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The Effect of HIV Programs in South Africa on National HIV Incidence Trends, 2000–2019

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Background: Recent studies have shown HIV incidence declines at a population level in several African countries. However, these studies have not directly quantified the extent to which incidence declines are attributable to different HIV programs.

Methods: We calibrated a mathematical model of the South African HIV epidemic to age- and sex-specific data from antenatal surveys, household surveys, and death registration, using a Bayesian approach. The model was also parameterized using data on self-reported condom use, voluntary medical male circumcision (VMMC), HIV testing, and antiretroviral treatment (ART). Model estimates of HIV incidence were compared against the incidence rates that would have been expected had each program not been implemented.

Results: The model estimated incidence in 15–49 year olds of 0.84% (95% CI: 0.75% to 0.96%) at the start of 2019. This represents a 62% reduction (95% CI: 55% to 66%) relative to 2000, a 47% reduction (95% CI: 42% to 51%) relative to 2010, and a 73% reduction (95% CI: 68% to 77%) relative to the incidence that would have been expected in 2019 in the absence of any interventions. The reduction in incidence in 2019 because of interventions was greatest for ART and condom promotion, with VMMC and behavior change after HIV testing having relatively modest impacts. HIV program impacts differed significantly by age and sex, with condoms and VMMC having greatest impact in youth, and overall incidence reductions being greater in men than in women.

Conclusions: HIV incidence in South Africa has declined substantially since 2000, with ART and condom promotion contributing most significantly to this decline.

Key Words: HIV/AIDS, antiretroviral treatment, condom promotion, male circumcision, HIV testing, South Africa

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INTRODUCTION

Across eastern and southern Africa, several studies have noted substantial declines in adult HIV incidence over the past decade.[1–6] These are consistent with the results of UNAIDS models that are calibrated to HIV prevalence data, which estimate a 43% reduction in the annual number of new HIV infections across the eastern and southern African region between 2010 and 2020.[7] Although these reductions may appear disappointing relative to the UNAIDS target of a 75% reduction in new HIV infections between 2010 and 2020,[8] they are nevertheless substantially greater than the reductions achieved in any other region.[7]

To strengthen and improve on these successes, it is important to understand which programs have contributed most significantly to the HIV incidence declines in the eastern and southern African region. Previous studies have focused mainly on the role of antiretroviral treatment (ART) and voluntary medical male circumcision (VMMC) in driving down HIV incidence rates and have noted that HIV incidence reductions have been greater in men than in women.[1–3,5] However, relatively less attention has been given to other programs, such as HIV testing and behavior change communication. HIV testing leads to reductions in HIV risk behavior, independently of whether individuals initiate ART,[9–11] and has been scaled up dramatically in sub-Saharan Africa over the past decade.[12] Evidence of the impact of behavior change communication has been mixed, but in several eastern and southern African countries, there have been increases in condom use since 2000, as well as increased reporting of multiple partnerships.[13,14]

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South Africa has the largest HIV epidemic globally, with close to 8 million South Africans living with HIV.[6] We previously estimated, using 2 different mathematical models, that adult HIV incidence rates in South Africa declined by approximately 30% between 2000 and 2008, with most of this decline being attributable to the impact of condom promotion campaigns.[15] However, minimal ART impact was estimated because of the relatively low levels of ART coverage at the time. In addition, the models did not assess the contribution of HIV testing programs and VMMC, which have emerged as particularly important components of South Africa's HIV response in recent years.[16] Since 2008, further declines in HIV incidence have been observed in South Africa,[6] but there has not yet been any systematic attempt to assess how much of this decline is attributable to different HIV programs.

This study updates our previous modelling study, by estimating HIV incidence trends over the 2000–2019 period. We aim to assess the extent to which changes in incidence are attributable to condom promotion, HIV testing, ART, and VMMC. We further aim to assess age and sex differences in adult HIV incidence trends and the factors accounting for these differences. Finally, we aim to assess South Africa's progress toward the UNAIDS target of a 75% reduction in new HIV infections, as well as the target of an incidence-to-prevalence ratio of less than 0.03 (the proposed threshold for "epidemic transition").[8]

METHODS

HIV incidence trends were estimated using the Thembisa model, an integrated HIV and demographic model developed for South Africa. A detailed description of the model is provided elsewhere[17]; in this article, we focus on describing those components of the model most relevant to the estimation of adult HIV incidence trends. The model divides the adult population into 2 broad risk groups: "high-risk" individuals are defined as those who have a propensity for concurrent partnerships and/or commercial sex, whereas "low-risk" individuals are serially monogamous and do not engage in commercial sex. The population is further stratified by sexual experience and marital status, with marital relationships being considered "long-term" relationships.

The HIV-positive adult population is stratified by CD4 count category, HIV testing history, and receipt of ART. The simulation of the HIV epidemic begins in 1985, based on an assumed initial HIV prevalence in high-risk women. The spread of HIV is simulated based on assumptions about HIV transmission probabilities per sex act, which depend on the HIV stage and CD4 count of the HIV-positive partner, the circumcision status of the susceptible partner, and the use of other prevention methods (condom use and preexposure prophylaxis [PrEP]).

Probabilities of condom use are assumed to depend on relationship type, year, age, sex, and (in the case of HIV-positive individuals) HIV diagnosis and receipt of ART. Assumptions about condom use in women are set by fitting a simple statistical model to data from 12 nationally representative surveys (1986–2017), stratified by age and marital status (see Section 2.2.1, Supplemental Digital Content 1, http://links.lww.com/QAI/B811). Two types of self-reported data are included: reporting on condom use at last sex and reporting on condom use for contraceptive purposes, with the statistical model assuming a constant proportional difference between the 2 self-reported measures. Time trends are included in the model using 2 cumulative Weibull distributions, the first to represent the effect of condom promotion campaigns introduced in the 1990s and early 2000s[18] and the second to represent a possible reversal in condom trends because of "ART optimism."[19–21] Rates of condom use in men are calculated to be consistent with those assumed for women.

Rates of HIV testing are assumed to depend on age, sex, sexual experience, HIV testing history, and CD4 count. The model accounts for changes over time in "general" rates of HIV testing and changes in rates of testing in pregnant women and patients with opportunistic infections. Assumptions about HIV testing rates are set by calibrating the model to data on the total numbers of tests in adults, proportions of test results that are positive, and proportions of adults who report having ever tested for HIV.[17,22] Rates of ART initiation after diagnosis are assumed to depend on CD4 count, sex and year, with the rates of ART initiation set so that the model matches separately estimated annual numbers of men and women starting ART.[17] The infectivity of treated individuals, per unprotected sex act, is assumed to reduce by a proportion that depends on their baseline CD4 count at ART initiation and their level of viral suppression (see Supplemental Materials, http://links.lww.com/QAI/B811). HIV diagnosis and ART initiation are both assumed to be associated with reductions in unprotected sex.

The model divides the male population into circumcised and uncircumcised men. Assumptions about rates of circumcision by age are set separately for "background" circumcision (circumcision that would be expected in the absence of VMMC campaigns, mostly in traditional settings) and circumcision in the context of VMMC campaigns aimed at reducing HIV risk. Rates of "background" circumcision are estimated from national surveys before 2005, after adjusting for misreporting, and rates of circumcision in the context of VMMC campaigns are estimated from annual reported numbers of VMMC operations by age.[23]

The model is calibrated to South African HIV prevalence and mortality data using a Bayesian approach. Prior distributions are assigned to represent the uncertainty in 21 of the model parameters that are considered most important to quantifying HIV incidence trends (Table 1). Because self-reported condom use at last sex is likely to be overstated,[15] we include a "condom bias" parameter (r) that determines the "true" rate of condom use (θ) from the statistical model estimates of condom use at last sex (θ_0) and condom use for contraceptive purposes (θ_1): $\theta = \theta_0(1 - r) + \theta_1 r$. Estimates of viral suppression from research cohorts in South Africa may also be biased, and we therefore similarly define a bias parameter, which represents the ratio of the true odds of viral suppression to that measured in research cohorts.[33] A likelihood function is specified to represent the goodness-of-model fit to 6 data sources: (1) HIV prevalence data in national surveys of pregnant women, from 1994 to 2019, stratified by 5-year age group; (2) HIV prevalence data in national

TABLE 1. Key Parameters and Prior Distributions

Parameter	Value (Mean)	SD*	Source†
% of men who are high risk	35%	—	24–26
% of women who are high risk	25%	—	24–26
Sexual mixing between high and low risk	0.53	0.12	S2.4.1
RR of short-term partner acquisition in low-risk men‡	0.50	0.29	S2.4.1
RR of short-term partner acquisition in low-risk women‡	0.50	0.29	S2.4.1
RR of short-term partner acquisition in high-risk married men‡	0.25	0.10	S2.4.1
RR of short-term partner acquisition in high-risk married women‡	0.25	0.10	S2.4.1
Bias in self-reported condom use at last sex	0.50	0.29	S2.2.1
Reduction in unprotected sex after HIV diagnosis	18%	15%	S2.2.4
Effect of ART on unprotected sex (h)	18%	—	S2.2.5
Gamma density of RR of short-term partner acquisition in women			
Mean age, yr	38.7	4.1	S2.4.1
Age standard deviation	19.3	2.8	S2.4.1
RR of HIV+ fertility before diagnosis/immune decline	1.30	0.13	S2.4.6
Initial HIV prevalence in high-risk women, ages 15–49 yr	0.10%	0.06%	S2.4.7
HIV transmission probability per unprotected sex act			
Male-to-female, short-term relationship	0.012	0.005	S2.4.4
Female-to-male, short-term relationship	0.008	0.003	S2.4.4
Male-to-male, short-term relationship	0.020	0.005	S2.4.4
Client-to-female sex worker	0.001	0.0005	S2.4.4
RR in long-term relationships, compared with short term	0.20	0.10	S2.4.4
Relative infectivity in acute HIV infection§	10	—	27
Relative infectivity at CD4 < 200, untreated§	7.0	—	28,29
% reduction in male susceptibility to HIV if circumcised	60%	—	30
Condom efficacy	90%	—	31,32
Odds of viral suppression in ART patients, relative to research cohorts	0.819	0.078	S2.4.5
Mean HIV survival in males aged 30 yr, in absence of ART	12.0	1.00	S2.4.2
RR disease progression/death in women	0.96	0.05	S2.4.2
Proportion increase in disease progression/death per 10-year age increase	0.18	0.06	S2.4.2
Reduction in log(mortality) per unit increase in rate of ART initiation (at CD4<200) over last 3 years	7.5	3.5	S2.4.2

*Standard deviations are presented only for those parameters that are allowed to vary in the model calibration process (for full details of the prior distributions see Table S9 of the Supplemental Digital Content materials, http://links.lww.com/QAI/B811).

†References to more detailed explanations in the supplementary materials are provided as section numbers (eg, "S2.4.1" refers to Section 2.4.1 in the Supplemental Digital Content, http://links.lww.com/QAI/B811).

‡Relative to high-risk unmarried individuals of the same sex.

§Relative to untreated chronic HIV with CD4 > 350 cells per microliter.

RR, relative rate.

household surveys, in 2005, 2008, 2012, 2016, and 2017, stratified by 5-year age group and sex; (3) antiretroviral metabolite data from national household surveys in 2012 and 2017, stratified by sex; (4) recorded numbers of deaths in adults, from 1997 to 2016, stratified by age and sex; (5) HIV prevalence data from surveys of female sex workers; and (6) HIV prevalence data from surveys of men who have sex with men (MSM). For each component of the likelihood, variance terms are set such that 95% confidence intervals were wide enough to include approximately 95% of observations in an out-of-sample validation (see Supplemental Materials, http://links.lww.com/QAI/B811). Posterior estimates that integrate the prior distributions and likelihood function are simulated using Incremental Mixture Importance Sampling.[34]

Program impacts (for each of ART, VMMC, and condom promotion) are estimated by comparing incidence rates with a counterfactual scenario in which the intervention was not introduced, and calculating the percentage difference in incidence rates between the main scenario and the counterfactual. In the case of HIV testing, we instead consider a counterfactual in which there was no HIV testing or ART because it would be illogical to define a counterfactual in which there was ART but no HIV testing. The behavior change counterfactual was defined as one in which the 2 cumulative Weibull distributions were set to zero (ie, assuming rates of condom use in undiagnosed individuals remain constant over time), while maintaining the same increased condom use after HIV diagnosis. The combined effect of all interventions was calculated with reference to a counterfactual in which there were no interventions. Estimates of HIV incidence trends and program impact were validated by comparing the results with those of MicroCOSM, an agent-based model of HIV in South Africa that models the same interventions[35] and with national survey estimates.[6,36,37]

RESULTS

Posterior estimates of model parameters were generally close to the prior means (see Table S16, Supplemental Digital Content, http://links.lww.com/QAI/B811). Model estimates for South Africa were consistent with survey estimates of HIV prevalence, recorded deaths, self-reported condom use, and HIV program data (Fig. 1). The model was also validated against HIV incidence estimates from national surveys (Fig. 2A): although the model estimates of HIV incidence in adults aged 15–49 years were mostly consistent with survey estimates, the estimate for 2016–2017 was 1.01% (95% CI: 0.91% to 1.13%), higher than the corresponding survey estimate of 0.79% (95% CI: 0.67% to 0.91%). The estimated HIV incidence in pregnant women in 2016–2017 (1.7%, 95% CI: 1.5% to 1.9%) was also slightly higher than that in a national survey in pregnant women (1.5%, 95% CI: 1.2% to 1.7%).[37]

Our model estimates that the HIV incidence rate in adults aged 15–49 years reduced from 2.22% (95% CI: 2.15% to 2.29%) at the start of 2000 to 1.59% (95% CI: 1.52% to 1.69%) at the start of 2010 and to 0.84% (95% CI: 0.75% to

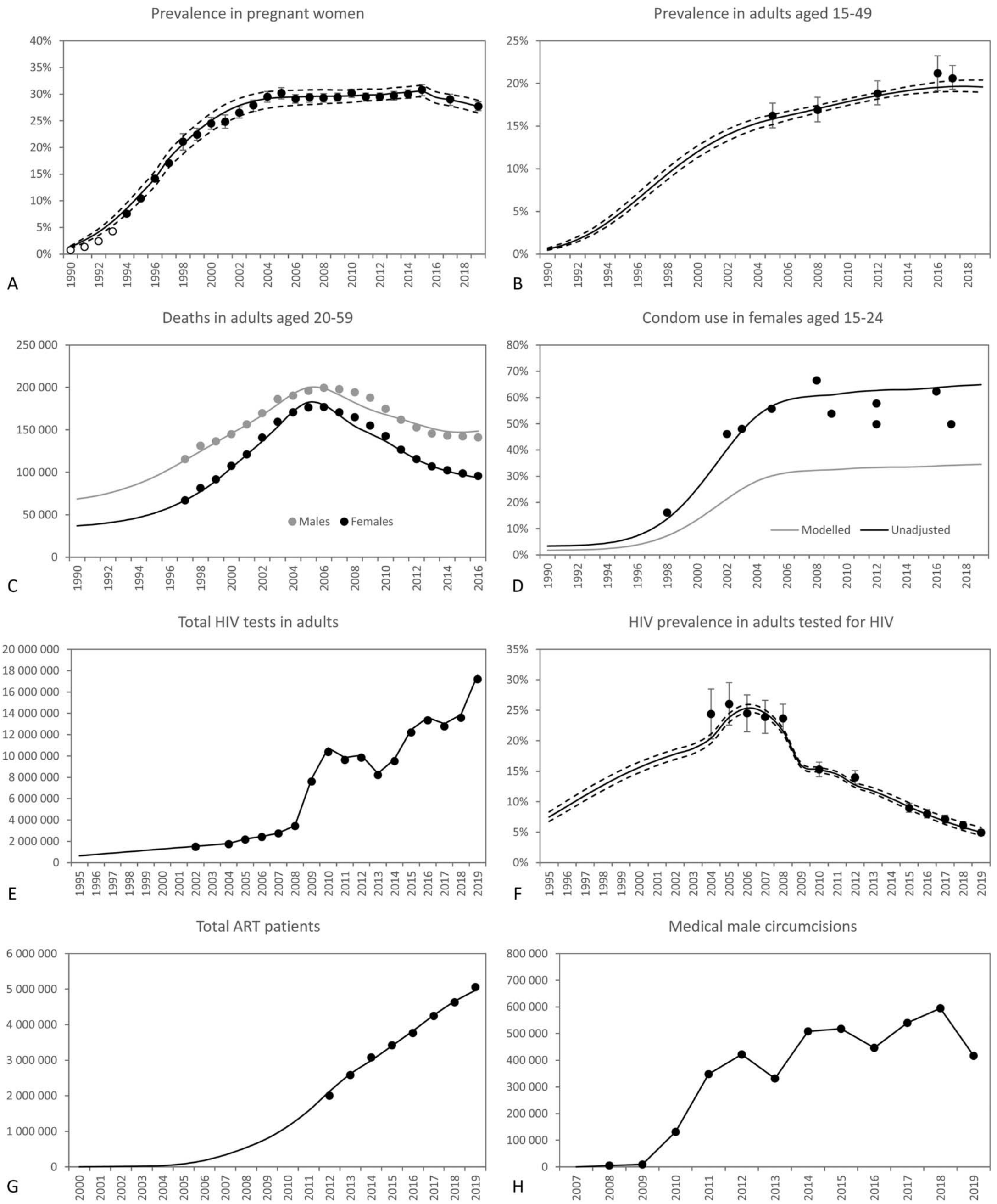

FIGURE 1. Model calibration to HIV survey data, vital registration data and program data. Solid lines represent posterior means of model estimates, and dashed lines represent 95% credible intervals around the model estimates. Dots represents data used in calibration (or as model inputs), whereas open circles represent data not used in calibration. In panel (C), recorded deaths have been adjusted for incomplete reporting. In panel D, the modeled "true" rate of condom use is represented by the grey line, whereas the black line represents the model estimate if not adjusting for bias in self-reported data. In panels (E–G), public sector data have been augmented with private sector data. ART data in panel G are shown only from 2012, as the public reporting system before 2012 reported mainly cumulative ART enrolment.

0.96%) at the start of 2019. This implies a 62% reduction (95% CI: 55% to 66%) in incidence over the 2000–2019 period, and a 47% reduction (95% CI: 42% to 51%) over the 2010–2019 period. The ratio of new infections to prevalent HIV at the start of 2019 was 0.032 (95% CI: 0.029 to 0.036). In the absence of any interventions, HIV incidence in the 15–49 age group would have increased from 2.75% (95% CI: 2.62% to 2.84%) at the start of 2000 to 3.15% (95% CI: 2.97% to 3.34%) at the start of 2010 and remained stable at this level up to 2019 (Fig. 2B). This implies that HIV

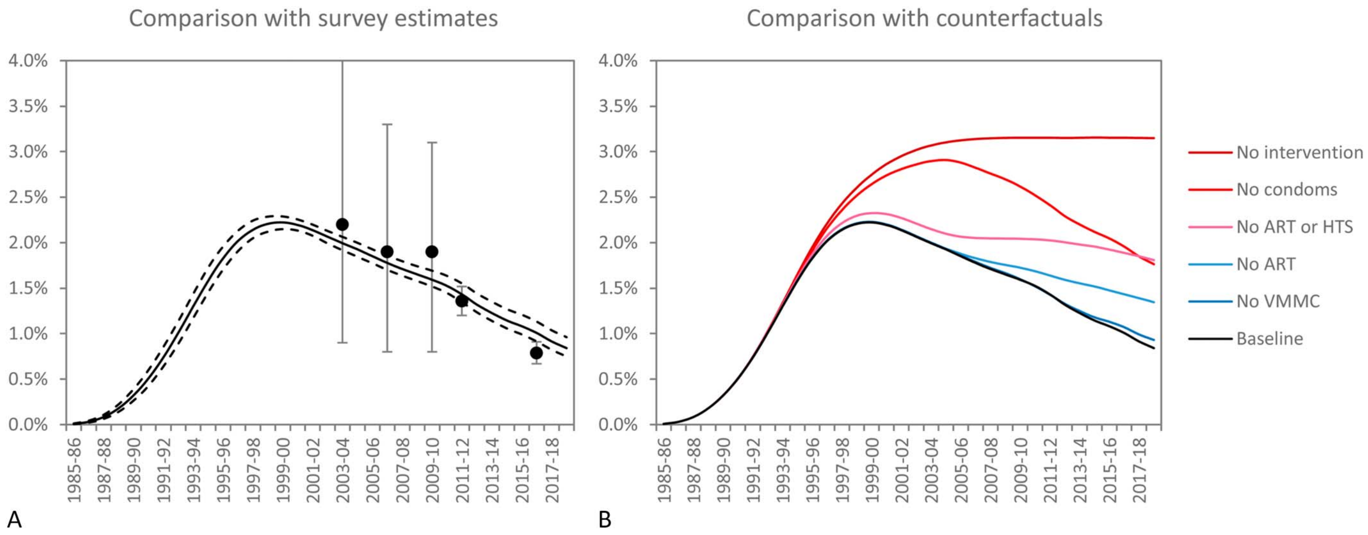

FIGURE 2. HIV incidence rates in adults aged 15–49 years. Solid lines represent posterior means of model estimates, and dashed lines represent 95% credible intervals around the model estimates. Dots represent HIV incidence estimates from national household surveys, obtained using the synthetic cohort method (first 3 estimates) and a recent infection testing algorithm that included the LAg avidity assay (last 2 estimates).[6,36] The results from the 2012 and 2017 surveys are plotted as estimates for 2011–2012 and 2016–2017, respectively, as the incidence estimates correspond to the 12 months before the survey. The "no intervention" scenario is one in which there is no condom promotion, HTS, ART or VMMC. HTS, HIV testing services.

incidence at the start of 2019 was 73% lower (95% CI: 68% to 77%) than would have been expected in the absence of HIV interventions. Estimates of HIV incidence trends in the main and counterfactual scenarios were slightly lower than those estimated by the MicroCOSM model (see Figure S14, Supplemental Digital Content, http://links.lww.com/QAI/B811).

When compared against the counterfactual estimates for individual interventions, the estimated incidence rate in 15–49 year olds at the start of 2019 was 9.7% lower than would have been expected without VMMC (95% CI: 9.3% to 10.1%), 52% lower than would have been expected without condom promotion (95% CI: 48% to 57%), 38% lower than would have been expected without ART (95% CI: 35% to 39%), and 53% lower than would have been expected without both ART and HIV testing (95% CI: 44% to 61%). Intervention impacts increased steadily over the 2004–2019 period, most rapidly in the case of ART and VMMC, and more slowly in the case of condom promotion (Table 2).

Intervention impacts differed by age and sex (Fig. 3). Overall, incidence reductions were greater in men than in women, driven largely by effects of VMMC and ART, which were more substantial in men than in women. Incidence reductions were also greater in younger adults because of higher uptake of HIV prevention (VMMC and condoms) at younger ages. Although ART had more impact on HIV incidence in 25–49 year olds than in 15–24 year olds, as a result of higher ART coverage in older HIV-positive adults, the impact of ART on HIV incidence at 50 years and older was substantially smaller, as fewer HIV-positive individuals would have survived to 50 years and older in the "no ART" counterfactual.

When compared against HIV incidence rates at the start of 2000, HIV incidence rates at the start of 2019 were significantly lower in all age and sex groupings, except in women aged 50 years and older, in whom incidence rates increased by 45% (95% CI: 21% to 72%). Incidence reductions over 2000–2019 were greatest in male subjects

TABLE 2. Proportionate Reductions in HIV Incidence (Ages 15–49 Years) Because of Interventions at Different Times

	2004	2009	2014	2019
Condom promotion	31% (28%–34%)	39% (35%–43%)	44% (40%–49%)	52% (48%–57%)
ART	0% (0%–0%)	6% (5%–7%)	21% (20%–22%)	38% (35%–39%)
ART and HTS	7% (3%–10%)	19% (13%–25%)	38% (29%–46%)	53% (44%–61%)
VMMC	—	1% (0%–1%)	2% (2%–2%)	10% (9%–10%)
All interventions	35% (33%–37%)	48% (43%–50%)	61% (55%–65%)	73% (68%–77%)

Results relate to the start of each calendar year. Proportionate reductions in incidence are calculated by comparing the actual incidence rate in the relevant year to the incidence rate that would have been expected in the same year if the intervention (or combination of interventions) had not been introduced. Results presented are means and 95% confidence intervals (in brackets).

HTS, HIV testing services.

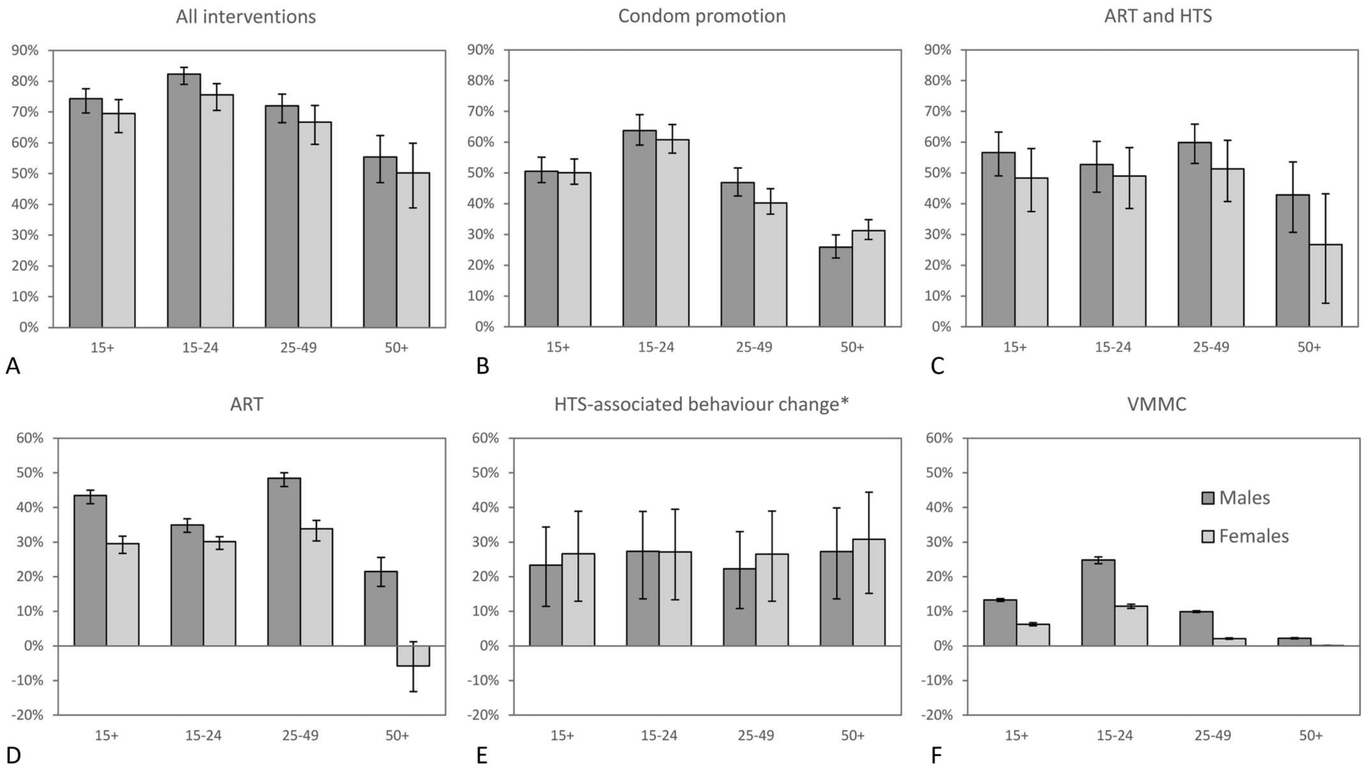

FIGURE 3. Reductions in HIV incidence at the start of 2019 because of HIV programs. Error bars represent 95% confidence intervals. The reductions are calculated by comparing the HIV incidence rates in 2019 against those that would have been expected in each of 5 counterfactual scenarios: no VMMC, no ART, no ART or HTS, no condom promotion, and no interventions. *The reduction in incidence because of behavior change after HIV diagnosis, however, is calculated by comparing the no ART and no ART or HTS scenarios, as we could not define a counterfactual in which there was ART but no HTS. HTS, HIV testing services.

aged 15–24 years (74%, 95% CI: 69% to 77%), men aged 25–49 years (65%, 95% CI: 60% to 69%), and female subjects aged 15–24 (63%, 95% CI: 56% to 67%) (see Figure S11, Supplemental Digital Content, http://links.lww.com/QAI/B811). The age distribution of HIV infections changed substantially over the 2000–2019 period, with the proportion of new infections in the 15- to 24-year age group decreasing from 37% to 24% in male subjects and from 55% to 44% in female subjects (see Figure S12, Supplemental Digital Content, http://links.lww.com/QAI/B811).

The model estimates that at the start of 2019, 29.6% (95% CI: 27.6% to 32.1%) of sexually acquired HIV was acquired from individuals who were undiagnosed, 32.5% (95% CI: 30.3% to 35.4%) was acquired from individuals

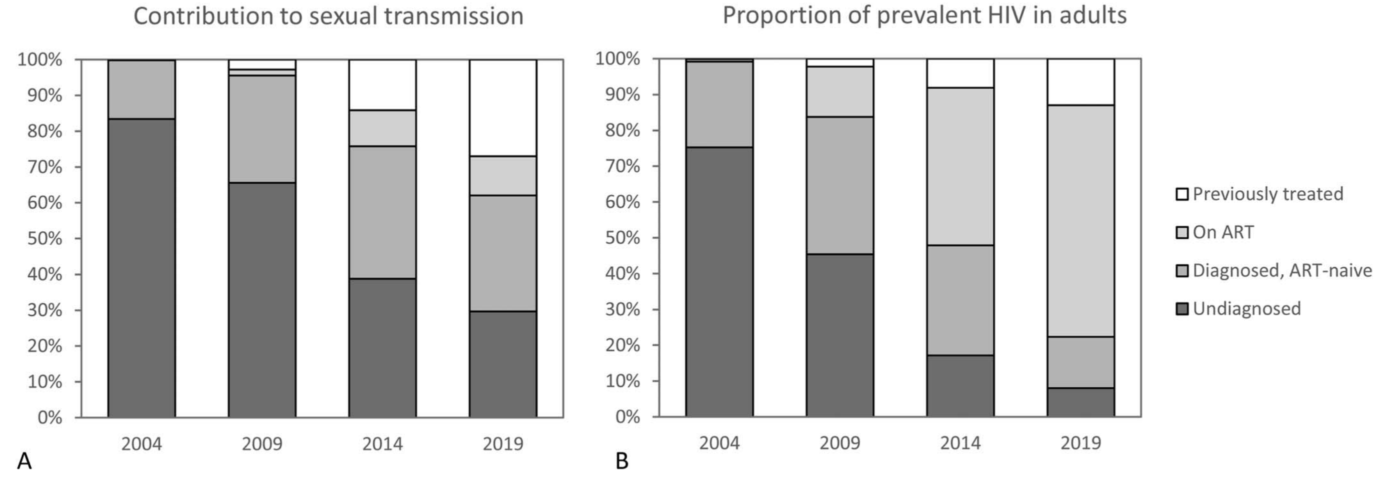

FIGURE 4. Contribution of different HIV disease stages to HIV transmission and to prevalent HIV.

who were diagnosed but ART naive, 10.9% (95% CI: 10.4% to 11.6%) was acquired from individuals who were on ART, and the remaining 27.0% (95% CI: 25.9% to 28.2%) was acquired from individuals who were interrupting ART (Fig. 4A). The latter is a significant increase in the proportion of sexual HIV transmission from ART interrupters at the start of 2009 (2.8%, 95% CI: 2.5%–3.1%) and at the start of 2014 (14.2%, 95% CI: 13.5%–15.0%). In 2019, 65% of adults living with HIV were on ART, while relatively modest proportions were undiagnosed (8%), diagnosed but ART naive (14%) or interrupting ART (13%) (Fig. 4b).

DISCUSSION

Our results suggest that South Africa has made encouraging progress in reducing HIV incidence over the past 2 decades. Although the estimated 47% reduction in HIV incidence over the 2010–2019 period falls short of the UNAIDS target of a 75% reduction over the 2010–2020 period, it is similar to the 43% average reduction in the region, and compares even more favorably with the average reduction of 31% globally over 2010–2020.[7] The incidence-to-prevalence ratio of 0.032 in 2019 is also close to the threshold of 0.03 for "epidemic transition" defined by UNAIDS.[8] Our results suggest that most of the HIV incidence reduction in South Africa is attributable to condom promotion and ART. To a lesser extent, increases in HIV testing and VMMC programs have also contributed significantly to incidence declines. Similar intervention impacts might be expected in other southern and eastern African countries, which mostly have similar levels of knowledge of HIV status,[12] ART coverage,[38] condom use,[13] and VMMC uptake[39] to South Africa.

Consistent with previous studies,[1,3] we find that HIV incidence rates in women have not declined to the same extent as those in men. To some extent, this is because VMMC programs mainly benefit men—although there is nevertheless a significant indirect benefit for women.[40] In addition, the higher rates of HIV diagnosis and ART coverage in women, relative to men, mean that men receive more of the ART prevention benefit. Our results suggest that VMMC and condom promotion have had more impact on HIV incidence at younger ages than at older ages, resulting in a shift in the age distribution of incidence toward older ages, consistent with other studies.[41,42] However, the change in age distribution is also partly the result of the natural dynamics of the epidemic: as people living with HIV age, they generate higher incidence rates at older ages. This is especially true for men: the 45% increase in HIV incidence in women aged ≥50 years over the 2000–2019 period is largely because of HIV-positive men aging into the ≥50-year age group.

Although there are concerns that ART optimism may have eroded some of the gains made by behavior change communication programs,[19–21] our analysis suggests that the impact of condom promotion has steadily grown over the past decade. This is likely to be because of the secondary prevention benefits of infections averted in the earlier stages of the epidemic, that is, the proportionate impact of prevention programs is greater in the long term than in the short term.[43] When fitting our statistical model to national survey data on condom use, we found no significant evidence to suggest reductions in condom use over the past decade (see Table S2, Supplemental Digital Content, http://links.lww.com/QAI/B811). Although the model estimated a slight increase in the proportion of adults with multiple partners, this was entirely because of declining rates of marriage (see Figure S21, Supplemental Digital Content, http://links.lww.com/QAI/B811). These results are consistent with trends in sexual behavior in other countries in the region.[13,14,44] However, a limitation of our analysis is that we have not considered the possibility of changes in age at sexual debut or secondary abstinence, as a result of concerns about weak and inconsistent evidence (for further discussion, see Section 4, Supplemental Digital Content, http://links.lww.com/QAI/B811).

Concerns about risk compensation have also been raised in the context of VMMC, although data do not support this,[45] and we have consequently not assumed any risk compensation to occur after circumcision. Although our estimated reductions in HIV incidence because of VMMC are modest, this is mainly because the uptake of VMMC has been highest in young adolescent boys who are not yet sexually active.[23] The prevention benefits of VMMC in South Africa are expected to grow substantially over the next decade as these young men reach their peak ages of sexual risk behavior and as the secondary benefits of reduced transmission to female partners become more substantial.[46]

Although not as significant as ART, our results suggest that behavior changes associated with HIV diagnosis may also have had a substantial impact on HIV incidence, consistent with previous studies.[9–11] This finding should be treated with some caution because there is substantial uncertainty regarding the proportionate reduction in unprotected sex after HIV diagnosis (see Table S16, Supplemental Digital Content, http://links.lww.com/QAI/B811), and this results in relatively wide confidence intervals around the estimated impact of HIV testing (Fig. 3E). In addition, MicroCOSM estimates a much smaller impact of HIV testing on HIV incidence and shows that this impact is sensitive to assumptions about interindividual heterogeneity in condom use (for further discussion see Section 3.5, Supplemental Digital Content, http://links.lww.com/QAI/B811).

The impact of PrEP was not considered in this analysis because uptake has to date been extremely low. By 2019, PrEP coverage levels in HIV-negative sex workers and MSM were 3% and 1%, respectively,[47] with negligible uptake in other risk groups. However, the impact of PrEP could become more substantial in future, particularly with the introduction of long-acting injectable PrEP.[48] Injectable PrEP is more effective than oral PrEP,[49] and local studies suggest a preference for injectable over oral HIV prevention methods,[50] which in turn suggests potential for significantly greater PrEP impacts in future.

A strength of our analysis is that it integrates data from several different sources—HIV prevalence data, mortality data, program data, and behavioral data—within a Bayesian modeling framework. Our estimates of HIV incidence reductions over 2010–2019 might be considered conservative because our recent estimates of HIV incidence are slightly higher than survey estimates,[6,37] which were not used in calibration. However, survey estimates depend on assumptions about parameters such as the mean duration of recent infection, which could vary across populations.[51] In addition, survey algorithms for defining recent infection exclude individuals on ART with suppressed viral loads, which may lead to HIV incidence being underestimated if there are significant numbers of individuals starting ART within a year of seroconversion. Our model suffers from the same limitation that incidence estimates depend on assumptions and structural simplifications, and our incidence estimates should therefore be treated with similar caution. A more detailed discussion of the strengths and limitations of different HIV incidence estimation approaches is included in the supplementary materials (see Section 5, Supplemental Digital Content, http://links.lww.com/QAI/B811).

Because we do not yet have HIV prevalence data after 2019, estimates of HIV incidence after 2019 are very uncertain and are not reported in our main results. However, extrapolating from trends in the previous years, our model estimates an HIV incidence rate in 15- to 49-year olds of 0.77% (95% CI: 0.68% to 0.89%) at the start of 2020, 52% (95% CI: 47% to 56%) lower than in 2010. HIV incidence rates in 2020 are particularly uncertain because of the unknown impact of COVID-19.[52] Early indications are that COVID-19 has severely impacted VMMC provision in South Africa[53] but that the impact on HIV testing and ART initiation has been more modest,[54–56] and there does not seem to have been any major drop in ART retention.[55–57] Mathematical models predict that HIV incidence rates are unlikely to be sensitive to short-term changes in VMMC, HIV testing, and ART initiation,[52] which suggests that South African HIV incidence estimates may be relatively unaffected by COVID-19, at least in the short term.

Another limitation of our model is that it does not include certain key populations at high HIV risk; although sex workers and MSM are included in the model, transgender women and people who inject drugs are not currently modeled. We also lack reliable data on intervention uptake in key populations, and although sex workers and MSM are estimated to contribute only modestly to new HIV infections in recent years,[58,59] this is nevertheless a source of uncertainty when estimating HIV incidence trends.

Although these results may be viewed positively, there is still much that needs to be done to improve South Africa's HIV response. With 26% of recent HIV transmission being from individuals interrupting ART, there is a clear need to improve retention in ART programs and reduce treatment interruptions. There is also an urgent need to address the relatively low rates of diagnosis and ART uptake in men, for example, through self-testing,[60] testing strategies that target men,[61,62] and community-based ART.[63] The shift in the age distribution of incident HIV to older ages also suggests a greater need for prevention programs in adults aged 25 years and older. Finally, structural interventions to address the social determinants of HIV—such as income inequality, inequitable gender norms, and hazardous drinking—also need to be considered.[64,65]

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