



What underpins the decline in syphilis in Southern and Eastern Africa? An exploratory ecological analysis



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SUMMARY

Background: AIDS mortality played an important role in the decline in syphilis prevalence in the USA, but its effect on the dramatic reduction in syphilis prevalence in Southern and Eastern Africa has not been explored. In this ecological study, we investigated the extent to which the relationship between syphilis and HIV prevalence at a population level varied between the early and late periods of the HIV epidemic. **Methods:** We performed linear regression analysis to measure the association between the national prevalence of syphilis and the peak-HIV prevalence in the early and late phases of the HIV epidemic in 11 countries of Southern and Eastern Africa.

Results: Our analysis showed a strong positive association between peak-HIV prevalence and syphilis prevalence early in the HIV epidemic ($R^2 = 0.59$; $p = 0.006$). Although only of borderline statistical significance, this linear relationship between HIV prevalence and syphilis prevalence switched to a negative direction late in the HIV epidemic ($R^2 = 0.32$; $p = 0.07$).

Conclusions: AIDS mortality may have played an important role in the decline in syphilis in this region. Consequently, with AIDS deaths declining in Sub-Saharan Africa, vigilant surveillance of syphilis prevalence will be necessary to detect a potential re-emergence, as has occurred in high-income countries, and to render a timely public health response.

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1. Introduction

There has been a dramatic decline in the prevalence of syphilis in Southern and Eastern Africa over the past two decades. In South Africa, for example, the prevalence dropped from 10.8% to 1.6% between 1998 and 2004 among women attending antenatal care.¹ Two explanations for this have dominated the literature. Authors of a paper entitled “Declining syphilis prevalence among pregnant women in northern Botswana: an encouraging sign for the HIV epidemic?” argued that reductions in higher-risk sex and the introduction of syndromic management of sexually transmitted infections (STIs) were responsible.² Similar explanations were offered in an analysis of factors responsible for the decline in syphilis prevalence among pregnant women in Nairobi since 1995.³ In contrast, a study from the USA that applied regression analysis to state-level AIDS mortality rates and syphilis

incidence rates found that AIDS mortality explained one-third to one-half of the decline in syphilis incidence among men.⁴ This can be explained by the strong association between HIV and syphilis at the individual-level, and that people at risk for syphilis are also at increased risk for HIV infection. In the era preceding the availability of antiretroviral therapy (ART), a relatively high proportion of individuals contributing to syphilis transmission would have been co-infected with HIV and subsequently died from AIDS. Although estimates of syphilis and HIV co-infection were not routinely reported, AIDS mortality could have been responsible for reducing a substantial portion of syphilis transmission and overall syphilis prevalence. Mathematical modelling of data from South Africa suggests that increased condom usage, improved treatment of STIs, and AIDS mortality were collectively responsible for the decline in syphilis prevalence between 1990 and 2005.⁵

From a public health perspective, it is important to establish which of these three factors may have produced the greatest reductions in syphilis prevalence in Southern and Eastern Africa. If

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improved STI treatment and behaviour change had the greatest impact, then recent suggestions are plausible that syphilis prevalence should remain low in future years and that syphilis is a reasonable candidate for elimination in the region.⁶ However, if AIDS mortality played a key role in reducing the population prevalence of syphilis, then the comparatively recent and widespread implementation of ART in the region may lead to a concomitant resurgence of syphilis. Since HIV has become a chronic disease that is manageable by ART in high-income countries, syphilis incidence has increased sharply, particularly among men who have sex with men.⁷ This has been due to a number of factors including reduced AIDS mortality, behavioural disinhibition, and other factors.^{8,9}

We used ecological regression analyses to test the hypothesis that AIDS mortality was an important driver of the decline in syphilis prevalence in Southern and Eastern Africa. Underlying our methodology is the hypothesis that if AIDS mortality has contributed to reductions, then areas with a higher peak-HIV prevalence should have experienced a more rapid and profound decline in syphilis incidence and prevalence than otherwise might have occurred. Thus, we compare the association between syphilis and HIV prevalence at a national level before and after the period of peak-HIV prevalence.

2. Methods

2.1. Syphilis prevalence data

National syphilis prevalence estimates were taken from sources as detailed in Table 1. We used national antenatal surveys wherever possible. However, to our knowledge there are no national antenatal survey data available for a number of countries, particularly from the early years of the HIV epidemic. In these cases, we drew data from antenatal surveys conducted from geographic regions within countries that had mainly been identified in two systematic reviews. One was a systematic review of the prevalence of malaria and curable STIs among pregnant women attending antenatal care in Sub-Saharan Africa between 1990 and 2011;¹⁰ this review excluded South Africa where malaria is no longer endemic. The other was a systematic review of STI prevalence in South Africa between 1985 and 2003 in selected sentinel populations.¹¹ We only used prevalence estimates from antenatal surveys in these systematic reviews. Antenatal data from additional sources were drawn from Botswana, Lesotho, Kenya, Malawi, and Tanzania. Further details for all sources are provided in Table 1. In addition, prevalence estimates were taken from several nationally representative surveys conducted in Uganda (2005 and 2011)^{12,13} and Madagascar (2003).¹⁴ These surveys provided syphilis prevalence estimates among 15–49-year-old women. Syphilis prevalence data from earlier in Uganda's HIV epidemic were obtained from two studies.^{15,16} Because the first of these two studies (1993 estimates) reported combined estimates for men and women, these were only used for the graphical representation of syphilis prevalence over time in Uganda and not in the calculation of syphilis prevalence from before the peak-HIV prevalence. The second study (1998 estimate) employed a population-based sampling strategy; these estimates for women were used as the pre-peak HIV syphilis prevalence.

A number of prevalence estimates were obtained from the World Health Organization's Global Data Repository, which has been an important source of national antenatal syphilis prevalence estimates since 2008.¹⁷ Insufficient data were found for Burundi, Rwanda, and Swaziland to warrant their inclusion in our study. In total, data from 11 countries were used to calculate the following variables: (1) 'Peak-HIV prevalence' defined as the highest HIV prevalence in the relevant area (country or province) between

1990 and 2009. The utility of peak HIV prevalence as a means of comparing different HIV epidemics has been detailed elsewhere.^{18,19} (2) 'Pre-peak-HIV syphilis prevalence' defined as the syphilis prevalence in the country from the first year this was measured. (3) 'Post-peak-HIV syphilis prevalence' defined as the nadir of syphilis prevalence reached in the period after the year that HIV prevalence reached its peak prevalence. (4) 'Change in syphilis prevalence' defined as the absolute difference (in percentage terms) between the mean syphilis prevalence in the period before the year that HIV reached its peak prevalence in that country and the mean syphilis prevalence in the post-peak-HIV period.

2.2. HIV prevalence data

We obtained country- and year-specific 15–49-year-old HIV prevalence estimates from UNAIDS for the period 1990–2010 (<http://www.unaids.org/en/dataanalysis/knowyourepidemic>).

2.3. Statistical analyses

We performed linear regression to analyze the relationship between syphilis prevalence and peak-HIV prevalence, and applied Pearson's correlation coefficient (R^2) to measure the proportion of explainable variance. Analyses were performed using Stata 12.1 (StataCorp LP, College Station, TX, USA).

3. Results

As shown in Figure 1, the only country not to experience a drop in syphilis prevalence during this time period was Madagascar, which was also the only country in Southern and Eastern Africa without a generalized HIV epidemic. The other 10 countries of our analysis experienced a decline in syphilis that occurred at some point after the onset of the HIV epidemic in the country. In one-half of these countries, syphilis prevalence declined within 10 years of HIV prevalence reaching 1% (Botswana, Lesotho, Kenya, Malawi, and South Africa), whereas in the remaining countries, syphilis declined some time later (Mozambique, Tanzania, Uganda, Zambia, and Zimbabwe).

There was a strong positive association between the syphilis prevalence (pre-peak-HIV) and the peak-HIV prevalence at a country level ($R^2 = 0.59$; $p = 0.006$; see Figure 2a). Although only of borderline statistical significance, the linear relationship between HIV prevalence and syphilis prevalence switched to a negative direction when peak-HIV prevalence was related to post-peak-HIV syphilis prevalence ($R^2 = 0.32$; $p = 0.07$; Figure 2b). There was also a statistically significant positive association between peak-HIV prevalence and the change in syphilis prevalence ($R^2 = 0.85$; $p = 0.0001$; Figure 2c).

4. Discussion

The syndromic management of STIs was introduced into all countries of Southern and Eastern Africa in the late 1990s. There is no evidence we could find that the method was less effectively implemented in Madagascar than elsewhere.²⁰ Madagascar is the only country in the region not to have experienced a generalized HIV epidemic or a decline in syphilis prevalence. One possible explanation is that AIDS mortality played an important role in the decline in syphilis prevalence rates. This is also a plausible interpretation for the observed shift in the relationship between syphilis and HIV prevalence at the country level, from a positive association early in the HIV epidemic to a negative association late in the HIV epidemic. This suggests that countries with higher peak HIV prevalence rates had greater declines in syphilis prevalence. As

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