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Dramatic increases in HIV prevalence after scale-up of antiretroviral treatment: a longitudinal population-based HIV surveillance study in rural kwazulu-natal

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Abstract

Objectives—To investigate HIV prevalence trends in a rural South African community after the scale-up of antiretroviral treatment (ART) in 2004.

Methods—We estimated adult HIV prevalence (ages 15–49 years) using data from a large, longitudinal, population-based HIV surveillance in rural KwaZulu-Natal, South Africa, over the period from 2004 (the year when the public-sector ART scale-up started) through 2011. We control for selection effects due to surveillance non-participation using multiple imputation. We further linked the surveillance data to patient records from the local HIV treatment programme to estimate ART coverage.

Results—ART coverage of all HIV-infected people in this community increased from 0% in 2004 to 31% in 2011. Over the same observation period adult HIV prevalence increased steadily from 21% to 29%. The overall increase in HIV prevalence was largely driven by the prevalence trends in women and men older than 24 years of age, i.e., the age group in which the largest proportions of HIV-infected people received ART.

Conclusions—The observed dramatic rise in adult HIV prevalence can be largely explained by increased survival of HIV-infected people due to ART. This interpretation is supported by the fact that the overall HIV prevalence trend is mostly due to increases in prevalence in older adults, i.e., in the age groups that currently benefit most from the local ART scale-up. Future studies should decompose HIV prevalence trends into HIV incidence and HIV-specific mortality changes to further improve the causal attribution of prevalence increases to treatment success rather than prevention failure.

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Conflicts of interest
All authors declare that they have no conflicts of interest.

Keywords

antiretroviral treatment; HIV prevalence; HIV surveillance; KwaZulu-Natal; population-based longitudinal cohort study

Introduction

Changes in HIV prevalence over time have in the past commonly been used to assess the success of national HIV responses, with increasing HIV prevalence taken to indicate failure of HIV prevention strategies [1–3]. However, such use of HIV prevalence data may become increasingly misleading, as large-scale antiretroviral treatment (ART) intervenes in the course of the HIV epidemic. Effective ART substantially increases survival of HIV-infected populations [4–7] and can decrease HIV transmission probabilities [8,9]. Mathematical models have predicted that the *net* impact of these two counteracting ART effects will be an increase in HIV prevalence, at least over the coming decades [10]. However, this impact has not been empirically documented.

We examine for the first time HIV prevalence trends following the start of ART scale-up in one of the HIV hyperendemic communities in sub-Saharan Africa, using data from the longitudinal, population-based HIV surveillance conducted by the Africa Centre for Health and Population Studies (Africa Centre) in rural Kwa-Zulu-Natal, South Africa [11]. KwaZulu-Natal is the province with the currently highest prevalence of HIV in South Africa and, as a consequence, with the highest adult mortality [12,13]. In this study, we quantify the HIV prevalence and ART coverage trends over the period 2004–2011 and examine trend differentials by sex and age group to inform hypotheses about the relationship between HIV prevalence and the local ART scale-up.

Methods

Setting

The Africa Centre setting and the HIV surveillance are described in the Appendix and elsewhere [11,14]. The Hlabisa HIV Treatment and Care Programme had 16,000 individuals actively on ART at the end of 2011, of which about 40% or 6,500 resided in the Africa Centre demographic surveillance area (DSA) [15].

Data for HIV prevalence estimation

To ensure comparability of the HIV data over time and across the sexes, we restricted our annual samples to men and women aged 15–49 years, even though since 2007 all adults 15 years or older were eligible for HIV testing in the surveillance. Sample sizes (and participation rates) in the years 2004 through 2011 were, respectively: 19,907 (57.6%); 27,303 (31.5%); 21,121 (37.7%); 20,211 (32.3%); 21,180 (30.6%); 18,339 (29.7%); 19254 (37.7%); 17,618 (36.9%). Participation rates by calendar year, sex and age group are reported in the appendix. The denominator of the participation rates is based on near-complete population enumeration (response rate greater than 99%) through the Africa Centre surveillance system. The denominator includes all individuals eligible for HIV

testing, i.e., both those who the surveillance fieldworkers successfully contacted for HIV testing consent and those who could not be contacted. Consent rates, i.e., the percentages of successfully contacted individuals who agreed to provide blood for an HIV test, were significantly higher (e.g., 51% in 2010 and 63% in 2011).

Data for ART coverage estimation

To estimate ART coverage of the HIV-infected people included in the samples described above, we matched the individuals who were eligible to participate in the population-based HIV surveillance to the patients in the local HIV treatment programme, using data on first name, last name, sex, birth date, and South African identification number [16].

Statistical Analysis

We computed crude HIV prevalence estimates for the entire eligible population, and sex and age subgroups, for each year from 2004 to 2011. To control HIV prevalence estimates for selective surveillance participation, we accounted for selection on a wide range of observed variables (age, sex, urban vs. rural residency status, household wealth, employment status, and educational attainment) using multiple imputation with chained equations (see Appendix for further details). Five complete data sets for HIV status were constructed from the imputation procedure using the R package MICE [17]. To obtain prevalence estimates and 95% confidence intervals from the five completed imputed datasets, we used the standard multiple imputation approaches [18,19]. All statistical analyses were performed in R version 2.14.2.

Results

We find a steady and substantial increase in both crude and imputed HIV prevalence for the adult population in this community over the observation period 2004–2011 (Table 1). When we stratify the prevalence estimates by sex and broad age groups, we find that the increases in overall HIV prevalence are largely driven by the prevalence trends in women and men aged 25–49 years (Fig. 1 and Appendix Tables S3 and S4). We do not find a similar trend in women and men aged 15–24 years. While there appears to be an increase over time in HIV prevalence in the youngest age group (15–19 years) in both men and women (which might be interpreted to indicate increasing HIV incidence), these increase does not reach statistical significance.

ART coverage increased rapidly over time, reaching levels >30% of all HIV-infected adults in 2011 (Table 1). In all years, ART coverage was higher in women aged 25–49 years compared to men in the same age group, and it was higher in both women and men aged 25–49 years than in younger age groups (Appendix Table S5).

To test the robustness of our findings, we conducted additional analyses using methods similar to those introduced by Floyd et al. [20]. We added HIV status data available at one point in time from the same individual who at another point in time refused an HIV test to proxy HIV status at the date of refusal. For this purpose, we used data closest in time to the date when an individual refused to participate in the HIV surveillance within specified time windows around this date: (i) +/− one year, (ii) +/− two years, and (iii) three +/- years. All

annual HIV prevalence estimates (both those based on complete cases and after multiple imputation) remained essentially unchanged in these three additional analyses (Appendix Figures S1 and S2).

Discussion

We find dramatic increase in overall adult HIV prevalence in a community in rural KwaZulu-Natal over the past eight years, following the public-sector scale-up of ART in South Africa. It is likely that this increase is a causal effect of the ART scale-up. ART was scaled up quickly over the observation period, reaching almost 40% (30%) of all HIV-infected women (men) aged 25–49 years. As a result, HIV-related mortality in this community has markedly declined [4,7,21]. At the same time, HIV incidence has remained high over the past years [22], but has not increased and has recently started to decline [23], so that it is unlikely that the HIV prevalences trend could have been caused by increasing incidence. Our result that HIV prevalence increases in older women and men, i.e., the age group with the highest proportions of people receiving ART, is largely responsible for the increase in overall adult prevalence lends further support to the interpretation that the ART scale-up is the cause of the observed trends.

Our findings confirm for the first time empirically the results of recent mathematical modelling studies, which predict that the net effects of ART will lead to HIV prevalence increases over the coming years despite the transmission-reducing effects of treatment [24,25]. While HIV prevalence has overall dramatically increased since 2004 in older women in this community, our data seem to indicate that prevalence is stabilizing in 2011, despite continuing increases in ART coverage. Plausible explanations of this most recent trend include changing composition of people initiating ARTand changing ART adherence over time. Further empirical and modeling studies are needed to continue tracking and explaining HIV prevalence trends in this community.

Our study has several limitations. For one, it is descriptive in nature and our interpretation that the observed HIV prevalence increases are due to ART is based on our understanding of HIV epidemic dynamics and background information on the community in which the study took place. Future studies in this and other population-based cohorts are needed to confirm that observed prevalence increases are causally attributable to the survival benefits of ART. Such studies could also contribute to decomposing the different effects of ART that can contribute to the net changes in HIV prevalence: the direct effect on survival in HIV-infected people receiving ART, the transmission-reducing ART effects, and any survival spillover effects in people not receiving ART. It is for instance possible that ART affects the delivery of other life-saving health services [26,27]. In as far as these services differentially benefit HIV-infected and –uninfected populations, ART spillover effects can lead to changes in HIV prevalence.

We have accounted for selection on a wide range of observed variables in multiple imputation and have further demonstrated the robustness of our results to widening the window of time within which HIV status data on an individual is used for the analyses. Despite these results indicating robustness, we cannot completely rule out that endogenous

selection has affected our findings. In particular, it is plausible that people who know of their positive HIV status are less likely to participate in HIV surveillance than other population sub-groups [16]. However, we can predict the direction of the potential bias due to this potential endogenous selection. As HIV status knowledge has increased in this community over time due to the local ART scale-up and intensified public HIV testing campaigns, we would have *underestimated* the steepness of the HIV prevalence time trend in this case. The only principled approach to control for endogenous selection is Heckman-type selection models, which have been applied to HIV prevalence estimation by Bärnighausen et al. using the identity of the HIV fieldworker as a selection variable [28,29]. Future studies in this community should replicate this approach to confirm the findings published in this article.

Our findings have a number of important implications for health policy and research. First, the common causal attribution of HIV prevalence trends to a failure of HIV prevention becomes untenable in areas where ART scale-up has reached high levels. It is likely that in other communities in Southern Africa that have benefited from the recent scale-up of ART observed HIV prevalence increases will be due to improved survival of HIV-infected people because of successful treatment programmes, rather than due to HIV incidence increases. As mathematical modelshaveshown,intheinitialyearsfollowingARTscaleup [24,30], the survival benefits outweigh the incidence reductionduetoART,leadingtoHIVprevalenceincreases, whileinthelongerruntheART-inducedreductionsinHIV incidence may decrease prevalence.

Second, methods to estimate HIV incidence based on HIV prevalence changes observed in independent cross-sectional samples of the same populations over time, become increasingly difficult to use in the dynamic stages of ART scale-up, when the survival of HIV-infected populations is constantly improving, leading to increasing HIV prevalence.

Third, as individuals, households and communities make decisions based on expectations about their health and survival, it will be important to ensure that people in areas with increasing HIV prevalence due to successful HIV treatment programmes understand that these increases are not the result of increases in the force of the epidemic, but rather reflect the good news that HIV treatment is improving the life expectancies of people who have been infected in the past. As HIV prevalence increases will likely soon be observed in other parts of Southern Africa, it will be crucial that governments and community organizations design effective messages to communicate the reasons for the increases.

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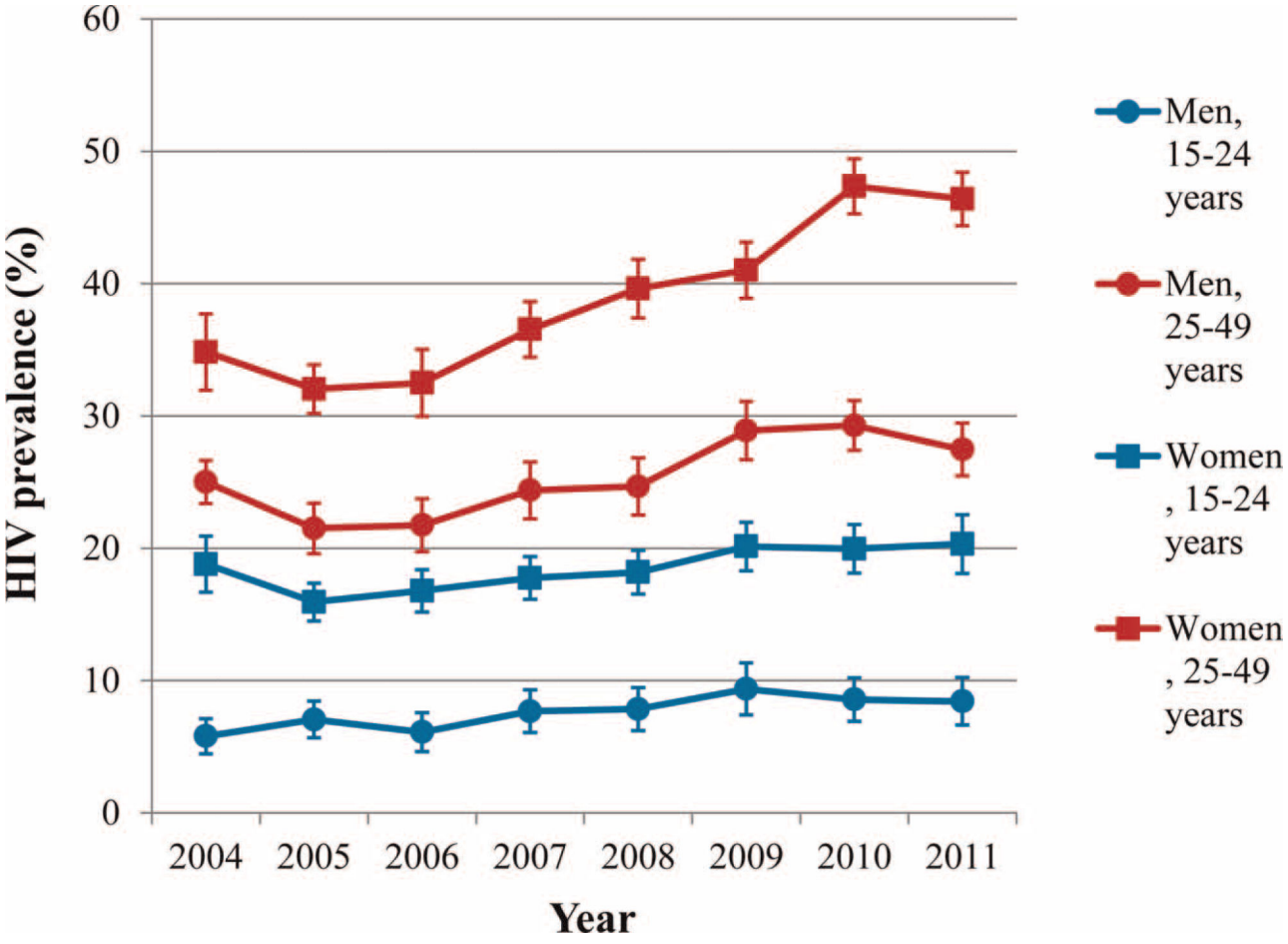

Fig. 1. HIV prevalence estimates by sex and age group

The estimates in this figure are imputation-adjusted. The error bars indicate the 95% confidence intervals.

Table 1

Overall adult prevalence estimates.

Year	Complete-case HIV prevalence estimates (95 % CI)	Imputation-adjusted HIV prevalence estimates (95% CI)	ART Coverage estimates (95% CI)
2004	21.8 (20.9–22.7)	22.4 (21.2–23.5)	0.0 (0.0–0.2)
2005	20.1 (19.2–21.0)	20.0 (19.2–20.9)	1.0 (0.61–1.4)
2006	19.8 (18.9–20.7)	20.3 (19.2–21.4)	3.8 (3.2–4.6)
2007	22.2 (21.1–23.1)	22.7 (21.3–24.1)	8.3 (7.4–9.3)
2008	22.9 (21.9–24.0)	24.0 (23.0–25.0)	14.3 (13.2–15.5)
2009	26.6 (25.4–27.9)	26.9 (25.8–28.0)	20.1 (18.8–21.3)
2010	29.2 (28.1–30.2)	28.5 (27.3–29.6)	24.7 (23.4–25.9)
2011	29.0 (27.9–30.1)	28.1 (26.9–29.2)	30.7 (29.3–32.1)

CI, confidence interval.