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

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A R T I C L E   I N F O

S U M M A R Y

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.

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

Table 1
Sources of syphilis prevalence data

Country	Year of sampling	Study design, testing modality and study reference
Botswana	1992–2003	Consecutive sample of 750 pregnant women per year (1992–2003) attending any one of Francistown's antenatal care sites. Francistown is Botswana's second biggest town. Approximately 3500 deliveries per year occur in Francistown healthcare facilities, and more than 95% of pregnant women have at least one visit for antenatal care. Syphilis testing with VDRL test only[2]
	2008–2011	WHO Global Health Observatory Data Repository[17]
Kenya	1992–1997	81 311 pregnant women from 10 antenatal sentinel sites in Nairobi were screened for syphilis on their first antenatal visit using the RPR only[3]
	2008–2011	WHO Global Health Observatory Data Repository[17]
Lesotho	1995	Random sample of 190 women from a rural area of Lesotho. Syphilis testing using RPR and TPHA tests[33]
	2003–2007	Data from three national antenatal surveys that assessed syphilis prevalence were used. The 2003 survey tested 2666 pregnant women aged 15–49 years from six sites around the country. They were all tested for syphilis with an RPR test only during their first visit to the antenatal clinic between July and October 2003. Surveys in 2005 and 2007 used the same methodology excluding the fact that they sampled at 10 sites, and in 2005 and 2007, 4542 and 4657 women were tested, respectively[34]
	2010	WHO Global Health Observatory Data Repository[17]
Madagascar	2003	As part of the 2003 Demographic and Health Survey, a nationally representative sample of 2783 women age 15–49 years were tested for syphilis with an RPR test only[14]
	2008–2011	WHO Global Health Observatory Data Repository[17]
Malawi	1990, 1993–1994, and 1996	Three major surveys carried out in 1990, 1993, and 1994 and a smaller survey sample of women in 1996 for a total sample of 10 401 consecutive first-visit pregnant women visiting antenatal care facilities in Blantyre. Syphilis was tested using RPR and TPHA or FTA testing[35]
	1990 and 1993	Two surveys conducted in Blantyre sampling 9890 first-visit pregnant women. Syphilis was tested using RPR and TPHA or FTA testing[36]
	2000–2004	Cross-sectional study of 3824 pregnant women in Blantyre. Syphilis tested using RPR and TPHA tests[37]
	2004–2005	2297 pregnant women recruited in three rural and one peri-urban antenatal clinic in southern Malawi as a part of the APPLe study (Azithromycin for the Prevention of Preterm Labor). Syphilis screening with VDRL only[38]
	2005	All pregnant women (n = 8953) attending antenatal clinics for the first time in the month of August at 19 sites in Malawi were tested for syphilis with the Abbott Determine Rapid Syphilis TP assay[39]
	2008–2011	WHO Global Health Observatory Data Repository[17]
Mozambique	1991–1992	Cross-sectional study among 201 pregnant women and 162 patients presenting with genital complaints. Syphilis testing with RPR and TPHA[40]
	1992–1993	Cross-sectional study conducted among 1728 consecutive antenatal attendees at 14 rural clinics in Zambézia. Syphilis testing with RPR and MHA-TP[41]
	2000	Age-stratified cross-sectional study recruiting 262 women in rural southern Mozambique. Syphilis testing with RPR and IgG ELISA[42]
	2003–2004	Study of 4789 women attending their first antenatal visit at six health facilities in Sofala Province, central Mozambique. Compared the sensitivity of the immunochromatographic strip (ICS) and RPR test[43]
	2003–2005	1030 pregnant women recruited at an antenatal clinic in Manhiça District, southern Mozambique. Syphilis testing with RPR only[44]
	2004	Cross-sectional study conducted among 1119 women attending antenatal care clinics in Tete Province. Syphilis testing with RPR and TPHA[45]
	2008–2011	WHO Global Health Observatory Data Repository[17]
South Africa	1990–1996	Johnson et al. systematic review[11]
	1996–2011	National antenatal surveys[46–51]
Tanzania	1992–2006	National antenatal surveys[52,53]
	2008–2011	WHO Global Health Observatory Data Repository[17,54]
Uganda	1993	A population-based survey of persons aged 15 years or older in two villages in Masaka, Uganda; 294 men and women were tested with both RPR and a TPHA. Reported results are for those who tested positive on both tests[15]
	1990–1993	A cross-sectional survey of all 15–54-year-old inhabitants of 15 neighbouring villages in rural south-western Uganda; 538 women were tested for syphilis with RPR and TPHA confirmatory testing[16]
	2004	250 pregnant women recruited for study in Entebbe, Uganda. Syphilis testing with RPR and TPHA[55]
	2005	A nationally representative sample of 9079 women aged 15–49 years were tested for syphilis with an RPR test and a confirmatory TPHA test[13]
	2011	A nationally representative sample of 10 794 women aged 15–49 years were tested for syphilis with the Bioline syphilis rapid diagnostic test. Those who tested positive had an RPR test to assess for active syphilis. Results reported are for those who tested positive for both tests[12]
Zambia	1994–2008	National antenatal surveys[56]
	2008–2011	WHO Global Health Observatory Data Repository[17]
Zimbabwe	1991	1433 pregnant women included in a study conducted in Umzingwane District. Syphilis testing with RPR test only[57]
	Not reported	Pregnant women recruited for cross-sectional study in Gutu District of Zimbabwe. Syphilis testing with RPR test only[58]
	Not reported	Random sampling of 2969 pregnant women at Harare Maternity Hospital, Harare. Syphilis testing with RPR and TPHA[59]
	2002–2003	Cross-sectional study of 691 pregnant women. Study was conducted from three peri-urban clinics around Harare. Syphilis testing with RPR and TPHA[60]
	2002–2004	Cross-sectional study that enrolled pregnant women in Harare (n = 691) and Moshi (n = 2654). Syphilis testing with RPR and Determine Syphilis TP[61]
	2011	WHO Global Health Observatory Data Repository[17]

VDRL, Venereal disease research laboratory; WHO, World Health Organization; RPR, rapid plasma reagin; TPHA, *Treponema pallidum* hemagglutination assay; FTA, Fluorescent Treponemal antibody-absorption test; MHA-TP, micro-hemagglutination assay–*Treponema pallidum*; IgG, Immunoglobulin G; ELISA, enzyme-linked immunosorbent assay.

observed in the USA, AIDS mortality could have been responsible for this effect in Southern and Eastern Africa. The effect of AIDS mortality could have been mediated via three pathways: (1) individuals most at risk of syphilis acquisition and transmission were removed from the population; (2) people living in areas with higher AIDS mortality may have been more likely to change their sexual behaviour;[4,21] and (3) depletion of the pool of high-risk persons might have made it difficult for the remaining high-risk
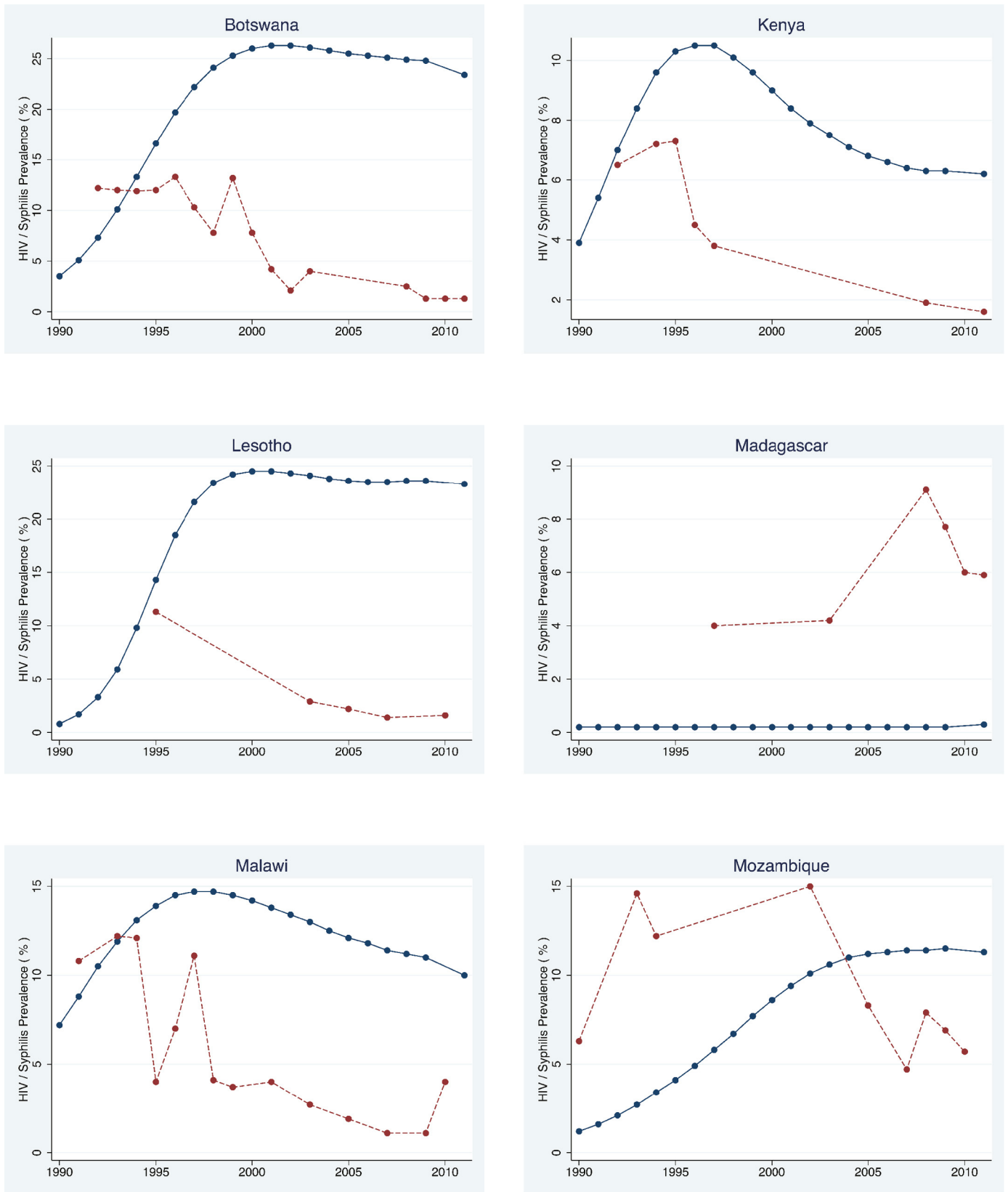
Figure 1. National prevalence of syphilis and HIV by year in 11 countries of Southern and Eastern Africa (data sources detailed in the Methods section).

persons to find sufficient partners with whom to engage in risky sex.[22]

Another potential interpretation of our findings is that optimal STI treatment was more effectively provided in countries with higher peak HIV prevalence estimates. However, an analysis using a number of data sources as proxy measures for the efficacy of STI treatment showed there to be no relationship between peak-HIV prevalence and STI treatment efficacy.[23] Alternatively, it is possible
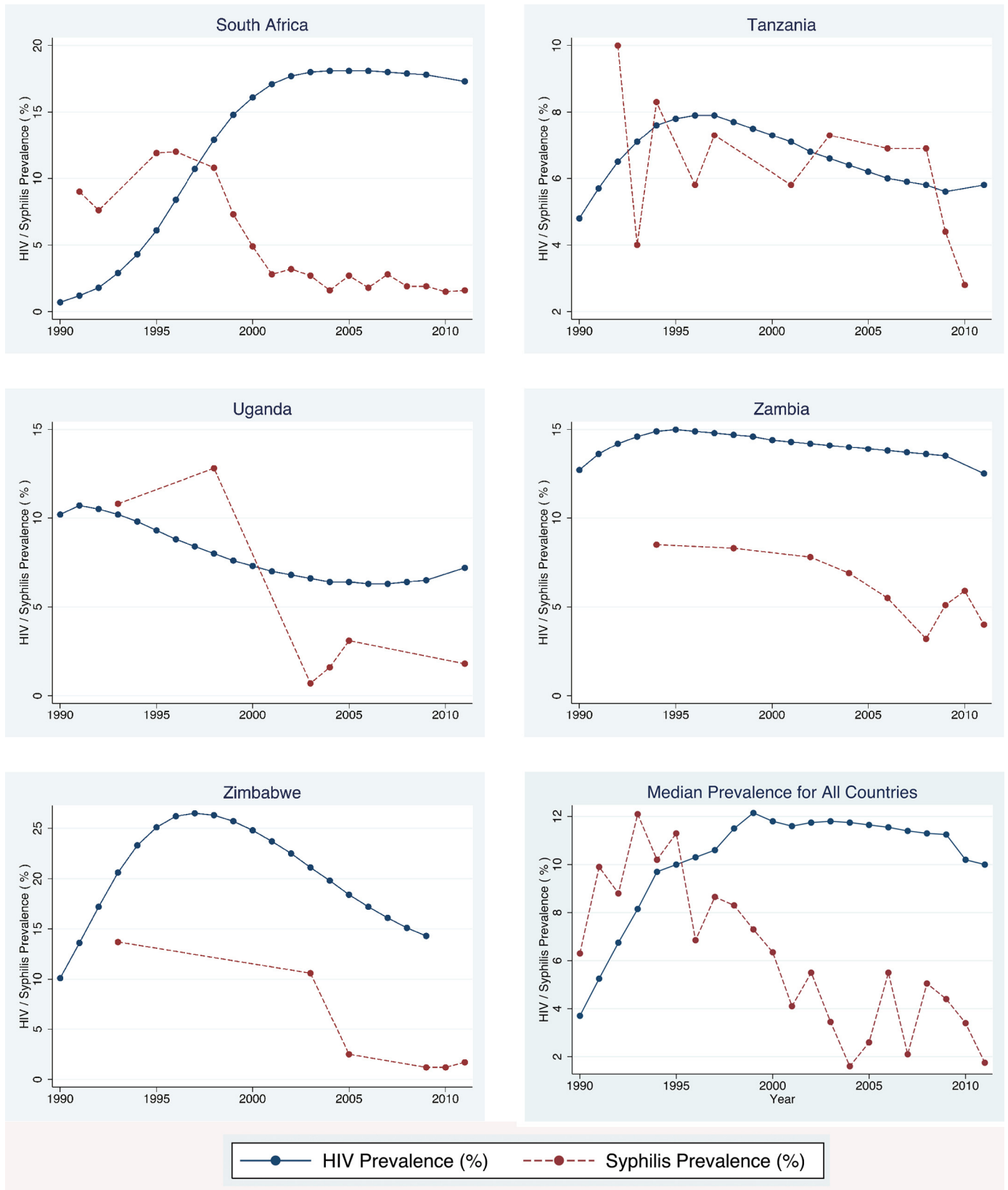
Fig. . (Continued).

that countries more heavily affected by HIV also responded more rapidly to the epidemic, thereby accelerating reductions in higher-risk sex within their borders. However, we could find scant evidence to support this theory. Analysis of changes in risk behaviour in South Africa's ethnic groups, for example, suggests that ethnic groups most affected by HIV also showed a more rapid increase in condom usage, but this did not translate into lower HIV prevalence because there was little change in their rates of
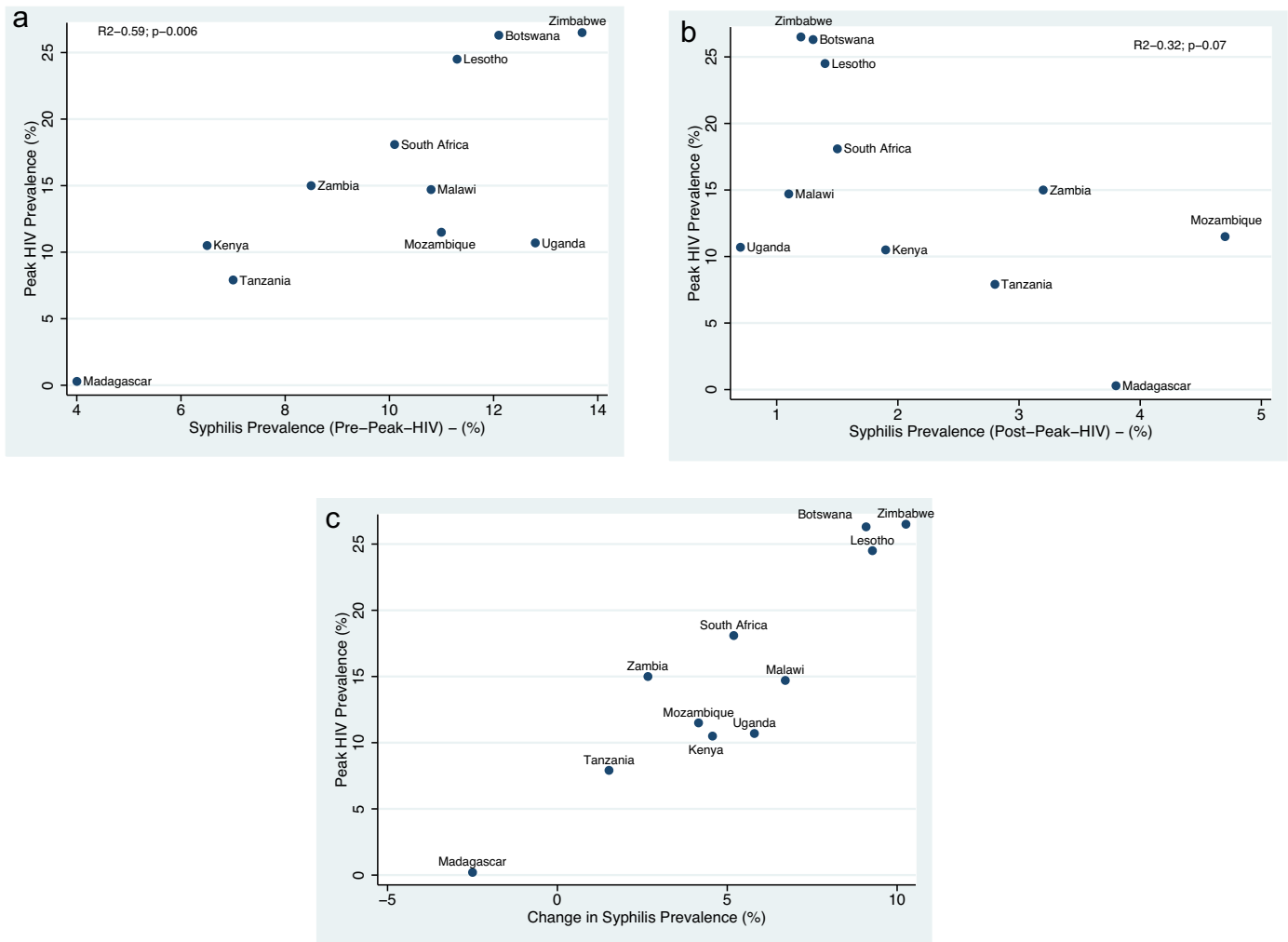
Figure 2. Association between national peak-HIV prevalence and syphilis prevalence from (a) early in the HIV epidemic (pre-peak) and (b) late in the epidemic (post-peak), and (c) the absolute change in syphilis prevalence between the pre- and post-peak-HIV periods in the countries of Southern and Eastern Africa. The data sources are described in the Methods section.

multiple and concurrent partnering, which remained considerably higher than among groups with a low prevalence of HIV.[24] Thirdly, the declines in syphilis prevalence may be due to some other unmeasured variable. The reasons behind the declines in syphilis prevalence are likely to be multifactorial and to vary somewhat among countries. This may explain the finding that in some countries syphilis prevalence declined relatively soon after the HIV epidemic began whereas in others it declined some time later.

There are a number of limitations with this analysis. The main problem is the paucity of accurate representative syphilis prevalence data. This is particularly the case in the 1980s and 1990s. We were thus forced in a number of instances to use data that were derived from local surveys that are unlikely to reflect national populations. Thus, our country-level findings of a positive relationship between peak-HIV prevalence and pre-peak-HIV syphilis prevalence should be interpreted with caution. However, it should be noted that syphilis prevalence estimates from surveys conducted prior to the peak of HIV were all high ($\geq 4\%$) and considerably lower following the peak-HIV period. This is in keeping with the findings of the systematic review of curable STIs among pregnant women attending antenatal care facilities in Sub-Saharan Africa and the World Health Organization reports on this topic.[10,25,26]

Since HIV is one of a number of causes of a false-positive diagnosis using rapid plasma reagin (RPR) assays, the HIV epidemic could have influenced RPR-based estimates of syphilis prevalence.[27] However, the fact that the syphilis prevalence dropped rather than rose as HIV prevalence increased suggests that this was unlikely to have played a large role. RPR results can also vary by a one-dilution titre between different batches, which adds a further potential misclassification bias.[28] The endemic treponematoses – yaws, bejel, and pinta – are other possible causes of false-positives with all the testing algorithms used in the studies. Thus, observed declines in syphilis prevalence may have been an artefact of reductions in these other treponematoses. This is however most unlikely, as none of the countries investigated here had reported any of these diseases between 1980 and 2012.[29]

A further reason we do not believe our results are a chance finding is that we have found the same association between syphilis and peak-HIV prevalence at a provincial level in South Africa and Zambia and at a district council level in South Africa. In each of these studies we found the same positive relationship between syphilis prevalence early in the HIV epidemic and peak-HIV epidemic and a negative relationship between syphilis prevalence late in the HIV epidemic and peak-HIV prevalence (C. Kenyon; unpublished results).

There has been a commendable reduction in syphilis prevalence in almost all the countries in this region. The data presented here, however, add to evidence from elsewhere that AIDS mortality likely played a significant role in this decline. The widespread availability of ART in high-income countries has indirectly contributed to a resurgence of syphilis in such settings through a combination of reduced AIDS mortality and behavioural disinhibition.[30] Both of these factors have been noted in Southern and Eastern Africa.[31,32] Vigilant surveillance is therefore necessary to detect a potential re-emergence of syphilis prevalence, as observed in high-income countries, and to render a timely public health response.

Conflict of interest: None declared.

References

1. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey, South Africa, 2010. South Africa: National Department of Health; 2011.
2. Creek TL, Thuku H, Kolou B, Rahman M, Kilmarx PH. Declining syphilis prevalence among pregnant women in northern Botswana: an encouraging sign for the HIV epidemic? *Sex Transm Infect* 2005;**81**:453–5.
3. Temmerman M, Fonck K, Bashir F, Inion I, Ndinya-Achola JO, Bwayo J, et al. Declining syphilis prevalence in pregnant women in Nairobi since 1995: another success story in the STD field? *Int J STD AIDS* 1999;**10**:405–8.
4. Chesson Harrell W, Dee Thomas S, Aral Sevgi O. AIDS mortality may have contributed to the decline in syphilis rates in the United States in the 1990s. *Sex Transm Dis* 2003;**30**:419–24.
5. Johnson LF, Dorrington RE, Bradshaw D, Coetzee DJ. The effect of syndromic management interventions on the prevalence of sexually transmitted infections in South Africa. *Sex Reprod Health* 2011;**2**:13–20.
6. Otieno-Nyunya B, Bennett E, Bunnell R, Dadabhai S, Gichangi AA, Mugo N, et al. Epidemiology of syphilis in Kenya: results from a nationally representative serological survey. *Sex Transm Infect* 2011;**87**:521–5.
7. Kerani RP, Handsfield HH, Stenger MS, Shafii T, Zick E, Brewer D, Golden MR. Rising rates of syphilis in the era of syphilis elimination. *Sex Transm Dis* 2007;**34**:154–61.
8. Fenton KA. A multilevel approach to understanding the resurgence and evolution of infectious syphilis in Western Europe. *Euro Surveill* 2004;**9**:3–4.
9. Stolte IG, Dukers NH, Geskus RB, Coutinho RA, de Wit JB. Homosexual men change to risky sex when perceiving less threat of HIV/AIDS since availability of highly active antiretroviral therapy: a longitudinal study. *AIDS* 2004;**18**:303–9.
10. Chico RM, Mayaud P, Ariti C, Mabey D, Ronsmans C, Chandramohan D. Prevalence of malaria and sexually transmitted and reproductive tract infections in pregnancy in sub-Saharan Africa: a systematic review. *JAMA* 2012;**307**:2079–86.
11. Johnson LF, Coetzee DJ, Dorrington RE. Sentinel surveillance of sexually transmitted infections in South Africa: a review. *Sex Transm Infect* 2005;**81**:287–93.
12. Uganda Ministry of Health. Uganda AIDS Indicator Survey 2011. Uganda Ministry of Health and ICF Kampala; 2012.
13. Ministry of Health. Uganda HIV/AIDS Sero-behavioural Survey 2004/2005. Uganda Ministry of Health and ORC Macro; 2006.
14. Institut National de la Statistique (INSTAT) Madagascar and ORC Macro. Enquête démographique et de santé, Madagascar 2003-2004: rapport de synthèse. INSTAT Madagascar and ORC Macro; 2005.
15. Wagner HU, Van Dyck E, Roggen E, Nunn AJ, Kamali A, Schmid DS, et al. Seroprevalence and incidence of sexually transmitted diseases in a rural Ugandan population. *Int J STD AIDS* 1994;**5**:332–7.
16. Kamali A, Nunn AJ, Mulder DW, Van Dyck E, Dobbins JG, Whitworth JA. Seroprevalence and incidence of genital ulcer infections in a rural Ugandan population. *Sex Transm Infect* 1999;**75**:98–102.
17. World Health Organization. Syphilis seropositivity among antenatal care attendees. Indicator and Measurement Registry version 1.6.0. Geneva: WHO; 2011.
18. Kenyon C, Colebunders R, Voeten H, Lurie M, Peak HIV. prevalence: a useful outcome variable for ecological studies. *Int J Infect Dis* 2013;**17**:e286–8.
19. Kenyon C, Buyze J. Should the threshold for generalized HIV epidemics be 1% or 5%? *Int J STDs AIDS* 2014;**25**(12):898–900.
20. Behets F, Andriamiadana J, Rasamilalao D, Ratsimbazafy N, Randrianasolo D, Dallabetta G, Cohen M. Sexually transmitted infections and associated socio-demographic and behavioural factors in women seeking primary care suggest Madagascar's vulnerability to rapid HIV spread. *Trop Med Int Health* 2001;**6**:202–11.
21. Boily MC, Brunham RC. The impact of HIV and other STDs on human populations. Are predictions possible? *Infect Dis Clin North Am* 1993;**7**:771–92.
22. Boily MC, Godin G, Hogben M, Sherr L, Bastos FI. The impact of the transmission dynamics of the HIV/AIDS epidemic on sexual behaviour: a new hypothesis to explain recent increases in risk taking-behaviour among men who have sex with men. *Med Hypotheses* 2005;**65**:215–26.
23. Kenyon C, Buyze J. Correlation between national peak HIV prevalence and concurrency, STI treatment capability, condom use and circumcision: an ecological study. *World J AIDS* 2014;**4**(2):249–57.
24. Kenyon C, Buyze J, Colebunders R. HIV prevalence by race co-varies closely with concurrency and number of sex partners in South Africa. *PLoS One* 2013;**8**:e64080.
25. World Health Organization. Global prevalence and incidence of selected curable sexually transmitted diseases: overview and estimates. Geneva: WHO; 1995.
26. World Health Organization. Global prevalence and incidence of selected curable sexually transmitted diseases: overview and estimates. Geneva: WHO; 2001.
27. Joyanes P, Borobio MV, Arquez JM, Perea EJ. The association of false-positive rapid plasma reagin results and HIV infection. *Sex Transm Dis* 1998;**25**:569–71.
28. Ratnam S. The laboratory diagnosis of syphilis. *Can J Infect Dis Med Microbiol* 2005;**16**:45–51.
29. Mitja O, Smajs D, Bassat Q. Advances in the diagnosis of endemic treponematoses: yaws, bejel, and pinta. *PLoS Negl Trop Dis* 2013;**7**:e2283.
30. Chesson HW, Gift TL. Decreases in AIDS mortality and increases in primary and secondary syphilis in men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2008;**47**:263–4.
31. Kembabazi A, Bajunirwe F, Hunt PW, Martin JN, Muzoora C, Haberer JE, et al. Disinhibition in risky sexual behavior in men, but not women, during four years of antiretroviral therapy in rural, southwestern Uganda. *PLoS One* 2013;**8**:e69634.
32. UNAIDS. UNAIDS reports on the global AIDS epidemic. Geneva: WHO; 2008.
33. Colvin M, Sharp B. Sexually transmitted infections and HIV in a rural community in the Lesotho highlands. *Sex Transm Infect* 2000;**76**:39–42.
34. Lesotho Ministry of Health. Antenatal HIV and syphilis sentinel surveillance 2003, 2005, 2007. Lesotho Ministry of Health; 2008.
35. Taha TE, Dallabetta GA, Hoover DR, Chiphangwi JD, Mtimavalye LA, Liomba GN, et al. Trends of HIV-1 and sexually transmitted diseases among pregnant and postpartum women in urban Malawi. *AIDS* 1998;**12**:197–203.
36. Taha TE, Gray RH, Kumwenda NI, Hoover DR, Mtimavalye LA, Liomba GN, et al. HIV infection and disturbances of vaginal flora during pregnancy. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999;**20**:52–9.
37. Kwiek JJ, Mwapasa V, Alker AP, Muula AS, Misiri HE, Molyneux ME, et al. Sociodemographic characteristics associated with HIV and syphilis seroreactivity among pregnant women in Blantyre, Malawi, 2000-2004. *Malawi Med J* 2008;**20**:80–5.
38. Van den Broek NR, White SA, Goodall M, Ntonya C, Kayira E, Kafulafula G, Neilson JP. The APPLe study: a randomized, community-based, placebo-controlled trial of azithromycin for the prevention of preterm birth, with meta-analysis. *PLoS Med* 2009;**6**:e1000191.
39. Malawi National AIDS Commission. HIV and syphilis sero-survey and national HIV prevalence estimates report. Malawi National AIDS Commission; 2005.
40. Vuylsteke B, Bastos R, Barreto J, Crucitti T, Folgosa E, Mondlane J, et al. High prevalence of sexually transmitted diseases in a rural area in Mozambique. *Genitourin Med* 1993;**69**:427–30.
41. Cossa HA, Gloyd S, Vaz RG, Folgosa E, Simbine E, Diniz M, Kreiss JK. Syphilis and HIV infection among displaced pregnant women in rural Mozambique. *Int J STD AIDS* 1994;**5**:117–23.
42. Menendez C, Castellsague X, Renom M, Sacarlal J, Quinto L, Lloveras B, et al. Prevalence and risk factors of sexually transmitted infections and cervical neoplasia in women from a rural area of southern Mozambique. *Infect Dis Obstet Gynecol* 2010. http://dx.doi.org/10.1155/2010/609315. pii: 609315.
43. Montoya PJ, Lukehart SA, Brentlinger PE, Blanco AJ, Floriano F, Sairosse J, Gloyd S. Comparison of the diagnostic accuracy of a rapid immunochromatographic test and the rapid plasma reagin test for antenatal syphilis screening in Mozambique. *Bull World Health Organ* 2006;**84**:97–104.
44. Menendez C, Bardaji A, Sigauque B, Romagosa C, Sanz S, Serra-Casas E, et al. A randomized placebo-controlled trial of intermittent preventive treatment in pregnant women in the context of insecticide treated nets delivered through the antenatal clinic. *PLoS One* 2008;**3**:e1934.
45. Lujan J, de Onate WA, Delva W, Claeys P, Sambola F, Temmerman M, et al. Prevalence of sexually transmitted infections in women attending antenatal care in Tete Province, Mozambique. *S Afr Med J* 2008;**98**:49–51.
46. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa: Department of Health; 2010.
47. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa, 2010: Department of Health; 2011.
48. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa, 2011: Department of Health; 2012.
49. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa: Department of Health; 2009.
50. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa: Department of Health; 2008.
51. National Department of Health. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey. South Africa: Department of Health; 2006.
52. The United Republic of Tanzania National AIDS Programme. HIV/AIDS/STDs Surveillance. Department of Health; 1995.
53. The United Republic of Tanzania National AIDS Programme. Surveillance of HIV and syphilis infections among antenatal clinic attendees 2003/2004. Department of Health; 2005.
54. The United Republic of Tanzania National AIDS Programme. Surveillance of HIV and syphilis infections among antenatal clinic attendees 2008. Department of Health; 2009.
55. Tann CJ, Mpairwe H, Morison L, Nassimu K, Hughes P, Omara M, et al. Lack of effectiveness of syndromic management in targeting vaginal infections in pregnancy in Entebbe, Uganda. *Sex Transm Infect* 2006;**82**:285–9.
56. Ministry of Health. Zambia Demographic and Health Survey. Central Statistical Office; 2007.
57. Rutgers S. Syphilis in pregnancy: a medical audit in a rural district. *Cent Afr J Med* 1993;**39**:248–53.

58. Majoko F, Munjanja S, Nystrom L, Mason E, Lindmark G. Field efficiency of syphilis screening in antenatal care: lessons from Gutu District in Zimbabwe. *Cent Afr J Med* 2003;**49**:90–3.

59. Pham L, Woelk GB, Ning Y, Madzime S, Mudzamiri S, Mahomed K, Williams MA. Seroprevalence and risk factors of syphilis infection in pregnant women delivering at Harare Maternity Hospital, Zimbabwe. *Cent Afr J Med* 2005;**51**: 24–30.

60. Kurewa NE, Mapingure MP, Munjoma MW, Chirenje MZ, Rusakaniko S, Stray-Pedersen B. The burden and risk factors of sexually transmitted infections and reproductive tract infections among pregnant women in Zimbabwe. *BMC Infect Dis* 2010;**10**:127.

61. Mapingure MP, Msuya S, Kurewa NE, Munjoma MW, Sam N, Chirenje MZ, et al. Sexual behaviour does not reflect HIV-1 prevalence differences: a comparison study of Zimbabwe and Tanzania. *J Int AIDS Soc* 2010;**13**:45.