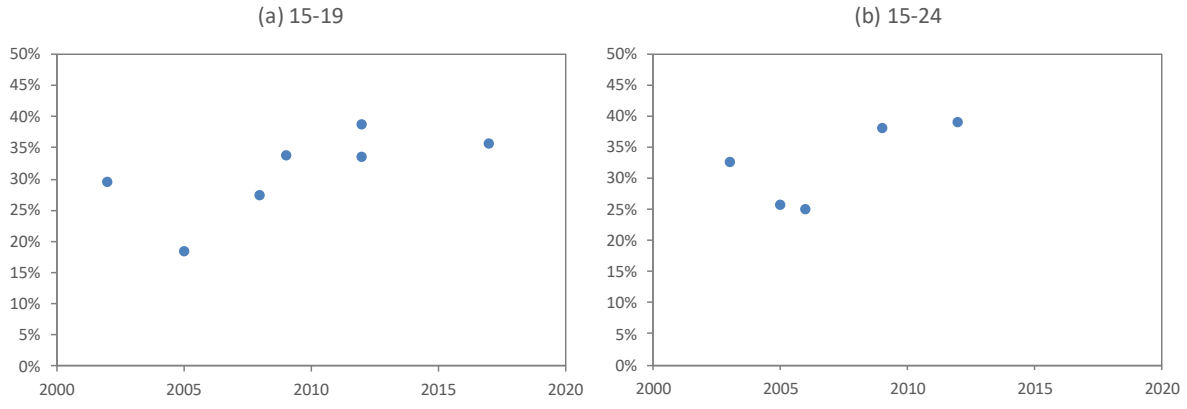

Figure S22: Proportion of young women reporting age-disparate relationships

4.5 Implications for Thembisa

In the Thembisa model we currently make provision for changes over time in rates of condom use (as described in section 2.2) and changes in rates of marriage (described in section 2.3). Because married individuals have lower rates of partner acquisition, the modelled trends towards lower rates of marriage imply a trend towards increased proportions of sexually active individuals with multiple partners (Figure S21), particularly in older age groups. However, the model makes no provision for exogenous changes in rates of partner acquisition (i.e. after controlling for age, sex, risk group and marital status, rates of short-term partnership formation are assumed to be constant over time). Similarly there is no assumption of any exogenous change over time in rates of sexual debut or partner age preferences. The evidence reviewed here does not strongly suggest that such changes have occurred, although the possibility of such changes should not be ruled out. If there has indeed been a trend towards increased levels of sexual risk behaviour in recent years (for example, due to earlier sexual debut or more age-disparate relationships), it is likely that Thembisa is either (a) under-estimating HIV incidence in recent years or (b) correctly estimating incidence but under-estimating the extent to which interventions have reduced HIV incidence in recent years.

5. Comparison with other estimation approaches

5.1 Alternative approaches to estimating HIV incidence

The gold standard in the estimation of HIV incidence is to repeatedly test the same group of individuals at regular intervals, and thus to directly identify seroconverters. This longitudinal approach has been applied both in community-wide studies and in studies of sub-populations (e.g. pregnant women, participants in randomized trials) [191, 192]. The main advantage of this approach, over our model-based approach, is that incidence is directly measured, without having to rely on model assumptions. However, applying this approach at a population level comes with challenges:

- Because of the expense of regularly testing individuals, it is usually only feasible to conduct such studies in narrowly defined geographical areas, and results might therefore not be nationally (or even regionally) representative.
- In settings where there are high rates of in- and out-migration it may be challenging to track the same cohort of individuals over time. If individuals who migrate are at increased risk of HIV, as some studies suggest [193], the difficulties associated with tracking these individuals could introduce a bias.
- In some cohorts, the small numbers of seroconversions that occur on an annual basis make it difficult to separate out statistical ‘noise’ from the true trend in HIV incidence.

In South Africa, a number of such studies have been conducted to estimate HIV incidence trends. Our incidence estimates are generally lower than those measured in these studies, both population-based studies [194, 195] and randomized trials [196-198]. However, these studies have almost all been conducted in KwaZulu-Natal, the province with the highest HIV prevalence in South Africa [15], and individuals recruited into HIV prevention trials are generally selected on the basis of high HIV risk behaviour. These incidence estimates are therefore not directly comparable with our estimates for South Africa as a whole.

Another HIV incidence approach that is widely used is to estimate HIV incidence from cross-sectional survey data, using novel assays that detect recent infection [199]. This requires assumptions about the average time that individuals remain classified as 'recently infected' by the assay, and the probability of a 'false recent' test result. This approach has the advantage that it is less costly (because it is not necessary to follow the same cohort of individuals over time) and can be more feasibly applied in producing nationally-representative estimates of HIV incidence. However, there are a number of challenges:

- The mean duration of recent infection can vary across settings [199], which introduces uncertainty into the estimation of HIV incidence.
- The false recent rate can also vary across settings, although most recent applications have relied on additional viral load and/or ART testing to exclude individuals who are unlikely to be recently infected, which helps to reduce the uncertainty due to 'false recent' test results.
- The above-mentioned exclusion of individuals who are on ART/virally suppressed could potentially introduce bias, particularly in the context of universal ART eligibility and high rates of HIV testing. Many seroconverters are likely to be diagnosed and start ART within a year of seroconversion, and excluding these individuals from the incidence calculation could lead to HIV incidence being under-estimated.

A number of previous South African studies have used this approach, both at a national level [15, 200, 201], and in smaller community surveys [202]. As noted in the main text, our recent model estimates of HIV incidence in South Africa are slightly higher than those estimated nationally using this approach [15, 201]. This difference could be due to biases in our model, or to the above-mentioned source of bias in the survey-based estimates.

A third possible HIV incidence approach is the 'synthetic cohort' approach [203]. This relies on age-specific HIV prevalence data from two cross-sectional surveys to estimate levels of HIV incidence over the inter-survey period, based on assumptions about mortality rates in people living with HIV. As with the previous approach, this approach has the advantage of being relatively inexpensive and appropriate in producing nationally-representative estimates. However, there are again challenges:

- Because HIV prevalence estimates have wide confidence intervals around them, the change in HIV prevalence between two surveys (which is the basis of the incidence estimate) has even wider confidence intervals. This means that these HIV incidence estimates are typically very imprecise [200].
- HIV incidence estimates can be sensitive to assumptions about HIV mortality rates, which are often very uncertain. For example, the estimate of HIV incidence in South Africans aged 15-49 over the 2005-2008 period, based on the synthetic cohort approach, changed from 1.3 per 100 person years [204] to 1.9 per 100 person years [200] as a result of changes to HIV survival assumptions.

Previous estimates of HIV incidence in South Africa, based on the synthetic cohort approach, are generally quite consistent with our model estimates, as shown in Figure 2a of the main text (the first three data points).

All of the previously described approaches can be used to produce estimates of changes over time in HIV incidence, at a population level. However, none of these approaches is able to assess how much of the change in incidence is attributable to the impact of different interventions. A major advantage of a model-based approach is that it allows us to estimate the impact of interventions on HIV incidence, based on comparing the model estimates of the

actual HIV incidence trends to the model estimates of what the incidence trend would have been in the absence of the intervention(s) of interest. Another major advantage of the modelling approach is that it allows us to combine multiple data sources (HIV prevalence data from household surveys and antenatal surveys, HIV programme data, mortality data and behavioural data) in the estimation of HIV incidence, whereas the other estimation approaches typically rely on a single data source. This inclusion of a greater range of data sources improves the precision of the model-based estimates and also reduces the risk of bias.

A major limitation of using a dynamic modelling approach to estimating HIV incidence is that estimates can be sensitive to assumptions about model structure. For example, in Thembisa we divide the population into 'high-risk' and 'low-risk' group, defined in terms of propensity for risk behaviour, but we do not allow for movement between the high-risk and low-risk groups over time. Due to the potential sensitivity of model results to structural assumptions, it is advisable to compare the estimates of different models (as we have done in section 3.6).

5.2 Alternative approaches to estimating population-level impact of HIV interventions

Although we have emphasized the value of mathematical modelling in evaluating the population-level impact of interventions, it is sometimes suggested that this impact can also be estimated through cluster-randomized controlled trials, in which the clusters are communities that are randomly assigned to be intervention or control communities. In sub-Saharan Africa, there have been a number of such trials to evaluate the impact of improved treatment for sexually transmitted infections [205, 206], community-based HIV testing [207], and 'treatment as prevention' [208-211]. Our model estimate of a modest population-level impact of HIV testing on HIV incidence is roughly consistent with the one cluster-randomized trial of this intervention, which found a non-significant 14% reduction in HIV incidence [207]. However, our model estimates of the population-level impact of ART on HIV incidence are much more substantial than those measured in the 'treatment as prevention' trials, two of which found no material reduction in HIV incidence due to ART [208, 210]. There are a number of reasons why the 'disappointing' results of the treatment as prevention trials are unlikely to reflect the true population-level impact of ART, and these reasons have been extensively discussed in previous commentaries [212-215]. Firstly, most of these trials assess the impact of changes in ART eligibility criteria, rather than the impact of ART *per se*. For example, the ANRS 12249 trial, which produced a null result [208], evaluated only the effect of a change in ART eligibility criteria, i.e. comparing universal ART eligibility to restricted ART eligibility, rather than comparing ART to no ART. Secondly, ART eligibility criteria in the control arms changed towards universal ART eligibility over the course of the trials, and this may have contributed to the relatively modest differences between intervention and control arms in these trials [212-214]. Thirdly, cluster RCTs of HIV interventions are usually conducted in contexts where individuals are highly mobile, often having sexual partners outside of the clusters in which the intervention is being tested, and this may cause a dilution of the intervention effect [212, 214, 215]. Finally, the population-level impact of an intervention is often greater over the long term than over the short term [216], but due to resource constraints, cluster-randomized trials typically only evaluate HIV incidence impacts over the short term.

References

1. Johnson LF, Dorrington RE. Thembisa version 4.4: A model for evaluating the impact of HIV/AIDS in South Africa. Centre for Infectious Disease Epidemiology and Research, University of Cape Town; 2021. Available: https://www.thembisa.org/
2. Johnson LF, Dorrington RE. Thembisa version 4.2: A model for evaluating the impact of HIV/AIDS in South Africa. University of Cape Town; 2019. Available: https://www.thembisa.org/
3. Trussell J. Contraceptive failure in the United States. *Contraception* 2011; **83**:397-404.
4. Mostert WP. Recent trends in fertility in South Africa. In: *South Africa's Demographic Future*. Edited by Mostert WP, Lötter JM. Pretoria: Human Sciences Research Council; 1990.
5. Department of Health. South Africa Demographic and Health Survey 1998: Full Report. 1999.
6. Human Sciences Research Council. South African national HIV prevalence, behavioural risks and mass media household survey 2002. 2002. Available: http://www.hsrcpress.ac.za. Accessed 18 Feb 2009
7. Department of Health. South Africa Demographic and Health Survey 2003: Preliminary Report. Pretoria; 2004. Available: http://www.doh.gov.za/docs/reports/2003/sadhs2003/part2.pdf. Accessed 6 Jan 2012
8. Pettifor AE, Rees HV, Steffenson A, Hlongwa-Madikizela L, MacPhail C, Vermaak K, *et al.* HIV and sexual behaviour among young South Africans: a national survey of 15-24 year olds. Johannesburg: Reproductive Health Research Unit, University of Witwatersrand; 2004.
9. Shisana O, Rehle T, Simbayi LC, Parker W, Zuma K, Bhana A, *et al.* South African National HIV Prevalence, HIV Incidence, Behaviours and Communication Survey, 2005. Cape Town: HSRC Press; 2005. Available: http://www.hsrcpress.ac.za. Accessed 1 Dec 2005
10. Shisana O, Rehle T, Simbayi LC, Zuma K, Jooste S, Pillay-van Wyk V, *et al.* South African national HIV prevalence, incidence, behaviour and communication survey, 2008: A turning tide among teenagers? Cape Town: Human Sciences Research Council; 2009. Available: http://www.hsrcpress.ac.za. Accessed 9 June 2009
11. Johnson S, Kincaid L, Laurence S, Chikwava F, Delate R, Mahlasela L. Second National HIV Communication Survey 2009. Pretoria: Johns Hopkins Health and Education in South Africa; 2010. Available: http://jhhesa.org.za/docs/NCS_2009.pdf. Accessed 8 March 2011
12. Shisana O, Rehle T, Simbayi LC, Zuma K, Jooste S, Zungu N, *et al.* South African National HIV Prevalence, Incidence, and Behaviour Survey, 2012. Cape Town: Human Sciences Research Council; 2014. Available: http://www.hsrc.ac.za/en/research-outputs/view/6871. Accessed 16 April 2014
13. Johnson S, Kincaid DL, Figueroa ME, Delate R, Mahlasela L, Magni S. The Third National HIV Communication Survey, 2012. Pretoria: Johns Hopkins Health and Education in South Africa; 2013. Available: http://jhhesa.org/sites/default/files/hiv_survey.pdf. Accessed 19 April 2014
14. Department of Health, Statistics South Africa, South African Medical Research Council, ICF. South Africa Demographic and Health Survey 2016. Pretoria; 2019. Available: https://www.dhsprogram.com/pubs/pdf/FR337/FR337.pdf. Accessed 19 March 2019

15. Simbayi LC, Zuma K, Zungu N, Moyo S, Marinda E, Jooste S, *et al.* South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2017. Cape Town: Human Sciences Research Council; 2019. Available: https://www.hsrcpress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-and-communication-survey-2017. Accessed 6 Nov 2019
16. Press WH, Flannery BP, Teukolsky SA, Vetterling WT. Minimization or maximization of functions. In: *Numerical Recipes*. Cambridge: Cambridge University Press; 1986. pp. 274-334.
17. Collinge J. Confronting HIV and AIDS through mass media and community action. In: *South African Health Review 2005*. Edited by Ijumba P, Barron P. Durban: Health Systems Trust; 2005. pp. 202-223.
18. Myer L. Barrier methods. In: *HIV/AIDS in South Africa*. Edited by Abdool Karim SS, Abdool Karim Q. 2nd ed. Cape Town: Cambridge University Press; 2010. pp. 183-200.
19. Thurston IB, Dietrich J, Bogart LM, Otwombe KN, Sikkema KJ, Nkala B, *et al.* Correlates of sexual risk among sexual minority and heterosexual South African youths. *Am J Public Health* 2014; **104**:1265-1269.
20. Peltzer K. Sexual orientation and HIV risk among youth in South Africa: a brief report. *J Psychol Afr* 2014; **24**:241-245.
21. Eaton LA, Pitpitan EV, Kalichman SC, Sikkema KJ, Skinner D, Watt MH, *et al.* Men who report recent male and female sex partners in Cape Town, South Africa: an understudied and underserved population. *Arch Sex Behav* 2013; **42**:1299-1308.
22. Peltzer K, Seoka P, Raphala S. Characteristics of female sex workers and their HIV/AIDS/STI knowledge, attitudes and behaviour in semi-urban areas in South Africa. *Curationis* 2004; **March 2004**:4-11.
23. Richter ML, Chersich M, Temmerman M, Luchters S. Characteristics, sexual behaviour and risk factors of female, male and transgender sex workers in South Africa. *S Afr Med J* 2013; **103**:246-251.
24. Sex Worker Education and Advocacy Taskforce. Beginning to build the picture: South African national survey of sex worker knowledge, experiences and behaviour. 2013.
25. Delva W, Richter M, De Koker P, Chersich M, Temmerman M. Sex work during the 2010 FIFA World Cup: results from a three-wave cross-sectional survey. *PLoS One* 2011; **6**:e28363.
26. University of California San Francisco, Anova Health Institute, Wits Reproductive Health and HIV Research Institute. South African Health Monitoring Study (SAHMS), Final Report: The Integrated Biological and Behavioural Survey among Female Sex Workers, South Africa 2013-2014. San Francisco; 2015. Available: https://www.health-e.org.za/wp-content/uploads/2016/03/South-African-Health-Monitoring-Survey-An-Integrated-Biological-and-Behavioral-Survey-among-Female-Sex-Workers-South-Africa-2013-2014.pdf. Accessed 9 June 2016
27. Weinhardt LS, Carey MP, Johnson BT, Bickham NL. Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985-1997. *Am J Public Health* 1999; **89**:1397-1405.
28. Matovu JKB, Gray RH, Makumbi F, Wawer MJ, Serwadda D, Kigozi G, *et al.* Voluntary HIV counseling and testing acceptance, sexual risk behavior and HIV incidence in Rakai, Uganda. *AIDS* 2005; **19**:503-511.
29. Cremin I, Nyamukapa C, Sherr L, Hallett TB, Chawira G, Cauchemez S, *et al.* Patterns of self-reported behaviour change associated with receiving voluntary

counselling and testing in a longitudinal study from Manicaland, Zimbabwe. *AIDS Behav* 2010; **14**:708-715.
30. Cawley C, Wringe A, Slaymaker E, Todd J, Michael D, Kumugola Y, *et al.* The impact of voluntary counselling and testing services on sexual behaviour change and HIV incidence: observations from a cohort study in rural Tanzania. *BMC Infect Dis* 2014; **14**:159.
31. Fonner VA, Denison J, Kennedy CE, O'Reilly K, Sweat M. Voluntary counseling and testing (VCT) for changing HIV-related risk behavior in developing countries. *Cochrane Database Syst Rev* 2012:CD001224.
32. Tiwari R, Wang J, Han H, Kalu N, Sims LB, Katz DA, *et al.* Sexual behaviour change following HIV testing services: a systematic review and meta-analysis. *J Int AIDS Soc* 2020; **23**:e25635.
33. Pence BW, Whetten K, Shirey KG, Yao J, Thielman NM, Whetten R, *et al.* Factors associated with change in sexual transmission risk behavior over 3 years among HIV-infected patients in Tanzania. *PLoS One* 2013; **8**:e82974.
34. Doyle JS, Degenhardt L, Pedrana AE, McBryde ES, Guy RJ, Stoové MA, *et al.* Effects of HIV antiretroviral therapy on sexual and injecting risk-taking behavior: a systematic review and meta-analysis. *Clin Infect Dis* 2014; **59**:1483-1494.
35. Risher K, Rehle T, Simbayi L, Shisana O, Celentano DD. Antiretroviral treatment and sexual risk behavior in South Africa. *AIDS Behav* 2016; **20**:710-716.
36. Johnson LF, Dorrington RE, Bradshaw D, Pillay-Van Wyk V, Rehle TM. Sexual behaviour patterns in South Africa and their association with the spread of HIV: insights from a mathematical model. *Demographic Res* 2009; **21**:289-340.
37. Statistics South Africa. Marriages and divorces, 2004. Pretoria; 2006. Available: http://www.statssa.gov.za/publications/Report-03-07-01/Report-03-07-012004.pdf. Accessed 2 Aug 2008
38. Porter L, Hao L, Bishai D, Serwadda D, Wawer MJ, Lutalo T, *et al.* HIV status and union dissolution in sub-Saharan Africa: the case of Rakai, Uganda. *Demography* 2004; **41**:465-482.
39. Bah S. The improvement of marriages and divorces statistics in South Africa: Relevance, registration issues and challenges. Population Studies Centre, University of Western Ontario; 1999. Available: http://sociology.uwo.ca/popstudies/dp/dp99-2.pdf. Accessed 17 Oct 2006
40. Hosegood V, McGrath N, Moultrie T. Dispensing with marriage: Marital and partnership trends in rural KwaZulu-Natal, South Africa 2000-2006. *Demographic Res* 2009; **20**:279-312.
41. Posel D, Rudwick S. Changing patterns of marriage and cohabitation in South Africa. In: *Marriage, Land and Custom: Essays on Law and Social Change in South Africa*. Edited by Claassens A, Smythe D: Juta; 2013. pp. 169-180.
42. Garenne M. A century of nuptiality decline in South Africa: A longitudinal analysis of census data. *African Population Studies* 2016; **30**:2403-2416.
43. Clark S, Brauner-Otto S. Divorce in sub-Saharan Africa: Are unions becoming less stable? *Pop Dev Rev* 2015; **41**:583-605.
44. Reniers G. Divorce and remarriage in rural Malawi. *Demographic Res* 2003; **Special Collection 1**:175-206.
45. Budlender D, Chobokoane N, Simelane S. Marriage patterns in South Africa: Methodological and substantive issues. *South Afr J Demography* 2004; **9**:1-26.
46. Bennett S. Log-logistic regression models for survival data. *J Roy Stat Soc C-App* 1983; **32**:165-171.

47. Schoen R, Weinick RM. The slowing metabolism of marriage: figures from 1988 U.S. marital status life tables. *Demography* 1993; **30**:737-746.
48. Raftery AE, Bao L. Estimating and projecting trends in HIV/AIDS generalized epidemics using Incremental Mixture Importance Sampling. *Biometrics* 2010; **66**:1162-1173.
49. Johnson LF, Dorrington RE. Modelling the impact of HIV in South Africa's provinces: 2019 update. University of Cape Town; 2019. Available: https://www.thembisa.org/
50. Johnson LF, Hallett TB, Rehle TM, Dorrington RE. The effect of changes in condom usage and antiretroviral treatment coverage on HIV incidence in South Africa: a model-based analysis. *J Roy Soc Interface* 2012; **9**:1544-1554.
51. Garnett G, Anderson R. Sexually transmitted diseases and sexual behaviour: insights from mathematical models. *J Infect Dis* 1996; **174**:S150-S160.
52. Touloumi G, Pantazis N, Antoniou A, Stirnadel HA, Walker SA, Porter K. Highly active antiretroviral therapy interruption: predictors and virological and immunologic consequences. *J Acquir Immun Defic Syndr* 2006; **42**:554-561.
53. Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, *et al.* Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Infect Dis* 2012; **205**:358-365.
54. Prins M, Meyer L, Hessol NA. Sex and the course of HIV infection in the pre- and highly active antiretroviral therapy eras. *AIDS* 2005; **19**:357-370.
55. Lessells RJ, Mutevedzi PC, Cooke GS, Newell ML. Retention in HIV care for individuals not yet eligible for antiretroviral therapy: rural KwaZulu-Natal, South Africa. *J Acquir Immun Defic Syndr* 2011; **56**:e79-86.
56. Todd J, Glynn JR, Marston M, Lutalo T, Biraro S, Mwita W, *et al.* Time from HIV seroconversion to death: a collaborative analysis of eight studies in six low and middle-income countries before highly active antiretroviral therapy. *AIDS* 2007; **21 (Suppl 6)**:S55-63.
57. Collaborative Group on AIDS Incubation and HIV Survival. Time from HIV-1 seroconversion to AIDS and death before widespread use of highly-active antiretroviral therapy: a collaborative re-analysis. *Lancet* 2000; **355**:1131-1137.
58. Bhaskaran K, Hamouda O, Sannes M, Boufassa F, Johnson AM, Lambert PC, *et al.* Changes in the risk of death after HIV seroconversion compared with mortality in the general population. *JAMA* 2008; **300**:51-59.
59. Johnson LF, May MT, Dorrington RE, Cornell M, Boulle A, Egger M, *et al.* Estimating the impact of antiretroviral treatment on adult mortality trends in South Africa: a mathematical modelling study. *PLoS Med* 2017; **14**:e1002468.
60. Lodi S, Phillips A, Touloumi G, Geskus R, Meyer L, Thiébaut R, *et al.* Time from human immunodeficiency virus seroconversion to reaching CD4+ cell count thresholds <200, <350, and <500 cells/mm^3: assessment of need following changes in treatment guidelines. *Clin Infect Dis* 2011; **53**:817-825.
61. Lodi S, Phillips A, Touloumi G, Pantazis N, Bucher HC, Babiker A, *et al.* CD4 decline in seroconverter and seroprevalent individuals in the precombination of antiretroviral therapy era. *AIDS* 2010; **24**:2697-2704.
62. Erikstrup C, Kallestrup P, Zinyama R, Gomo E, Mudenge B, Gerstoft J, *et al.* Predictors of mortality in a cohort of HIV-1-infected adults in rural Africa. *J Acquir Immun Defic Syndr* 2007; **44**:478-483.
63. Isingo R, Zaba B, Marston M, Ndege M, Mngara J, Mwita W, *et al.* Survival after HIV infection in the pre-antiretroviral therapy era in a rural Tanzanian cohort. *AIDS* 2007; **21 (Suppl 6)**:S5-S13.

64. Hogg RS, Strathdee SA, Craib KJ, O'Shaughnessy MV, Montaner JS, Schechter MT. Lower socioeconomic status and shorter survival following HIV infection. *Lancet* 1994; **344**:1120-1124.
65. Pezzotti P, Phillips AN, Dorrucci M, Lepri AC, Galai N, Vlahov D, *et al.* Category of exposure to HIV and age in the progression to AIDS: longitudinal study of 1199 people with known dates of seroconversion. *BMJ* 1996; **313**:583-586.
66. Auvert B, Males S, Puren A, Taljaard D, Carael M, Williams B. Can highly active antiretroviral therapy reduce the spread of HIV? A study in a township of South Africa. *J Acquir Immun Defic Syndr* 2004; **36**:613-621.
67. Rehle TM, Shisana O. Estimates of eligibility for antiretroviral treatment (ART) and projected ART impact on AIDS mortality among South African educators. *SAHARA J* 2005; **2**:304-310.
68. Connelly D, Veriava Y, Roberts S, Tsotetsi J, Jordan A, DeSilva E, *et al.* Prevalence of HIV infection and median CD4 counts among health care workers in South Africa. *S Afr Med J* 2007; **97**:115-120.
69. Kranzer K, Lawn SD, Johnson LF, Bekker LG, Wood R. Community viral load and CD4 count distribution among people living with HIV in a South African township: implications for treatment as prevention. *J Acquir Immun Defic Syndr* 2013; **63**:498-505.
70. Malaza A, Mossong J, Bärnighausen T, Viljoen J, Newell ML. Population-based CD4 counts in a rural Area in South Africa with high HIV prevalence and high antiretroviral treatment coverage. *PLoS One* 2013; **8**:e70126.
71. van Rooyen H, Barnabas RV, Baeten JM, Phakathi Z, Joseph P, Krows M, *et al.* High HIV testing uptake and linkage to care in a novel program of home-based HIV counseling and testing with facilitated referral in KwaZulu-Natal, South Africa. *J Acquir Immun Defic Syndr* 2013; **64**:e1-8.
72. Huerga H, Maman D, Etard JF, Farhat JB, Bouhenia M. Mbongolwane and Eshowe HIV Impact in Population Survey. Epicentre and Medecins sans Frontieres; 2014.
73. Kharsany ABM, Cawood C, Khanyile D, Lewis L, Grobler A, Puren A, *et al.* Community-based HIV prevalence in KwaZulu-Natal, South Africa: results of a cross-sectional household survey. *Lancet HIV* 2018; **5**:e427-e437.
74. Johnson LF. Access to antiretroviral treatment in South Africa, 2004-2011. *South Afr J HIV Med* 2012; **13**:22-27.
75. Johnson LF, Dorrington RE. Thembisa version 4.1: A model for evaluating the impact of HIV/AIDS in South Africa. 2018.
76. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, *et al.* Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005; **191**:1403-1409.
77. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, *et al.* Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010; **375**:2092-2098.
78. Boily MC, Baggaley RF, Wang L, Masse B, White RG, Hayes RJ, *et al.* Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. *Lancet Infect Dis* 2009; **9**:118-129.
79. Johnson LF, Mossong J, Dorrington RE, Schomaker M, Hoffmann CJ, Keiser O, *et al.* Life expectancies of South African adults starting antiretroviral treatment: Collaborative analysis of cohort studies. *PLoS Med* 2013; **10**:e1001418.
80. Kaplan SR, Oosthuizen C, Stinson K, Little F, Euvrard J, Schomaker M, *et al.* Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: A cohort study. *PLoS Med* 2017; **14**:e1002407.

81. Clouse K, Vermund SH, Maskew M, Lurie MN, MacLeod W, Malete G, *et al.* Mobility and clinic switching among postpartum women considered lost to HIV care in South Africa. *Journal of Acquired Immune Deficiency Syndrome* 2017; **74**:383-389.
82. Kranzer K, Lewis JJ, Ford N, Zeinecker J, Orrell C, Lawn SD, *et al.* Treatment interruption in a primary care antiretroviral therapy program in South Africa: cohort analysis of trends and risk factors. *J Acquir Immun Defic Syndr* 2010; **55**:e17-23.
83. Johnson LF, Dorrington RE. Modelling the impact of HIV in South Africa's provinces: 2021 update. Centre for Infectious Disease Epidemiology and Research, University of Cape Town; 2021. Available: https://www.thembisa.org/
84. Weiss HA, Halperin D, Bailey RC, Hayes RJ, Schmid G, Hankins CA. Male circumcision for HIV prevention: from evidence to action? *AIDS* 2008; **22**:567-574.
85. Pettifor AE, Hudgens MG, Levandowski BA, Rees HV, Cohen MS. Highly efficient HIV transmission to young women in South Africa. *AIDS* 2007; **21**:861-865.
86. Auvert B, Ballard R, Campbell C, Caraël M, Carton M, Fehler G, *et al.* HIV infection in a South African mining town is associated with herpes simplex virus-2 seropositivity and sexual behaviour. *AIDS* 2001; **15**:885-898.
87. Baeten JM, Richardson BA, Lavreys L, Rakwar JP, Mandaliya K, Bwayo JJ, *et al.* Female-to-male infectivity of HIV-1 among circumcised and uncircumcised Kenyan men. *J Infect Dis* 2005; **191**:546-553.
88. Mahiane SG, Legeai C, Taljaard D, Latouche A, Puren A, Peillon A, *et al.* Transmission probabilities of HIV and herpes simplex virus type 2, effect of male circumcision and interaction: a longitudinal study in a township of South Africa. *AIDS* 2009; **23**:377-383.
89. Morison L, Weiss HA, Buvé A, Caraël M, Abega S-C, Kaona F, *et al.* Commercial sex and the spread of HIV in four cities in sub-Saharan Africa. *AIDS* 2001; **15**:S61-S69.
90. Gray R, Wawer M, Brookmeyer R, Sewankambo N, Serwadda D, Wabwire-Mangen F, *et al.* Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet* 2001; **357**:1149-1153.
91. Allen S, Tice J, Van de Perre P, Serufilira A, Hudes E, Nsengumuremyi F, *et al.* Effect of serotesting with counselling on condom use and seroconversion among HIV discordant couples in Africa. *BMJ* 1992; **304**:1605-1609.
92. Gilbert PB, McKeague IW, Eisen G, Mullins C, Guéye-NDiaye A, Mboup S, *et al.* Comparison of HIV-1 and HIV-2 infectivity from a prospective cohort study in Senegal. *Stat Med* 2003; **22**:573-593.
93. Kimani J, Kaul R, Nagelkerke NJ, Luo M, MacDonald KS, Ngugi E, *et al.* Reduced rates of HIV acquisition during unprotected sex by Kenyan female sex workers predating population declines in HIV prevalence. *AIDS* 2008; **22**:131-137.
94. Ramjee G, Williams B, Gouws E, Van Dyck E, De Deken B, Abdool Karim S. The impact of incident and prevalent herpes simplex virus-2 infection on the incidence of HIV-1 infection among commercial sex workers in South Africa. *J Acquir Immun Defic Syndr* 2005; **39**:333-339.
95. Ramjee G, Weber AE, Morar NS. Recording sexual behavior: comparison of recall questionnaires with a coital diary. *Sex Transm Dis* 1999; **26**:374-380.
96. Ramjee G, Gouws E. Prevalence of HIV among truck drivers visiting sex workers in KwaZulu-Natal, South Africa. *Sex Transm Dis* 2002; **29**:44-49.
97. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission (Cochrane Review). In: *The Cochrane Library*. Chichester, UK: John Wiley & Sons; 2004.

98. Chen L, Jha P, Stirling B, Sgaier SK, Daid T, Kaul R, *et al.* Sexual Risk Factors for HIV Infection in Early and Advanced HIV Epidemics in Sub-Saharan Africa: Systematic Overview of 68 Epidemiological Studies. *PLoS One* 2007; **2**:e1001.
99. Jin F, Jansson J, Law M, Prestage GP, Zablotska I, Imrie JC, *et al.* Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART. *AIDS* 2010; **24**:907-913.
100. Scott HM, Vittinghoff E, Irvin R, Sachdev D, Liu A, Gurwith M, *et al.* Age, race/ethnicity, and behavioral risk factors associated with per contact risk of HIV infection among men who have sex with men in the United States. *J Acquir Immun Defic Syndr* 2014; **65**:115-121.
101. De Gruttola V, Seage GR, Mayer KH, Horsburgh CR. Infectiousness of HIV between male homosexual partners. *J Clin Epidemiol* 1989; **42**:849-856.
102. Cornell M, Grimsrud A, Fairall L, Fox MP, van Cutsem G, Giddy J, *et al.* Temporal changes in programme outcomes among adult patients initiating antiretroviral therapy across South Africa, 2002-2007. *AIDS* 2010; **24**:2263-2270.
103. Pillay T. Determinants of HIV viral suppression in South Africans receiving antiretroviral treatment. Cape Town: University of Cape Town; 2019.
104. Fraser C, Hollingsworth TD, Chapman R, de Wolf F, Hanage WP. Variation in HIV-1 set-point viral load: epidemiological analysis and an evolutionary hypothesis. *Proc Natl Acad Sci U S A* 2007; **104**:17441-17446.
105. Quinn T, Wawer M, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, *et al.* Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000; **342**:921-929.
106. Fideli US, Allen SA, Musonda R, Trask S, Hahn BH, Weiss H, *et al.* Virologic and immunologic determinants of heterosexual transmission of human immunodeficiency virus type 1 in Africa. *AIDS Res Hum Retroviruses* 2001; **17**:901-910.
107. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al.* Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**:493-505.
108. Anglemyer A, Rutherford GW, Horvath T, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database Syst Rev* 2013; **4**:CD009153.
109. Fox MP, Van Cutsem G, Giddy J, Maskew M, Keiser O, Prozesky H, *et al.* Rates and predictors of failure of first-line antiretroviral therapy and switch to second-line ART in South Africa. *J Acquir Immun Defic Syndr* 2012; **60**:428-437.
110. Pillay T, Cornell M, Fox MP, Euvrard J, Fatti G, Technau K, *et al.* Recording of HIV viral loads and viral suppression in South African patients receiving antiretroviral treatment: a multicentre cohort study. *Antivir Ther* 2020; **25**:257-266.
111. Johnson LF, Mutemaringa T, Heekes A, Boulle A. The effect of HIV and antiretroviral treatment on pregnancy rates in the Western Cape province of South Africa. *J Infect Dis* 2020; **221**:1953-1962.
112. Myer L, Carter RJ, Katyal M, Toro P, El-Sadr WM, Abrams EJ. Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study. *PLoS Med* 2010; **7**:e1000229.
113. Sedgh G, Larsen U, Spiegelman D, Msamanga G, Fawzi WW. HIV-1 disease progression and fertility in Dar es Salaam, Tanzania. *J Acquir Immun Defic Syndr* 2005; **39**:439-445.
114. Loko MA, Toure S, Dakoury-Dogbo N, Gabillard D, Leroy V, Anglaret X. Decreasing incidence of pregnancy by decreasing CD4 cell count in HIV-infected women in Côte d'Ivoire: a 7-year cohort study. *AIDS* 2005; **19**:443-445.

115. Johnson LF, Kubjane M, Eaton JW. Challenges in estimating HIV prevalence trends and geographical variation in HIV prevalence using antenatal data: insights from mathematical modelling. *PLoS One* 2020; **15**:e0242595.
116. Voluntary HIV-1 Counselling and Testing Efficacy Study Group. Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania and Trinidad: a randomised trial. *Lancet* 2000; **356**:103-112.
117. Marlow HM, Maman S, Moodley D, Curtis S, McNaughton Reyes L. HIV status and postpartum contraceptive use in an antenatal population in Durban, South Africa. *Contraception* 2015; **91**:39-43.
118. Hoffman IF, Martinson FE, Powers KA, Chilongozi DA, Msiska ED, Kachipapa EI, *et al.* The year-long effect of HIV-positive test results on pregnancy intentions, contraceptive use, and pregnancy incidence among Malawian women. *Journal of Acquired Immune Deficiency Syndrome* 2008; **47**:477-483.
119. Kaida A, Laher F, Strathdee SA, Janssen PA, Money D, Hogg RS, *et al.* Childbearing intentions of HIV-positive women of reproductive age in Soweto, South Africa: the influence of expanding access to HAART in an HIV hyperendemic setting. *Am J Public Health* 2011; **101**:350-358.
120. Taulo F, Berry M, Tsui A, Makanani B, Kafulafula G, Li Q, *et al.* Fertility intentions of HIV-1 infected and uninfected women in Malawi: a longitudinal study. *AIDS Behav* 2009; **13 (Suppl 1)**:20-27.
121. Brahmbhatt H, Santelli J, Kaagayi J, Lutalo T, Serwadda D, Makumbi F. Pregnancy incidence and fertility desires among couples by HIV status in Rakai, Uganda. *Journal of Acquired Immune Deficiency Syndrome* 2019; **80**:494-502.
122. Mbita G, Renju J, Lija G, Conserve DF, Todd J. Effect of antiretroviral therapy on fertility rate among women living with HIV in Tabora, Tanzania: An historical cohort study. *PLoS One* 2019; **14**:e0222173.
123. Patel RC, Onono M, Gandhi M, Blat C, Hagey J, Shade SB, *et al.* Pregnancy rates in HIV-positive women using contraceptives and efavirenz-based or nevirapine-based antiretroviral therapy in Kenya: a retrospective cohort study. *Lancet HIV* 2015; **2**:e474-482.
124. Elul B, Wools-Kaloustian KK, Wu Y, Musick BS, Nuwagaba-Biribonwoha H, Nash D, *et al.* Untangling the relationship between antiretroviral therapy use and incident pregnancy: a marginal structural model analysis using data from 47,313 HIV-positive women in East Africa. *Journal of Acquired Immune Deficiency Syndrome* 2016; **72**:324-332.
125. Johnson LF, Patrick M, Stephen C, Patten G, Dorrington RE, Maskew M, *et al.* Steep declines in pediatric AIDS mortality in South Africa, despite poor progress towards pediatric diagnosis and treatment targets. *Pediatr Infect Dis J* 2020; **39**:843-848.
126. National Breastfeeding Consultative Group. The Tshwane declaration of support for breastfeeding in South Africa. *S Afr J Clin Nutr* 2011; **24**:214.
127. Küstner H, Swanevelder J, van Middelkoop A. National HIV surveillance - South Africa, 1990 - 1992. *S Afr Med J* 1994; **84**:195-199.
128. Montana LS, Mishra V, Hong R. Comparison of HIV prevalence estimates from antenatal care surveillance and population-based surveys in sub-Saharan Africa. *Sex Transm Infect* 2008; **84 (Suppl 1)**:i78-i84.
129. Williams BG, Gouws E, Colvin M, Sitas F, Ramjee G, Abdool Karim SS. Patterns of infection: using age prevalence data to understand the epidemic of HIV in South Africa. *S Afr J Sci* 2000; **96**:305-312.

130. Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *Br J Obstet Gynaecol* 1998; **105**:836-848.
131. Statistics South Africa. Mortality and causes of death in South Africa: Findings from death notification 2017. Pretoria; 2020. Available: https://www.statssa.gov.za/publications/P03093/P030932017.pdf. Accessed 10 May 2021
132. Groenewald P, Nannan N, Bourne D, Laubscher R, Bradshaw D. Identifying deaths from AIDS in South Africa. *AIDS* 2005; **19**:193-201.
133. Dorrington RE, Moultrie TA, Timæus IM. Estimation of mortality using the South African Census 2001 data. Centre for Actuarial Research; 2004. Available: http://www.commerce.uct.ac.za/Research_Units/CARE/Monographs/Monographs/Mono11.pdf. Accessed 3 Dec 2015
134. Statistics South Africa. Mortality and causes of death in South Africa, 2011: Findings from death notification. Pretoria; 2014. Available: http://beta2.statssa.gov.za/publications/P03093/P030932011.pdf. Accessed 15 April 2014
135. Dorrington RE, Bradshaw D. Maternal mortality in South Africa: lessons from a case study in the use of deaths reported by households in censuses and surveys. *J Pop Res* 2011; **28**:49-73.
136. Dorrington R, Bradshaw D, Laubscher R. Rapid Mortality Surveillance Report 2012. Cape Town; 2014. Available: http://www.mrc.ac.za/bod/RapidMortalitySurveillanceReport2012.pdf. Accessed 21 April 2014
137. Johnson LF, Dorrington RE, Laubscher R, Hoffmann CJ, Wood R, Fox MP, *et al.* A comparison of death recording by health centres and civil registration in South Africans receiving antiretroviral treatment. *J Int AIDS Soc* 2015; **18**:20628.
138. Poliah V, Paruk S. Depression, anxiety symptoms and substance use amongst sex workers attending a non-governmental organisation in KwaZulu-Natal, South Africa. *S Afr Fam Pract* 2017; **59**:116-122.
139. Slabbert M, Venter F, Gay C, Roelofsen C, Lalla-Edward S, Rees H. Sexual and reproductive health outcomes among female sex workers in Johannesburg and Pretoria, South Africa: Recommendations for public health programmes. *BMC Public Health* 2017; **17 (Suppl 3)**:442.
140. Rohr JK, Xavier Gomez-Olive F, Rosenberg M, Manne-Goehler J, Geldsetzer P, Wagner RG, *et al.* Performance of self-reported HIV status in determining true HIV status among older adults in rural South Africa: a validation study. *J Int AIDS Soc* 2017; **20**:21691.
141. Dunkle KL, Beksinska ME, Rees VH, Ballard RC, Htun Y, Wilson ML. Risk factors for HIV infection among sex workers in Johannesburg, South Africa. *Int J STD AIDS* 2005; **16**:256-261.
142. Leggett T. Drugs, sex work, and HIV in three South Africa cities. *Society in Transition* 2001; **32**:101-109.
143. Williams B, Gilgen D, Campbell C, Taljaard D, MacPhail C. *The natural history of HIV / AIDS in South Africa: A biomedical and social survey in Carletonville*. Johannesburg: Council for Scientific and Industrial Research; 2000.
144. Ndhlovu L, Searle C, Van Dam J, Mzaidume Y, Rasego B, Moema S. Reducing the transmission of HIV and sexually transmitted infections in a mining community: Findings from the Carletonville Mothusimpilo intervention project: 1998 to 2001.

Washington, DC: Population Council; 2005. Available: http://www.popcouncil.org/pdfs/horizons/crltnvll.pdf. Accessed 1 Dec 2006
145. van Loggerenberg F, Mlisana K, Williamson C, Auld SC, Morris L, Gray CM, *et al.* Establishing a cohort at high risk of HIV infection in South Africa: challenges and experiences of the CAPRISA 002 acute infection study. *PLoS One* 2008; **3**:e1954.
146. Luseno WK, Wechsberg WM. Correlates of HIV testing among South African women with high sexual and substance-use risk behaviours. *AIDS Care* 2009; **21**:178-184.
147. Greener R, Rambally L, Lafort Y, Beksinksa M, Drace M, Smit J. Condom use and access amongst female sex workers in eThekwini District, KwaZulu-Natal [Abstract MOPE266]. *20th International AIDS Conference*. Melbourne, Australia; 2014.
148. Schwartz S, Lambert A, Phaswana-Mafuya N, Kose Z, McIngana M, Holland C, *et al.* Engagement in the HIV care cascade and barriers to antiretroviral therapy uptake among female sex workers in Port Elizabeth, South Africa: findings from a respondent-driven sampling study. *Sex Transm Infect* 2017; **93**:290-296.
149. Black V, Williams BG, Maseko V, Radebe F, Rees HV, Lewis DA. Field evaluation of Standard Diagnostics' Bioline HIV/Syphilis Duo test among female sex workers in Johannesburg, South Africa. *Sex Transm Infect* 2016; **92**:495-498.
150. Coetzee J, Jewkes R, Gray GE. Cross-sectional study of female sex workers in Soweto, South Africa: Factors associated with HIV infection. *PLoS One* 2017; **12**:e0184775.
151. Johnson LF, Mulongeni P, Marr A, Lane T. Age bias in survey sampling and implications for estimating HIV prevalence in men who have sex with men: insights from mathematical modelling. *Epidemiol Infect* 2018; **146**:1036-1042.
152. Cloete A, Simbayi LC, Rehle T, Jooste S, Mabaso M, Townsend L, *et al.* The South African Marang Men's Project: HIV bio-behavioral surveys using respondent-driven sampling conducted among men who have sex with men in Cape Town, Durban and Johannesburg. Cape Town: Human Sciences Research Council; 2014. Available: http://www.hsrcpress.ac.za/product.php?productid=2328&cat=0&page=1&featured&freedownload=1. Accessed 20 Nov 2014
153. Lane T, Osmand T, Marr A, Shade SB, Dunkle K, Sandfort T, *et al.* The Mpumalanga Men's Study (MPMS): Results of a baseline biological and behavioral HIV surveillance survey in two MSM communities in South Africa. *PLoS One* 2014; **9**:e111063.
154. Lane T, Raymond HF, Dladla S, Rasethe J, Struthers H, McFarland W, *et al.* High HIV prevalence among men who have sex with men in Soweto, South Africa: results from the Soweto Men's Study. *AIDS Behav* 2011; **15**:626-634.
155. Rispel LC, Metcalf CA, Cloete A, Reddy V, Lombard C. HIV prevalence and risk practices among men who have sex with men in two South African cities. *J Acquir Immun Defic Syndr* 2011; **57**:69-76.
156. Tucker A, Liht J, de Swardt G, Jobson G, Rebe K, McIntyre J, *et al.* An exploration into the role of depression and self-efficacy on township men who have sex with men's ability to engage in safer sexual practices. *AIDS Care* 2013; **25**:1227-1235.
157. Sandfort TG, Lane T, Dolezal C, Reddy V. Gender expression and risk of HIV infection among black South African men who have sex with men. *AIDS Behav* 2015; **19**:2270-2279.
158. Kufa T, Lane T, Manyuchi A, Singh B, Isdahl Z, Osmand T, *et al.* The accuracy of HIV rapid testing in integrated bio-behavioral surveys of men who have sex with men across 5 Provinces in South Africa. *Medicine* 2017; **96**:e7391.

159. Sandfort TGM, Dominguez K, Kayange N, Ogendo A, Panchia R, Chen YQ, *et al.* HIV testing and the HIV care continuum among sub-Saharan African men who have sex with men and transgender women screened for participation in HPTN 075. *PLoS One* 2019; **14**:e0217501.
160. Fearon E, Tenza S, Moodley K, Mokoena C, Smith AD, Bourne A, *et al.* A population-based assessment of HIV prevalence and engagement in the HIV care cascade amongst gay, bisexual and other men who have sex with men and transgender women (MSM/TG) in Johannesburg. 2018.
161. Schoub BD, Lyons SF, McGillivray GM, Smith AN, Johnson S, Fisher EL. Absence of HIV infection in prostitutes and women attending sexually-transmitted disease clinics in South Africa. *Trans R Soc Trop Med Hyg* 1987; **81**:874-875.
162. Johnson LF, Geffen N. A comparison of two mathematical modeling frameworks for evaluating sexually transmitted infection epidemiology. *Sex Transm Dis* 2016; **43**:139-146.
163. van Schalkwyk C, Moodley J, Welte A, Johnson LF. Are associations between HIV and human papillomavirus transmission due to behavioural confounding or biological effects? *Sex Transm Infect* 2019; **95**:122-128.
164. Esra RT, Johnson LF. Modelling the impact of screening for chlamydia and gonorrhoea in youth and other high-prevalence groups in a resource-limited setting. *International Journal of Public Health* 2020; **65**:413-423.
165. Johnson LF, Kubjane M, Moolla H. MicroCOSM: a model of social and structural drivers of HIV and interventions to reduce HIV incidence in high-risk populations in South Africa. *BioRxiv* 2018:310763.
166. Johnson LF, van Rensburg C, Govathson C, Meyer-Rath G. Optimal HIV testing strategies for South Africa: a model-based evaluation of population-level impact and cost-effectiveness. *Sci Rep* 2019; **9**:12621.
167. Rigby SW, Johnson LF. The relationship between intimate partner violence and HIV: a model-based evaluation. *Infectious Disease Modelling* 2017; **2**:71-89.
168. Reniers G, Armbruster B. HIV status awareness, partnership dissolution and HIV transmission in generalized epidemics. *PLoS One* 2012; **7**:e50669.
169. Johnson LF, Dorrington RE, Bradshaw D, Coetzee DJ. The role of sexually transmitted infections in the evolution of the South African HIV epidemic. *Trop Med Int Health* 2012; **17**:161-168.
170. Hargreaves JR, Morison LA, Kim JC, Busza J, Phetla G, Porter JD, *et al.* Characteristics of sexual partnerships, not just of individuals, are associated with condom use and recent HIV infection in rural South Africa. *AIDS Care* 2009; **21**:1058-1070.
171. Hendriksen ES, Pettifor A, Lee SJ, Coates TJ, Rees HV. Predictors of condom use among young adults in South Africa: the Reproductive Health and HIV Research Unit National Youth Survey. *Am J Public Health* 2007; **97**:1241-1248.
172. Department of Health. Annual Report 2008/09. 2009. Available: http://www.health.gov.za/annualreports.php. Accessed 19 Feb 2014
173. Department of Health. Annual Report 2010/11. 2011. Available: http://www.doh.gov.za/docs/reports/annual/2011/annual_report2010-11.pdf. Accessed 31 May 2013.
174. Massyn N, Day C, Barron P, Haynes R, English R, Padarath A. District Health Barometer 2011/12. Durban: Health Systems Trust; 2013. Available: http://www.hst.org.za/publications/district-health-barometer-201112. Accessed 23 Oct 2013

175. Massyn N, Day C, Peer N, Padarath A, Barron P, English R. District Health Barometer 2013/14. Durban; 2014.
176. Massyn N, Peer N, English R, Padarath A, Barron P, Day C. District Health Barometer 2015/16. Durban; 2016. Available: http://www.hst.org.za/publications/district-health-barometer-201516-0. Accessed 5 March 2017
177. Massyn N, Barron P, Day C, Ndlovu N, Padarath A. District Health Barometer 2018/19. Durban: Health Systems Trust; 2020.
178. Massyn N, Day C, Ndlovu N, Padayachee T. District Health Barometer 2019/20. Durban: Health Systems Trust; 2020.
179. Myer L, Mathews C, Little F, Abdool Karim SS. The fate of free male condoms distributed to the public in South Africa. *AIDS* 2001; **15**:789-793.
180. Meekers D, Van Rossem R. Explaining inconsistencies between data on condom use and condom sales. *BMC Health Serv Res* 2005; **5**:5.
181. Guthrie T, Chaitkin M, Khoza N, Zulu N, Madisha V, Ndlovu N, *et al.* Consolidated Spending on HIV and TB in South Africa (2014/15–2016/17). Pretoria: National Department of Health, Health Finance and Governance Project, Results for Development Institute; 2018. Available: https://www.r4d.org/wp-content/uploads/South-Africa-HIV-and-TB-Expenditure-Review-2014-15-2016-17-Full-Report_vf.pdf. Accessed 1 July 2019
182. Guthrie T, Hecht R, Rychman T. Consolidated Spending on HIV and TB in South Africa: Investment Case. Washington DC, USA: Results for Development; 2015.
183. Fraser-Hurt N, Zuma K, Njuho P, Chikwava F, Slaymaker E, Hosegood V, *et al.* The HIV epidemic in South Africa: What do we know and how has it changed?: World Bank, Human Sciences Research Council, Health and Development Africa, UNAIDS; 2011. Available: http://www.genderjustice.org.za/external-resources/external-resources. Accessed 13 June 2011
184. Bradshaw D, Pettifor A, MacPhail C, Dorrington RE. Trends in youth risk for HIV. In: *South African Health Review 2003*. Edited by Ijumba P, Day C, Ntuli A: Health Systems Trust; 2004.
185. Reddy SP, Panday S, Swart D, Jinabhai CC, Amosun SL, James S, *et al.* Umthenthe Uhlaba Usamila - The South African Youth Risk Behaviour Survey 2002. Cape Town: South African Medical Research Council; 2003. Available: http://www.mrc.ac.za/healthpromotion/healthpromotion.htm. Accessed 15 Dec 2003
186. Reddy SP, James S, Sewpaul R, Koopman F, Funani NI, Sifunda S, *et al.* Umthente uhlaba usamila - The South African Youth Risk Behaviour Survey 2008. Cape Town: South African Medical Research Council; 2010.
187. Gregson S, Zhuwau T, Ndlovu J, Nyamukapa CA. Methods to reduce social desirability bias in sex surveys in low-development settings: experience in Zimbabwe. *Sex Transm Dis* 2002; **29**:568-575.
188. Mensch BS, Hewett PC, Erulkar AS. Reporting of sensitive behavior by adolescents: a methodological experiment in Kenya. *Demography* 2003; **40**:247-268.
189. Health and Development Africa. Impact Assessment of the Khomanani Campaign 2004 - 2006. 2007.
190. Boily M, Bastos FI, Desai K, Mâsse B. Changes in the transmission dynamics of the HIV epidemic after the wide-scale use of antiretroviral therapy could explain increases in sexually transmitted infections. *Sex Transm Dis* 2004; **31**:100-113.
191. Joshi K, Lessler J, Olawore O, Loevinsohn G, Bushey S, Tobian AAR, *et al.* Declining HIV incidence in sub-Saharan Africa: a systematic review and meta-analysis of empiric data. *J Int AIDS Soc* 2021; **24**:e25818.

192. Risher KA, Cori A, Reniers G, Marston M, Calvert C, Crampin A, *et al.* Age patterns of HIV incidence in eastern and southern Africa: a modelling analysis of observational population-based cohort studies. *Lancet HIV* 2021; **8**:e429-e439.
193. Bärnighausen T, Hosegood V, Timæus IM, Newell ML. The socioeconomic determinants of HIV incidence: evidence from a longitudinal, population-based study in rural South Africa. *AIDS* 2007; **21 (Suppl 7)**:S29-38.
194. Vandormael A, Akullian A, Siedner M, de Oliveira T, Barnighausen T, Tanser F. Declines in HIV incidence among men and women in a South African population-based cohort. *Nat Commun* 2019; **10**:5482.
195. Kharsany ABM, Cawood C, Lewis L, Yende-Zuma N, Khanyile D, Puren A, *et al.* Trends in HIV prevention, treatment, and incidence in a hyperendemic area of KwaZulu-Natal, South Africa. *JAMA Netw Open* 2019; **2**:e1914378.
196. Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, *et al.* Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010; **329**:1168-1174.
197. Delany-Moretlwe S, Lombard C, Baron D, Bekker LG, Nkala B, Ahmed K, *et al.* Tenofovir 1% vaginal gel for prevention of HIV-1 infection in women in South Africa (FACTS-001): a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet Infect Dis* 2018; **18**:1241-1250.
198. Ramjee G, Wand H, Whitaker C, McCormack S, Padian N, Kelly C, *et al.* HIV incidence among non-pregnant women living in selected rural, semi-rural and urban areas in KwaZulu-Natal, South Africa. *AIDS Behav* 2012; **16**:2062-2071.
199. Global HIV Strategic Information Working Group. Recent infection testing algorithm technical update: Applications for HIV surveillance and programme monitoring. UNAIDS; 2018. Available: https://www.unaids.org/sites/default/files/media_asset/infection_testing_algorithm_en.pdf. Accessed 20 May 2021
200. Rehle T, Johnson L, Hallett T, Mahy M, Kim A, Odido H, *et al.* A comparison of South African national HIV incidence estimates: a critical appraisal of different methods. *PLoS One* 2015; **10**:e0133255.
201. Woldesenbet S, Kufa-Chakezha T, Lombard C, Manda S, Cheyip M, Ayalew K, *et al.* Recent HIV infection among pregnant women in the 2017 antenatal sentinel cross-sectional survey, South Africa: Assay-based incidence measurement. *PLoS One* 2021; **16**:e0249953.
202. Grebe E, Welte A, Johnson LF, van Cutsem G, Puren A, Ellman T, *et al.* Population-level HIV incidence estimates using a combination of synthetic cohort and recency biomarker approaches in KwaZulu-Natal, South Africa. *PLoS One* 2018; **13**:e0203638.
203. Hallett TB, Zaba B, Todd J, Lopman B, Mwita W, Biraro S, *et al.* Estimating incidence from prevalence in generalized HIV epidemics: methods and validation. *PLoS Med* 2008; **5**:e80.
204. Rehle TM, Hallett TB, Shisana O, Pillay-van Wyk V, Zuma K, Carrara H, *et al.* A decline in new HIV infections in South Africa: estimating HIV incidence from three national HIV surveys in 2002, 2005 and 2008. *PLoS One* 2010; **5**:e11094.
205. Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Senkoro K, *et al.* Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised control trial. *Lancet* 1995; **346**:530-536.
206. Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N, *et al.* Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. *Lancet* 1999; **353**:525-535.

207. Coates TJ, Kulich M, Celentano DD, Zelaya CE, Chariyalertsak S, Chingono A, *et al.* Effect of community-based voluntary counselling and testing on HIV incidence and social and behavioural outcomes (NIMH Project Accept; HPTN 043): a cluster-randomised trial. *Lancet Glob Health* 2014; **2**:e267-277.
208. Iwuji CC, Orne-Gliemann J, Larmarange J, Balestre E, Thiebaut R, Tanser F, *et al.* Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial. *Lancet HIV* 2018; **5**:e116-125.
209. Hayes RJ, Donnell D, Floyd S, Mandla N, Bwalya J, Sabapathy K, *et al.* Effect of universal testing and treatment on HIV incidence - HPTN 071 (PopART). *N Engl J Med* 2019; **381**:207-218.
210. Havlir DV, Balzer LB, Charlebois ED, Clark TD, Kwarisiima D, Ayieko J, *et al.* HIV testing and treatment with the use of a community health approach in rural Africa. *N Engl J Med* 2019; **381**:219-229.
211. Makhema J, Wirth KE, Pretorius Holme M, Gaolathe T, Mmalane M, Kadima E, *et al.* Universal testing, expanded treatment, and incidence of HIV infection in Botswana. *N Engl J Med* 2019; **381**:230-242.
212. Abdool Karim SS. HIV-1 epidemic control - insights from test-and-treat trials. *N Engl J Med* 2019; **381**:286-288.
213. Brault MA, Spiegelman D, Hargreaves J, Nash D, Vermund SH. Treatment as prevention: concepts and challenges for reducing HIV incidence. *Journal of Acquired Immune Deficiency Syndrome* 2019; **82 (Suppl 2)**:S104-S112.
214. Havlir D, Lockman S, Ayles H, Larmarange J, Chamie G, Gaolathe T, *et al.* What do the universal test and treat trials tell us about the path to HIV epidemic control? *J Int AIDS Soc* 2020; **23**:e25455.
215. Tanser F, Kim HY, Vandormael A, Iwuji C, Barnighausen T. Opportunities and challenges in HIV treatment as prevention research: results from the ANRS 12249 cluster-randomized trial and associated population cohort. *Curr HIV/AIDS Rep* 2020; **17**:97-108.
216. Alsallaq RA, Baeten JM, Celum CL, Hughes JP, Abu-Raddad LJ, Barnabas RV, *et al.* Understanding the potential impact of a combination HIV prevention intervention in a hyper-endemic community. *PLoS One* 2013; **8**:e54575.