Epidemics 3 (2011) 88–94

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

Declining HIV prevalence and incidence in perinatal women in Harare, Zimbabwe ☆

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ARTICLE INFO

Article history:
Received 24 June 2010
Revised 10 December 2010
Accepted 23 February 2011
Available online 2 March 2011

Keywords:
HIV-1 prevalence
HIV-1 incidence
Behavior change
Zimbabwe

ABSTRACT

Background: In several recent papers it has been suggested that HIV prevalence and incidence are declining in Zimbabwe as a result of changing sexual behavior. We provide further support for these suggestions, based on an analysis of more extensive, age-stratified, HIV prevalence data from 1990 to 2009 for perinatal women in Harare, as well as data on incidence and mortality.

Methodology/principal findings: Pooled prevalence, incidence and mortality were fitted using a simple susceptible-infected (SI) model of HIV transmission; age-stratified prevalence data were fitted using double-logistic functions. We estimate that incidence peaked at 5.5% per year in 1991 declining to 1% per year in 2010. Prevalence peaked in 1998/9 [35.9% (CI95: 31.3–40.7)] and decreased by 67% to 11.9% (CI95: 10.1–13.8) in 2009. For women <20 y, 20–24 y, 25–29 y, 30–34 y and ≥35 y, prevalence peaked at 25.4%, 34.2%, 47.1%, 44.0% and 33.5% in 1993, 1996, 1997, 1998 and 1999, respectively, declining thereafter in every age group. Among women <25 y, prevalence peaked in 1994 at 28.8% declining thereafter by 69% to 8.9% (CI95: 6.8–11.5) in 2009.

Conclusion/significance: HIV prevalence declined substantially among perinatal women in Harare after 1998 consequent upon a decline in incidence starting in the early 1990s. Our model suggests that this was primarily a result of changes in behavior which we attribute to a general increase in awareness of the dangers of AIDS and the ever more apparent increases in mortality.

Introduction

Zimbabwe is at the center of the HIV pandemic: 1.2 million of its 12 million people are infected with HIV (UNAIDS, 2010). However, several recent reports indicate that HIV prevalence is declining rapidly. In the Eastern highlands of Zimbabwe, between 1998 and 2003, prevalence declined by 12% among all reproductive-aged women and by 49% among those aged 17–29 years; moreover these declines were linked to sexual behavioral change (Gregson et al., 2006). Among women attending antenatal sentinel surveillance sites throughout the country, HIV-1 prevalence declined by one-half between 1999 and 2009 (Gregson et al., 2010; Mahomva et al., 2006; MOH, 2009a). Similarly, in the ZVITAMBO trial a study of 14,110 postpartum women enrolled from maternity hospitals in Greater Harare between November 1997 and January 2000, the monthly prevalence increased from 28.5% (CI95: 23.9–33.4) in December 1997 to 35.9% (CI95: 31.3–40.7) in December 1998 and then declined to 29.5% (CI95: 25.2–34.0) in December 1999 ($p = 0.002$ and 0.003 for linear and quadratic terms, respectively) (Humphrey et al., 2007). These changes remained statistically significant after adjustment for a number of independent factors suggesting that the ZVITAMBO trial had spanned the peak of the epidemic among perinatal women in Harare.

Several modeling studies have led to suggestions that HIV incidence in Zimbabwe peaked around 1990 (Lopman and Gregson, 2008), and

☆ Previously presented in part: at the *Harare National HIV and AIDS Conference: taking stock, looking to the future*, Harare, Zimbabwe, 15–18th June 2004, and at the UNAIDS/WHO/CDC/UNICEF Meeting: *Evidence and causes of declines in HIV prevalence and incidence in countries with generalized epidemics*. Harare, Zimbabwe, 15–17th November 2004.

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doi:10.1016/j.epidem.2011.02.004

that at least part of the decline in HIV incidence could be ascribed to changing sexual behavior (Gregson et al., 2010; Hallet et al., 2009; Hallett et al., 2006).

This paper complements and extends these findings by presenting an analysis of HIV prevalence, incidence and mortality data collected between 1990 and 2009 from 22,684 perinatal women in Greater Harare.

Methods

Sources of data

Prevalence data were drawn from nine data sets (Table 1) from public sector antenatal sites located in high-density urban neighborhoods of Greater Harare. The three sites included in the 1990 study were all part of the 1994/5 study, and the four sites included in the 1994/5 study were all included in ZVITAMBO. One of two Zimbabwe Ministry of Health and Child Welfare (MoHCW) sentinel sites included in the national surveys in 1999–2009 had also been a site in the ZVITAMBO Trial, though neither had been included in the earlier studies (further details of this trial provided in the Supplementary Information).

The HIV sentinel surveys in antenatal clinic sites were conducted by the MoHCW in 1999/2000, 2001, 2002, 2004, 2006 and 2009 (Mahomva et al., 2006; MOH, 2007, 2009b). All women presenting for antenatal care at designated sentinel surveillance sites during the recruitment periods for each of the six surveys were eligible for inclusion. Data for two of these sites, which are located in Greater Harare and were included in all four surveys, were extracted for the current analysis. Women were tested for HIV by ELISA on an unlinked and anonymous basis.

Incidence data were available for a cohort of 372 HIV-negative antenatal women who were enrolled in an observational study between September 1991 and January 1993 and were followed for 24 months postpartum (Mbizvo et al., 2004), and among 9562 women enrolled in ZVITAMBO between October 1997 and January 2000 who were HIV-negative at delivery and were followed for 12 to 24 months postpartum (Humphrey et al., 2006a). Mortality data were obtained from records provided by the City of Harare (Harare City Health Department, 2004). Condom distribution and sales were extracted from published reports of the Zimbabwe National Family Planning Council (PSI, 2004), and program records of Population Services International.

Modeling

HIV status, age, and date of testing were extracted from the nine databases and merged; the combined database included 22,684 women who provided unequivocal HIV test results. HIV prevalence in each of the databases analyzed was estimated for women of all ages pooled, and for age-stratified data.

We use a standard susceptible-infected (SI) model which we fit to data on HIV prevalence, incidence and mortality, all pooled on age. We let $S(t)$ and $I(t)$ be the number of susceptible and infected adults over the age of 25 years at time t, with $N(t)=S(t)+I(t)$. Adults enter the population at risk at a rate b times the population 15 years earlier so that the total population growth rate matches the reported value. To allow for heterogeneity in sexual behavior and to fit the observed asymptotic prevalence of infection the transmission parameter takes the value λ_0 at the start of the epidemic and declines exponentially at rate α times the prevalence of infection. The background death rate is μ. We use a Weibull survivorship, $W(t)$, with a median of 9.8 years and a shape parameter of 2.25 to capture the dependence of HIV-related mortality on time since infection. The model is then

$$\frac{dS}{dt} = bN(t-25) - \lambda_0 e^{-\alpha I/N} SI/N - \mu S \qquad (1)$$

Table 1
Details of studies and sites for the collection of HIV prevalence data in Greater Harare, 1990–2009.

Dates	Sites	Eligibility	N	HIV test	Confirmation	Prevalence (%)	Additional data
Mahomed et al. May–Oct 1990 (Mahomed et al., 1991)	1, 2, 3	1st antenatal visit or at labor	1008	Serial ELISA tests (Abbott and Wellcozyme Recombinant)	Ancoscreen Western Blot	18 [16–21]	Demographics by questionnaire.
Mbizvo et al. May 1994–June 1995 (Mbizvo et al., 1996)	1, 2, 3, 4	1st antenatal visit	1168	Capillus HIV-1/HIV-2 kit	Western Blot, Recombinant ELISA (Cambridge Biotech, Galway, Ireland). HIV rapid test	30 [27–33]	Demographics by questionnaire
ZVITAMBO Nov 1997–Jan 2000 (Humphrey et al., 2007; Humphrey et al., 2006a, 2006bMalaba et al., 2005)	1–14	Within 96 h post partum	14,057	ELISA tests (HIV 1.0.2 ICE: Murex Diagnostics, Edenvale, SA, and GeneScreen HIV 1/2: Sanofi Diagnostics Pasteur, Johannesburg, SA)	Western Blot, (HIV Blot 2.2: Genelabs Diagnostics SA, Genevitamin A, Switzerland)	32 [31–33]	Baseline characteristics by questionnaire and hospital records transcription.
MoHCW ANC Sentinel Surveillance 1999/2000 2001 (Mahomva et al., 2006)	14, 15	Antenatal care visit	841 1043	ELISA test (Biorad Genscreen)		30 [27–33] 31 [28–34]	Age by questionnaire
MoHCW ANC Sentinel Surveillance 2002, 2004 {Mahomva et al., 2006}2006 (Zimbabwe National HIV/AIDS estimates, 2009) 2009 (Central Statistical Office HZ, 1995)	14, 15	Antenatal care visit	1097 1118 1115 1237	Parallel ELISA tests (Biorad Genscreen and Thermo Labsystems)	Western Blot	24 [22–27] 20 [18–23] 16 [14–18] 12 [10–14]	Age by questionnaire

Legend: Sites (clinics unless stated as being hospitals) 1 = Harare Hospital; 2 = Edith Opperman; 3 = Glen View; 4 = Warren Park; 5 = Chitungwiza Hospital; 6 = Epworth; 7 = Highfield; 8 = Rutsanana; 9 = Mabvuku; 10 = Kambuzuma; 11 = Mufakose; 12 = Budiriro; 13 = Dzivarasekwa-Rujeko; 14 = Kuwadzana; 15 = St Mary's (Chitungwiza).
The sample size (N) refers to the number of unequivocal HIV-1 results obtained.

$$\frac{dI}{dt} = \lambda_0 e^{-\alpha I/N} SI/N - \mu I - D \quad (2)$$

$$D = \left(\lambda_0 e^{-\alpha I/N} SI/N\right) \otimes W \quad (3)$$

where $\otimes$ indicates convolution and D is number of HIV-related deaths per unit time. In order to explore the possibility that the decline in prevalence is due to changes in behavior resulting from increased awareness of the epidemic or behaviour change programs, replace λ_0 in Eqs. (1) to (3) by, $\lambda_0(t)$, a logistic function decreasing at a rate α, reaching half-height at time τ and converging to an asymptotic value of b so that

$$\lambda_0(t) = \lambda_0 \left\{ (1-b) \frac{e^{\alpha(t-\tau)}}{1+e^{\alpha(t-\tau)}} + b \right\}. \quad (4)$$

We then adjust b, α and τ to fit the data. To explore the possibility that the decline in prevalence is due to changes in behavior arising from peoples' increased awareness of deaths in the population we replace λ_0 in Eqs. (1) to (3) by $\lambda_0(D/N)$, an exponential function decreasing at a rate ε as the mortality D/N increases, so that

$$\lambda_0(D/N) = \lambda_0 e^{-\varepsilon D/N} \quad (5)$$

We then adjust ε to fit the data. In all cases we carry out a weighted least squares fit jointly to the incidence, prevalence and mortality data.

Statistical methods

We did not have sufficient information on age-specific fertility, as a function of time, to construct such a model for the age-stratified data, which were accordingly fitted using a double-logistic function:

$$P(t) = \frac{e^{\alpha(t-\tau)}}{1+e^{\alpha(t-\tau)}} \left[2a \frac{e^{-\beta(t-\tau)}}{1+e^{-\beta(t-\tau)}} + b \right] \quad (6)$$

where α is the initial rate of increase in prevalence to a peak level proportional to a, and where prevalence converges, at rate β, to $b \geq 0$ for large t; τ is an offset parameter which determines the timing of the peak in prevalence. This model was fitted to prevalence calculated separately for five age categories: <20, 20–24, 25–29, 30–34, and ≥35 years: it was a statistical fit aimed simply at estimating the underlying prevalence trends in the age-specific data and serving as a check on the results emerging from the fit to the age-pooled data. All analyses were performed using Stata (Stata, College Station, Texas, USA), SAS (SAS Institute Inc., Cary, North Carolina, USA) and Microsoft Excel.

Mortality rates in Harare

Death certificates in Zimbabwe do not generally record HIV as a cause of death. To estimate the mortality from causes other than AIDS we fitted an exponential function to the declining mortality between 1981 and 1988, before there were significant numbers of deaths attributable to HIV, assuming an asymptotic mortality value of 1 per thousand. We then extrapolate this background mortality for the period after 1998 and subtract it from the total mortality to estimate the mortality attributable to HIV-AIDS over this period.

Results

Estimated mortality due to HIV

Following the end of the liberation war in 1980, international relations were normalized in Zimbabwe and there was a sharp inflow of international aid; there was also a marked, steady decline in mortality until 1988. Thereafter, in line with the appearance of the first AIDS cases in the late 1980s, total mortality increased by a factor of six by the end of the 1990s, and began to decline again in 2003 (Fig. 1).

We cannot be certain that non-AIDS mortality would have continued to decrease after 1988 in the manner predicted in Fig. 1. Nonetheless, the difference between the very high mortality at the end of the 1990s, overwhelmingly attributable to HIV-AIDS, and low levels in the middle 1980s, before the epidemic took hold, suggests that the assumed patterns of change in the background mortality provide a good approximation to the true situation.

Similarly, while the available mortality data was not stratified by gender it seems likely that the pattern of death in males and females was similar so that Fig. 1 gives a reasonable estimate of trends in HIV mortality among adult women, though not the absolute levels.

HIV-1 prevalence and incidence pooled on age

The prevalence of HIV increased from close to zero in the early 1980s (Blair Research Institute OU, 1996) to 35.9% (95% CI: 31.3–40.7) in December 1998, and then decreased by about 10% per year to 11.9% (95% CI: 10.1–13.8) in 2009 (Fig. 2). AIDS-related mortality began to increase in the late 1980s and peaked in 2001/2002. The data on incidence of HIV in Harare are limited and we have only two point estimates: 4.8% (CI95: 3.1–6.5) per year among pregnant women recruited in 1990/1 (Mbizvo et al., 2004), and 3.4% (CI95: 3.0–3.8) among post partum women recruited to the ZVITAMBO study in 1998/9 (Humphrey et al., 2006a).

Fitting the dynamical model to the pooled data we find that, if no assumption is made about a decline in HIV incidence, prevalence stabilizes at 27%, the level dictated by the balance between the accumulation of new infections and losses due to AIDS deaths (dashed lines in Fig. 2A) and clearly fails to fit the prevalence data after the year

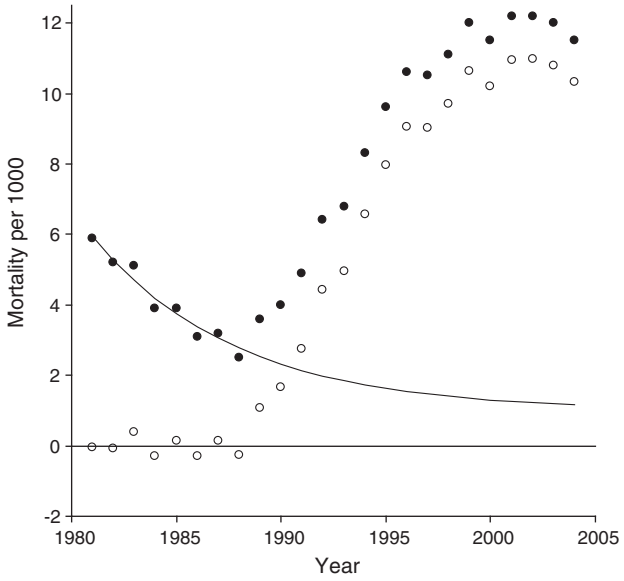

Fig. 1. Mortality (M) in Harare as a function of calendar year (t). The dots indicate the raw data. The data for 1981–1988 were fitted by the exponential function $M = 1 + 4.956 \exp(-0.147(t-1981))$ where exp indicates the exponential function. Subtracting the functional values from the raw data for each year provides an estimate of the mortality due to AIDS (open circles).

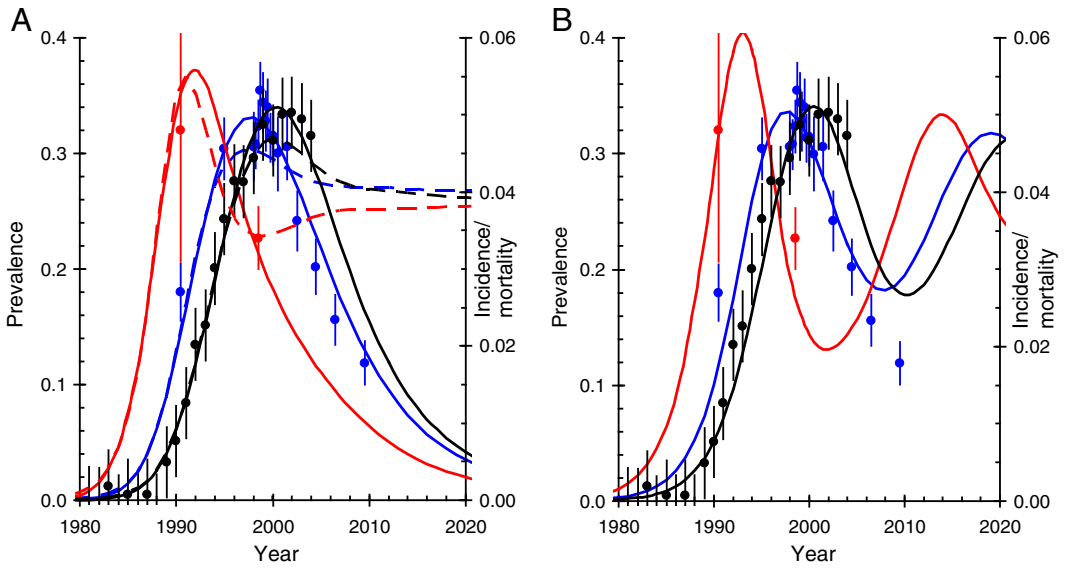

Fig. 2. HIV prevalence (blue), incidence (red) and mortality (black) among women attending maternity clinics in Harare and Chitungwiza. Dots show observed values: incidence from follow-up of cohorts of pregnant (Mbizvo et al., 2004) and post partum women (Humphrey et al., 2006a). Lines show the fitted prevalence, incidence and mortality. The models allow for reductions in transmission as a result of behavior change (A) or in response to mortality (B) as described in the text. Lines show results of fitting model. The best fits under the assumption of no change in behavior is indicated by the dashed lines in (A).

2000. We therefore assumed that behavior changes arising from education about HIV resulted in increasing awareness of the epidemic, which led to a reduction in risky sexual behavior as described by Eq. (4). The best fit (solid lines in Fig. 2A) is achieved if we assume that changes in behavior reduced the risk of infection by about 93% between the late 1980s and the early 1990s. We also investigated an alternative explanation that the change in behavior and corresponding decline in incidence, resulted from peoples' response to observed mortality using Eq. (5). In this case the best fit suggests that transmission must have fallen by 30% for each 1% increase in mortality (Fig. 2B). There is, however, a delay between changes in incidence and changes in mortality. Changes in behavior, and hence incidence, in response to mortality therefore lead to oscillations in the epidemic curves (Fig. 2B). This model, on its own, does not provide a satisfactory fit to the later prevalence data but we cannot, and do not, rule out the possibility that both factors contributed to the decline in prevalence to some degree.

Age structure of perinatal attendees, 1990 to 2009

The proportion of perinatal attendees less than 20 years old increased from 10.5% in 1990 to 23.0% in 2002, declining thereafter to 12.7% in 2009 (Fig. 3; filled circles); over the same periods the proportion of mothers ≥35 years fell from 13% to 3.6% in 2002, increasing to 6.0% by 2009 (Fig. 3; open diamonds). Changing age structure could have resulted from older women experiencing proportionately greater HIV-associated death, reduced fertility, reduced family size, and/or emigration (Terceira et al., 2003). Regardless of the cause, the temporary shift to a younger age distribution among perinatal attendees would have resulted in a decline in the overall HIV prevalence, even if HIV incidence was unchanged, since prevalence increases rapidly between the ages of 16 and 30 years (Humphrey et al., 2007). Further analyses accordingly accounted for maternal age.

Age-specific HIV-1 prevalence and incidence

Age-specific prevalence peaked in all age groups between 1990 and 1999 and has since declined significantly ($P<0.001$) by >65% among all women <35 years old (Fig. 4; Table S1, Supplementary Information). The decline in prevalence seen in Fig. 1 is not thus an artifact of age-pooling. Prevalence peaked progressively later, and at higher levels, with increasing age up to 30 years. For women <20 y, 20–24 y, 25–29 y, 30–34 y and ≥35 y, peak prevalences estimated from separate age group analyses were 25.4%, 34.2%, 47.1%, 44.0% and 33.5% and occurred in about 1993, 1996, 1997, 1998 and 1999, respectively.

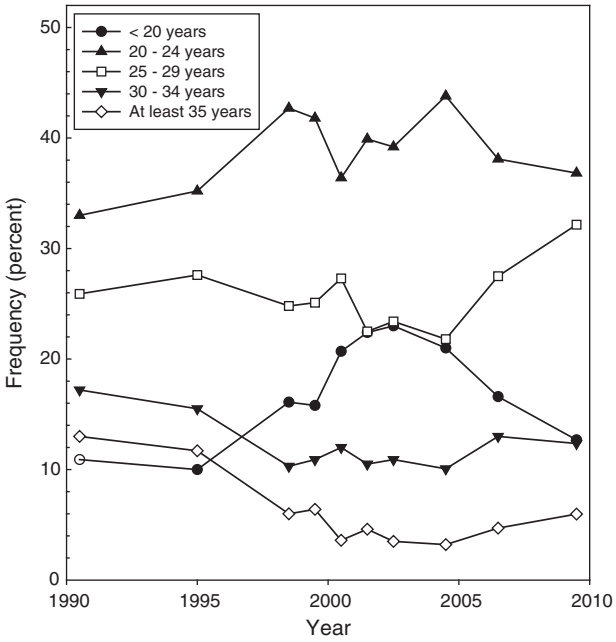

Fig. 3. The age structure among mothers attending maternity clinics in Harare and Chitungwiza, 1991–2009. Sources of data: 1990 — HIV-1 prevalence survey among antenatal women (Fabiani et al., 2001), n = 1008; 1994/95 — HIV-1 and HIV-2 prevalence survey among antenatal women in Harare in 1994/95 (Zaba et al., 2003), n = 1168; 1998 — women enrolled in ZVITAMBO from November 1997–December 1998 (Humphrey et al., 2007), n = 7253; 1999 — women enrolled in ZVITAMBO from January 1999–January 2000, n = 6857; 2000, 2001, 2002, 2004, 2006 and 2009 — women enrolled in the Harare sites of the Zimbabwe Ministry of Health and Child Welfare sentinel survey (Mahomva et al., 2006) conducted in each of these years, n = 841, 1043, 1097, 1118, 1115 and 1237, respectively.

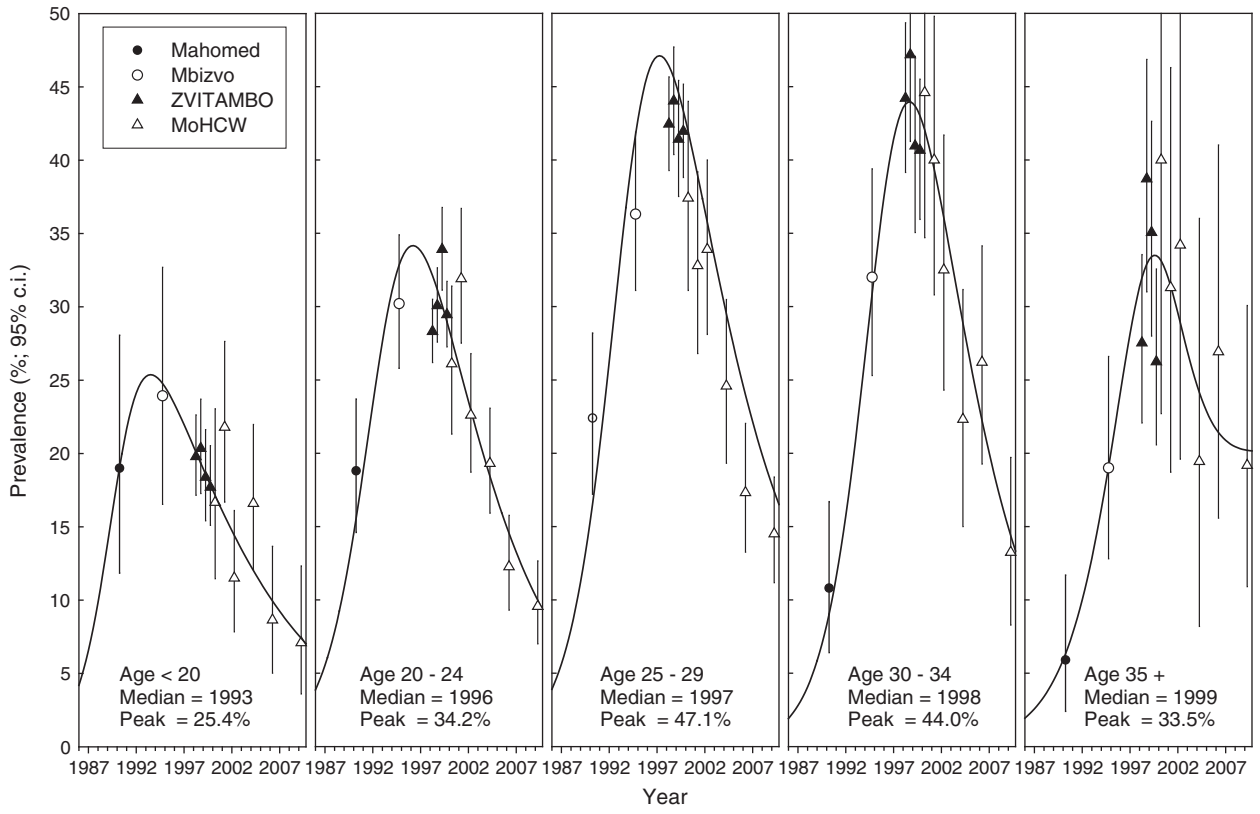

Fig. 4. Time trends in HIV-1 prevalence, stratified by age, among women attending maternity clinics in Greater Harare, Zimbabwe. The data were fitted using a double logistic function. For the ZVITAMBO trial data were pooled for November 1997 to June 1998, July to December 1998, January to June 1999 and July 1999 to January 2000. Parameter estimates, with 95% confidence intervals, for the optimal fit of the model are provided in Table S1 of the Supplementary Materials.

Trends in prevalence among young people (15–24 years old) reflect recent HIV-1 infections and are therefore good indicators of trends in incidence (Gregson et al., 2002; Kilian et al., 1999; Shelton et al., 2006; Zaba et al., 2000). Among women <24 years old, prevalence increased between 1991 and 1994 by 52%, from 18.9% (15.2–23.0) in 1991 to 28.8 (25.0–32.9) in 1994, then declined by 67% to 8.9% (CI95: 6.8–11.5) between 1994 and 2009. An explanation that is consistent with these observed changes in prevalence, is that incidence among young women continuously increased up to the early 1990s and then substantially and continuously declined thereafter (Williams et al., 2003).

The importance of the age-stratified analysis is that it applies to fuller data than are available for HIV-prevalence changes in Zimbabwe as a whole. The age stratified data for young women make it clearer than it is possible to see from any other data set that incidence has been in decline since 1993. The fits to the age-stratified data thus support both the timing of the onset of the decline in incidence, and the magnitude suggested by the model fitted to the age-pooled data (Fig. 2). To emphasize this point, in Fig. 5 we compare the modeled incidence with the HIV-1 prevalence in women of the youngest age-class (Fig. 4), normalized to match the area under the estimated incidence curve (Fig. 2) and shifted back in time by two years. The scaled incidence and shifted prevalence matches the estimated incidence quite precisely.

The shift stems from the fact that current prevalence reflects incidence averaged over the time exposed to HIV. The lowest age-group includes women 15 to 19 years of age, but with very few fifteen year olds, so that the range of ages during which these women have been exposed to HIV is four years and the average time since infection must be about two years. This in itself is an important finding since if age-specific prevalence curves for teenage pregnant women are to be used as a surrogate for time-trends in incidence they need to be shifted down by about two years. The fact that age-specific trends in HIV-prevalence in young women, which are available for many countries, can be used to determine historical trends in HIV incidence is of great importance.

Discussion

This paper introduces novel approaches to modeling HIV in Africa. For the first time, we have fitted a compartmental model simultaneously to data on HIV-1 prevalence, incidence and mortality. We

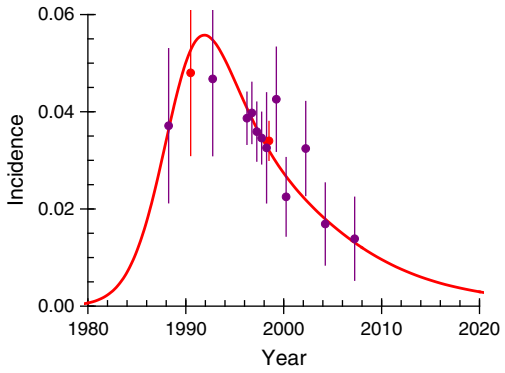

Fig. 5. Red line: Estimated incidence of HIV for women attending antenatal clinics (from the model results in Fig. 2). Purple dots: HIV-1 prevalence in women <20 years old (from Fig. 4) scaled vertically to match the area under the incidence curve and shifted down by two years. Red dots: HIV incidence from follow-up of cohorts of pregnant (Mbizvo et al., 2004) and post partum women (Humphrey et al., 2006a) (see Fig. 2).

have also used a more extensive set of prevalence data than has been analyzed previously for Zimbabwe, thereby providing an unusually high level of internal consistency. The quality and quantity of the data have also allowed us to disaggregate the prevalence by age which, in turn, allowed us to describe changes in HIV prevalence among young women, an indicator of incidence in the population. This analysis demonstrates, for the first time, that incidence has been declining in Harare for nearly two decades. Finally we were able to show good agreement between the disaggregated data and the result of the model fitted to the age-pooled data, which also suggests that HIV-1 incidence has been declining steadily since the early 1990s.

The data on HIV incidence, mortality and pooled prevalence among perinatal clinic attendees in Harare (Fig. 2) shows that prevalence peaked at 35.9% in late 1998 and declined to 11.9% in 2009, and that mortality peaked at 1.22% in 2001/2 then began to fall (Fig. 1). More importantly, fitting a transmission model to the data suggests that HIV-1 incidence peaked at 5.5% in 1992 and fell to 1% by 2010. The model suggests that the incidence, prevalence and mortality will all continue to decline.

Disaggregating the prevalence data by age (Fig. 4) shows a similar pattern across all age groups but with prevalence peaking progressively later as age increases — in 1993 for the youngest age-group and in 1999 for the oldest. Prevalence in young women has been used as a surrogate measure of population incidence and, provided we shift the age-specific prevalence in the youngest age group down by two years, the time trend in the prevalence matches very closely the time trend in incidence estimated by fitting the dynamical model to the pooled incidence, prevalence and mortality data (Fig. 5). This provides, for the first time, direct evidence that time trends in the prevalence of infection in young women can be used as a surrogate measure for time trends in incidence with a small time delay.

Analysis of the ZVITAMBO data (Humphrey et al., 2007) demonstrates that the decline in prevalence was independent of parental education and occupation, maternal parity, and religious, marital, housing and financial status, and recruitment clinic, and not due to differences in testing algorithms, which remained constant over the 27 months of recruitment, or laboratory errors, since 91% of positive cases were confirmed from a subsequent blood sample. Since others have shown that, in Zimbabwe, the prevalence of HIV among antenatal attendees is a good approximation to the prevalence among reproductive-aged women in the general population (Gregson et al., 2002), these declines are probably occurring among all reproductive-aged women in Harare.

In the absence of ART, most women infected between 16 and 24 years old will die before they are 35 years old (Morgan et al., 1997). In addition, fertility declines with age among women older than 30 years and among women infected with HIV (Terceira et al., 2003). These factors tend to reduce the proportion of all HIV positive women attending maternity clinics, with the greatest effect among older women. They explain both the transient reduced proportion of older women in the whole sample (Fig. 3) and the eventual decline in peak prevalence (Fig. 4) in the oldest age group.

What is driving the declines in HIV prevalence and incidence in Zimbabwe?

We offer no unequivocal explanation for the dramatic, sustained declines in HIV-1 prevalence in Zimbabwe over the past 12 years, and in incidence for more than 15 years — greater by far than in any other country in the region. Increased emigration, consequent on the economic downturn at the end of the 1990s, could not have caused the reversal of the trend in HIV incidence since this started six years earlier. Moreover, emigration would only reduce prevalence if HIV-positive people were more likely than HIV-negative people to emigrate, whereas HIV prevalence among Zimbabwe women attending antenatal clinics in the UK was between 9% and 11% in 2002–2004 (Gregson et al., 2010), compared to 20% at the time in Harare.

Similarly, our model for Harare indicates that behavior changes, as a direct response to the observed rapid increases in mortality between 1990 and 2000, may explain at least part of the decline in incidence during the 1990s but do not account for the continued decline in prevalence after 2004(Fig. 2B).

UNAIDS estimates that in 2005 only 2% of all HIV-positive people were on ART increasing to 19% in 2009 (UNAIDS, 2010). Since our mortality data only extend to 2004, ART will have a negligible effect on the mortality figures presented here. As ART becomes more available, substantial reductions in mortality and more modest reductions in prevalence would be expected. Our findings are consistent with several previous studies suggesting that the observed decline in HIV prevalence in Zimbabwe could only occur under the assumption of declining risky sexual behavior with ensuing declines in incidence (Gregson et al., 2010; Lopman and Gregson, 2008; Hallet et al., 2009; Hallett et al., 2006). In support of this we note that, although VCT and MTCT services only began in late 1999 and 2001, respectively, education campaigns had begun so that, by 1994, virtually all adults had heard of AIDS, 75% knew that a healthy-looking person could be infected, more than 50% personally knew somebody with AIDS, more than 90% knew AIDS could not be cured, and the most commonly stated means of avoiding AIDS were given as condom use and having only one sexual partner (Central Statistical Office HZ, 1995).

In this regard it may be relevant that, between 1990 and 1995, the number of condoms distributed in the country doubled from 21.5 million to 42.7 million. By 2004 it had doubled again to 81.1 million and increased to more than 90 million by 2009 (PSI, 2004). With an estimated adult male population of about 3.6 million the number of condoms distributed increased from 6 to 25 condoms per adult male per year. Furthermore, the proportion of condoms sold, rather than distributed free, rose from 1% in 1990 to 54% in 2004 and to more than 70% in 2008 suggesting an increased awareness of the dangers of HIV and increasing efforts to avoid them. This is consistent, at least, with an increased awareness in the population of the dangers of unprotected sex.

Limitations and prospects

Our analysis has two major limitations. First, our analysis included only pregnant and post-partum women, and thus most specifically applies to sexually active, reproductive-aged women who become pregnant. However, ANC data are widely used for monitoring HIV epidemics and their inference to the general population has been carefully analyzed and discussed (Fabiani et al., 2001; Zaba et al., 2000, 2003). Second, though the ANC surveillance system is designed to be nationally representative, the data from the two Harare sites are not necessarily representative of Harare. In addition, the research studies included in this analysis were not population-based studies. However, the single factor most likely to bias the estimated change in prevalence is a concurrent change in age structure: this indeed did occur, but we demonstrate substantial and significant declines in HIV-1 prevalence across all age groups. Finally, we acknowledge that it would have been preferable to use mortality figures specifically for females. Such data were not available and, in their absence, we have minimized the dangers of any inherent bias by using only the trend in, and not the absolute, mortality values. The important point to emerge from the data is the timing of the peak in mortality which should be little affected by any such bias or incompleteness in the data.

We have estimated that the annual incidence of HIV infection in Harare peaked at about 5.5% in 1998 and fell to about 1.0% in 2008. An annual incidence of 1% is still very high and continued diligence in primary prevention will be essential, particularly since continued decline cannot be assumed.

Contributors

J Humphrey designed the ZVITAMBO Trial and contributed to all facets of data collection and analysis. J Hargrove contributed to the analysis of the data and wrote the paper. A Mahomva contributed to the ZVITAMBO study design and contributed to the collection, collation, analysis, and interpretation of the MoHCW ANC surveys. B Williams contributed to data analysis and mathematical modeling. M Mbizvo contributed to the early studies on HIV prevalence and incidence in Harare and, with K Nathoo, P Iliff, H Chidawanyika and E Marinda to the design, data collection and interpretation in the ZVITAMBO Trial. K Mutasa oversaw all analyses and interpretation of laboratory data.

Conflict of interest

None of the authors has any commercial or other association that might pose a conflict of interest. The ZVITAMBO project was supported by the Canadian International Development Agency (CIDA) (R/C Project 690/M3688), United States Agency for International Development (USAID) (cooperative agreement number HRN-A-00-97-00015-00 between Johns Hopkins University and the Office of Health and Nutrition — USAID) and a grant from the Bill and Melinda Gates Foundation, Seattle WA. Additional funding was received from the Rockefeller Foundation (NY, NY) and BASF (Ludwigshafen Germany).

Acknowledgments

We thank the Zimbabwe Ministry of Health and Child Welfare for providing antenatal sentinel HIV-1 survey data for Harare and Chitungwiza and Dr. A.D. McNaughten, Centers for Disease Control and Prevention, for preparing databases of some of these data and advising on their analysis and interpretation. We gratefully acknowledge Clemens Benedikt and Annemarie Schuller of UNFPA for collating data on condom distribution in Zimbabwe, and Yasmin Madan of Population Services International for providing data on socially marketed condoms. We thank Liz Corbett, Frances Cowan, Simon Gregson and Eleanor Gouws for helpful comments on the manuscript. SACEMA receives major funding from the Department of Science and Technology, Government of South Africa and from the Canadian International Development Agency (CIDA) Project A033749.

Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.epidem.2011.02.004.

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