Critique of early models of the demographic impact of HIV/AIDS in sub-Saharan Africa based on new empirical data from Zimbabwe

Simon Gregson[1,2], Constance Nyamukapa[1,2], Ben Lopman[1], Phyllis Mushati[2], Geoffrey P Garnett[1], Stephen K Chandiwana[2,3] and Roy M Anderson[1]

[1] Department of Infectious Disease Epidemiology, Imperial College London, [2] Biomedical Research and Training Institute, and [3] Faculty of Health Sciences Research and Postgraduate Studies, University of Witwatersrand. Correspondence should be addressed to S.G. (s.gregson@imperial.ac.uk).

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Early mathematical models varied in their predictions of the impact of HIV/AIDS on population growth from minimal impact to reductions in growth, in pessimistic scenarios, from positive to negative values over a period of 25 years. Models predicting negative rates of natural increase forecast little effect on the dependency ratio. Twenty years later, HIV prevalence in small towns, estates and rural villages in Manicaland, Zimbabwe's eastern province, has peaked within the intermediate range predicted by the early models but the demographic impact has been more acute than was predicted. Despite concurrent declines in fertility, fuelled in part by HIV infections (total fertility is now 8% lower than expected without an epidemic), and a doubling of the crude death rate due to HIV/AIDS, the rate of natural population increase between 1998 and 2005 remained positive in each socio-economic stratum. In the worst-affected areas (towns with HIV prevalence of 33%), HIV/AIDS reduced growth by two-thirds from 2.9% to 1.0%. The dependency ratio fell from 1.21 at the onset of the HIV epidemic to 0.78; the impact of HIV-associated adult mortality being out-weighed by the effects of fertility decline. With the benefit of hindsight, the more pessimistic early models over-estimated the demographic impact of HIV epidemics by over-extrapolating initial HIV growth rates or not allowing for heterogeneity in key parameters such as transmissability and sexual risk behaviour. Data collected since the late 1980s show that there was a mismatch between the observed growth in the HIV epidemic and assumptions made about viral transmission.

The initial observation of a growing AIDS epidemic amongst heterosexual populations in the Americas and Africa generated concern over the eventual scale and impact of the pandemic. A range of models was developed to explore the future spread of infection and its impact on mortality based on the available pattern of growth in HIV prevalence, patterns of sexual behaviour, transmissibility of the virus, and progression from infection to AIDS and death. Initial predictions, based on the initial growth of the epidemic and a long duration of infectiousness, predicted that, over a period of decades, HIV could well turn population growth rates negative (1, 2). However, others disagreed (3) and the consensus at a United Nations and World Heath Organisation workshop held in December 1989 was that the epidemic could have an important effect on population growth but that negative rates of natural increase were unlikely (4). A maximum reduction of 30% in the growth rate over a period of less than 50 years was predicted. The relationship between mortality in young adults and decreased births meant that, even in models with an extreme impact, dependency ratios were predicted to remain unchanged (1, 2)

Over time, our understanding of the spread of HIV and its impact on fertility and mortality has improved and has been included in more recent models (5-7). Model predictions can be compared with empirical estimates of demographic impact obtained in surveys, census and vital registration (8). However, discrepancies can still arise leading to debate over the validity of both model and empirical estimates (9). With the benefit of hindsight, we can explore the validity of the assumptions made in the different models of the heterosexual spread of HIV and, in particular, re-evaluate the approaches taken in predicting the demographic impact of AIDS.

HIV prevalence has now reached moderate to high levels in several countries in southern and eastern Africa with rates generally being highest in cities and other centres of high labour migration (10). Since the mid-1980s, previous gains in under-five mortality have been reversed (11, 12) and adult death rates have doubled or tripled in countries with high HIV prevalence (13). Data from community studies indicate that, in the absence of other causes of death, 33% and 61% of infants with HIV infection would die before the ages of 1 year and 5 years,

respectively (14), and that upwards of 75% of deaths in economically-active age-groups are associated with HIV infection (15-19). In Masaka, Uganda, a relatively low HIV prevalence of 8% was estimated to have reduced life expectancy at birth in the period 1990-1992 from 58.6 years to 42.5 years (20).

In the Rakai district of Uganda, 1990-1991, Sewankambo and colleagues (21) observed substantial reductions in the rate of natural increase but continued population growth in three geographic strata in which HIV prevalence ranged from 13-35%. Using 1991 national census data for the same country, Low-Beer and colleagues (22) found instances of negative population growth at parish level but not at district or national levels. Population pyramids for severely affected areas exhibited deficits of adults and young children consistent with the distribution of reported AIDS cases. Despite much interest in the demographic impact of AIDS, these appear to be the only direct empirical measurements published to date on the impact of large-scale HIV epidemics on population growth and structure. Furthermore, we are aware of no previous reports of this kind in the countries in southern Africa that have experienced the most widely-disseminated epidemics (23).

In Zimbabwe, nationally, the HIV/AIDS epidemic took hold in the mid-1980s and HIV prevalence in adults aged 15-49 years is estimated to have peaked at 29% in 1997 and to have fallen to 20% by 2005 (24). Over a similar period, Census reports estimated that the annual average inter-censal population growth rate declined from 3.1% between 1982 and 1992 to 1.1% between 1992 and 2002 (25, 26). This decline resulted from a combination of rising mortality (the crude death rate [CDR] almost doubled from 9.5 to 17.2 between 1992 and 2002), falling fertility (the total fertility rate [TFR] fell by a third from 5.5 live births per women in 1984-1988 to 3.8 in 2001-2005) (27, 28), and increasing international out-migration (United Nations Office for the Coordination of Humanitarian Affairs. “Zimbabwe Government taps into remittances to ease forex shortage.” Integrated Regional Information Networks News. 9 June 2004).

Against this background, we present data on the impact of HIV/AIDS on mortality, fertility, population age-structure, and population growth in small towns, estates and rural villages subject to a maturing, large-scale HIV epidemic in Manicaland, Zimbabwe’s eastern province. To inform future modelling of the impact of infectious disease, we use these data as the basis for a critique of early model predictions of the demographic impact of HIV/AIDS in sub-Saharan Africa. Empirical measurements are compared with model projections and likely explanations for observed discrepancies are discussed.

RESULTS

Demographic impact of HIV/AIDS in Manicaland, eastern Zimbabwe

Adult HIV prevalence and mortality

Table 1 shows HIV prevalence and mortality rates per 1000 person years (PY) by sex, age, socio-economic stratum, and HIV-infection status for 1998-2005. HIV prevalence in adults fell from 23% to 18% over an average 5-year inter-survey interval and substantial declines were observed in young men and women (29). During the same period, adult mortality appears to have stabilised in both males and females (30). Adult mortality was much higher amongst HIV-infected individuals, 81.6 per 1000 PY, than in uninfected individuals, 7.2 per 1000 PY (Cox proportional hazard ratio adjusted for sex, age and location, AHR, 12.1; 95% CI, 9.9-14.9). In HIV-infected individuals, death rates were highest in males (AHR, 1.3; 95% CI, 1.0-1.5) and in village locations (AHR, 1.3, 95% CI, 1.0-1.6).

The proportion of deaths associated with HIV infection was similar in both sexes and across socio-economic locations (Range: 75-87%). The proportion of all deaths that would have been averted in the absence of HIV (Attributable risk) was 73% in both males and females – the higher HIV prevalence in females balancing the greater mortality in infected males. Female HIV-associated deaths typically occurred at younger ages with 70% of deaths in females *versus* 56% of deaths in males occurring before the age of 40.

Fertility

Fertility in the Manicaland study sites declined between 1998 and 2005 (31) and an average TFR of 3.46 was recorded for the period as whole. Based on the fertility experience of uninfected women, this would have been 3.73 in the absence of the HIV epidemic. Thus, the population-attributable reduction in fertility associated with HIV/AIDS in 1998-2005 was 8%. Table 2 shows similar comparisons for the town, estate and village populations.

Population structure and dependency ratios

The sex- and age-structures of the town, estate and village populations for 2003-2005 are shown in Fig. 1. The town and estate populations had a more even sex ratio than the village populations (0.98 and 1.02 *versus* 0.81 males per female) and greater numbers of males aged 25-54 years and females aged 25-34 years. The dependency ratio - defined here as the number

of children below age 15 years and elderly people over 65 years, divided by the number of adults aged 15 to 64 years - before and after including adult AIDS cases as dependents, is higher in the villages (0.85 and 0.91, respectively) than in the towns (0.55 and 0.61) or estates (0.55 and 0.61).

The dependency ratios for the combined study population were similar at the beginning (1998-2000: 0.78 and 0.81) and end of the study period (2003-2005: 0.78 and 0.84). In the absence of data for these areas prior to the onset of the HIV epidemic, the observed dependency ratios and age-structures were compared with those observed in rural populations nationally in the mid-1980s (32). This comparison suggests a considerable reduction in the dependency ratio from 1.21 in the mid-1980s and that individuals in the age-range 15-44 years have increased as a proportion of the total population whilst the proportion accounted for by children up to the age of 14 has reduced (Fig. 2).

Population growth

Table 3 shows the observed crude birth and death rates and rate of natural population increase and estimates of these rates in the absence of the HIV epidemic, for each of the three socio-economic strata. In the absence of HIV/AIDS, the rate of natural increase is greater in the towns and estates due to the concentration of young adults with high fertility and low mortality (Fig. 2). The presence of HIV/AIDS more than doubles the crude death rate and reduces the crude birth rate in each population stratum. In the towns, where HIV prevalence is highest, the rate of natural increase is estimated to have been cut by two thirds from 2.9% per annum to 1.0% per annum but remains substantially above zero. Smaller reductions were recorded in the estates and villages. If the HIV-infected adults living in the towns are taken to have experienced the higher death rates recorded in the villages (to allow for migration during terminal illness), the rate of natural increase reduces further to 0.7%, but still remains positive.

Comparison of empirical estimates from Zimbabwe with early model predictions

At the United Nations and World Health Organisation workshop held in December 1989, mathematical modellers were given a standard set of inputs for demographic trends in the absence of HIV, patterns of marriage and extramarital relationships and parameters describing the natural history and transmissibility of the virus. They were then requested to provide estimates for the spread and impact of HIV after 25 years. i.e. by 2010 from a starting point based on HIV prevalence levels in east Africa around 1985 (33). The intermediate and worst case predictions made at the workshop are presented in Table 4. It is important to note that the

HIV prevalence estimates presented were for all age-groups not prevalence within the most sexually-active age-range (typically 15-49 years) which is commonly used today. Based on best estimates of the biological, behavioural and demographic parameters, it was found that the HIV epidemic would have a moderate demographic effect 'at most 30%' (4) rather than the profound impact predicted by Anderson et al. 1988 (1). Many other simulations did generate negative population growth rates but with parameter values that 'may prove exaggerated when more complete and accurate evidence is gathered' (4). These parameter values included high transmission probabilities of HIV which, in turn, generated a high prevalence of infection and a large demographic impact.

In this exercise, Anderson and colleagues did not use the standard inputs but generated results based on doubling times of the epidemic, where a doubling time of 4.5, 3.5, 2.5 and 1.5 generated a prevalence of approximately 10%, 20%, 40% and 48%, respectively, after 25 years. Only in the first case, with a doubling time of 4.5, did population growth remain positive; however, it took more than 25 years to become negative with a doubling time of 3.5 years. In the mid-1990s, the same research group applied a model which additionally included heterogeneity in sexual behaviour with parameter settings based on data from Zimbabwe. The model projected that HIV prevalence in adults would peak at around 25% and, with concurrent fertility decline stabilising at a TFR of 3.5 live births per women, would cause the rate of natural increase to fall slightly below zero (34). A similar prediction was made by the United States Bureau of the Census at around the same time (35).

The empirical estimates for HIV prevalence across all ages in Zimbabwe fall near the centre of the range of the intermediate projections at the United Nations and World Health Organisation workshop (Table 4). In populations where the underlying rate of natural increase was slightly lower than the 3.5% per annum used at the workshop, the Dietz and Brouard models provided seemingly accurate predictions of the impact on population growth. However, these impacts were predicted to be later than observed and were predicted to continue increasing. The later projections for Zimbabwe (34) correctly predicted the peak in HIV prevalence but over-estimated the impact on population growth.

Anderson's initial model had also predicted that HIV epidemics would have only a modest impact on the dependency ratio. The group's later model for Zimbabwe indicated that any impact would be out-weighed by the effects of rapid fertility decline. These predictions are consistent with the empirical data, although recent high out-migration has led to deficits in the 15-34 year age-groups, particularly amongst males (Fig. 2).

DISCUSSION

Empirical evidence – summary and consistency with other empirical studies

HIV has spread extensively within rural areas of Manicaland, eastern Zimbabwe, but our data indicate that, 20 years into the epidemic, the rate of natural increase remains positive, even in the areas of highest HIV prevalence. Demographic and epidemiological trends in Manicaland broadly reflect those for Zimbabwe as a whole. In both cases, antiretroviral treatment for HIV/AIDS only began to become available late in the study period.

Our findings are consistent with those obtained by Sewankambo and colleagues between 1990 and 1991 in three rural socio-economic strata in the Rakai District of Uganda. The HIV epidemic took hold in Rakai District more than a decade earlier than in Manicaland and HIV prevalence levels and the underlying rate of population increase were similar to those seen in the current study areas (21). HIV-associated sub-fertility was not accounted for in the Rakai study but mortality in HIV-infected individuals was lower in Manicaland, possibly due to the longer periods of follow-up resulting in greater under-reporting (18).

Perhaps the most surprising finding is the continued excess of fertility over mortality in the small towns. As in the trading centres in Rakai, Uganda (21), an adult HIV prevalence of over 30% proved insufficient to reduce the annual rate of natural increase below 1%. There appear to be two main reasons for this. First, a strong concentration of women of peak childbearing age results in a high crude birth rate despite lower age-specific fertility rates than in the other socio-economic strata. Second, age-specific mortality rates amongst HIV-positive adults in the towns - and also in the estates - are lower than in the villages. Migration could have contributed to this since Zimbabweans living in centres of employment frequently retain strong links with their "rural homes" (36). We minimised the effect of terminally-ill individuals returning to rural villages once they become too ill to work by accounting for deaths according to place of residence when last interviewed and, in earlier research, we found no evidence for selective out-migration of HIV-infected individuals from our study populations (37). A larger proportion of the deaths of HIV-infected adults in the towns and estates could have gone unreported in the survey given the greater social isolation in these locations but the rate of natural increase remained above zero even when HIV-infected adults in the towns were taken to experience the higher death rates observed in villages. A further possibility is that circular migration could have led to under-estimates in the true number of person-years of residence in towns and estates

in the age-groups with highest HIV-associated mortality and, thereby, to under-estimates of the crude death rates in these areas. Urban and estate residents frequently visit their rural homes during holidays and near the end of the month shortly after being paid. However, our surveys were conducted on a *de jure* basis which should have minimised this bias.

Other sources of bias could have affected our estimates of the impact of HIV/AIDS on population growth in eastern Zimbabwe. We assumed that no AIDS deaths occurred within the age-groups not covered by the individual cohort survey (i.e. 5-14 years and 55 years and above) which tends to make our findings conservative. We assumed that the levels of mortality and fertility seen in uninfected individuals represented the levels that would have pertained in the absence of the HIV epidemic. If infected individuals would have had higher mortality or lower fertility than other individuals even in the absence of infection, our estimates would tend to overstate the true impact of HIV/AIDS.

The data from eastern Zimbabwe indicate a reduction rather than an increase in the dependency ratio and, unlike in south-west Uganda in the early 1990s (22), we found no evidence for deficits (relative to the pre-AIDS period) in the adult age-groups with greatest HIV-associated mortality. This is probably because, unlike Uganda prior to 1990, Zimbabwe experienced a substantial fall in fertility during the 1980s and 1990s (31) which typically causes population ageing. However, fertility declines have yet to commence or have been less pronounced in a number of other countries with large national epidemics (e.g. Zambia and Malawi). In these countries, deficits of – particularly, older middle-aged - adults could occur (38). We did find deficits in the early-childhood age-groups. Low-Beer and colleagues noted that reduced numbers of births due to smaller proportions of women being in the primary child-bearing age-groups - as well as HIV-associated sub-fertility and paediatric mortality - could contribute to such deficits (22).

The recent collapse of the economy in Zimbabwe has led to substantial international migration of young adults to South Africa and other countries in the region as well as to western countries since around 2000. This phenomenon is unlikely to have affected our findings that the rate of natural increase of the population has remained positive and that the combined effect of HIV/AIDS and fertility decline has reduced the dependency ratio. However, when migration is taken into account, the net growth rate since 2000 has almost certainly been negative in some parts of Zimbabwe. Migration has probably also increased the dependency ratio during this period although the economic effects of this have been offset, in part, by a substantial increase in remittances received from the newly expanded Diaspora.

Empirical measurements are subject to bias of the forms just discussed. However, HIV prevalence over the complete age-range has not reached the levels feared in the early model worst case scenarios. Whilst the data from Zimbabwe are consistent with two of the intermediate scenarios, with the benefit of hindsight, one can question the wide range of predicted demographic impact, particularly when the anticipated prevalence of infection was similar.

At the time, early models were classified depending upon whether they adopted a standard demographic cohort projection approach (39, 40) or built from epidemiological foundations. However, the major differences in their predictions came from elsewhere. The predicted impact of HIV on population growth depends upon: (1) the background demography, i.e. the expected birth and death rates in the absence of HIV and the patterns of migration; (2) the incidence of HIV infections over time as a function of sex and age; and (3) the impact that infection has on fertility and mortality in the individual. The major differences between the models depend upon both the HIV prevalence level achieved and how quickly it is attained and all the models failed to capture what has subsequently been observed. Whilst the intermediate predictions for Auvert (41), Brouard (42) and Dietz (43) generate high prevalence, these increase more gradually than observed to the recorded levels. Projections from Anderson's models, based on initial HIV epidemic growth rates and without heterogeneity in risk behaviour within age-groups, go on increasing until most of the population is infected. The IWG (44) and Palloni (40) models (and the Bongaarts and John model applied before this exercise (4)) did not reach the high HIV prevalence levels observed with the parameters provided for the exercise. The model of Bulatao, from the World Bank (39), is an outlier, in that, even at high prevalence, population growth is little affected. For some unexplained reason the crude fertility rate (CFR) in this model increases along with increased HIV prevalence and also, despite a continued high prevalence of HIV, the projected life expectancy bounces back after an initial decline.

The subsequent HIV epidemics in eastern and southern Africa can broadly be described as less widespread than those predicted by models with a rapid rise in prevalence, but more widespread than the other predictions. These discrepancies came mainly from an attempt to fit the models to HIV prevalence levels observed in 1985 whilst using the observed per act transmission probabilities of 0.001 from female to male and 0.003 from male to female (45). In those models that started from the 1985 HIV prevalence levels, these transmission probabilities led to slow growth thereafter whilst, those models that generated the 1985 HIV prevalence

levels could only do so with extreme risk behaviours leading to the predicted epidemic eventually spreading too far.

The low per act transmission probabilities assumed that transmission likelihood was independent of partnership. At the time, there was concern over changing transmissibility, but this was largely ignored. The question asked of experts was whether HIV was transmissible at all in the long asymptomatic incubation period, rather than whether it was less transmissible (44). Further in, those models which did allow variation in transmissibility over the course of the infection assumed that this mostly took the form of an increase towards the end of the incubation period. It is now clear that the high viral load associated with primary HIV infection leads to a high transmission probability per act early in the infection (46, 47) and this generates a rapidly growing and saturating epidemic (48). Early models which assumed a per partnership transmission probability, like that of Anderson and colleagues, would have better captured the heterogeneity in transmission probabilities per partnership. However, the model of Anderson et al (1991) (49) failed to include behavioural heterogeneity which is needed to generate saturation effects. Dietz's model (43) is interesting in that it explicitly includes sexual partnerships as state variables. However, in that formulation, partnerships were protective which slowed the spread of infection. Subsequent models describing the network of sexual partnerships show how overlapping partnerships combined with the high transmissibility early in infection can generate rapid epidemic spread (50).

Translating a given HIV prevalence into a demographic impact depends upon the rate at which infection leads to AIDS and then death. A median period of 10 years from infection to AIDS was assumed for the standard United Nations and World Health Organisation workshop. More rapid progression requires greater HIV incidence to maintain the observed prevalence, so observed urban prevalence levels could have led to a negative population growth rate if progression had been faster than in western countries (51). However, subsequent data suggest that the incubation period assumed initially was reasonable (52). None of the models took account of reduced fertility in those infected with HIV. At the time the evidence was slim, but subsequent work has shown a decline of about 25% in births to women infected (53-55). Nonetheless, this may be offset by the lower than assumed mother-to-child transmission rate and the countervailing reduction in fallopian tube occlusion associated with declines in bacterial sexually transmitted diseases (56).

Models for Zimbabwe developed in the mid-1990s (34, 35) provided accurate forecasts of the timing and level of peak HIV prevalence within the sexually active age-range but predicted a greater impact on population growth than is indicated by the data. Mortality may not have

been fully captured in the survey for the reasons discussed above. However, errors in model assumptions (e.g. an under-estimation of the median survival time from seroconversion) also contributed to this discrepancy.

Conclusion

In Zimbabwe and some other parts of sub-Saharan Africa, HIV prevalence has reached the levels predicted in some intermediate case scenarios in the late 1980s. Whilst HIV/AIDS has not turned positive growth rates negative, the impact has exceeded the maximum 30% reduction envisaged at the time. The more pessimistic projections over-estimated the demographic impact by over-extrapolating initial epidemic growth rates or by not allowing for heterogeneity in transmissibility. It was not realised at the time that heightened transmissability during the early stages of infection was combining with overlapping sexual partnerships to cause a rapid initial spread of epidemics. The more optimistic projections under-estimated the potential for future growth in HIV epidemics and the more pessimistic projections over estimated this.

Whilst the demographic impact of large-scale HIV epidemics may be less dramatic than was first feared, the effects are nonetheless very substantial and still unfolding. In the predominantly rural populations studied here, life expectancy has been reduced by a median of 19 years for males and 22 years for females (18), total fertility has been reduced by approximately 0.3 live births per woman, and the rate of natural increase has been reduced by up to two-thirds. The proportion of children under the age of 15 years who were orphans doubled from 12% to 25% between 1998-2000 and 2003-2005, during which period the rates at which children lost their mothers and became double orphans continued to rise (57).

METHODS

Study setting. The study was conducted in 12 locations – 2 small towns, 2 tea and coffee estates, 2 forestry plantations, 2 roadside trading centres and 4 subsistence farming areas – in Manicaland province, eastern Zimbabwe between 1998 and 2005.

Data collection and laboratory procedures. The detailed procedures followed in the study have been published previously (29). In brief, we conducted a baseline census of all households in each of the 12 study locations in a phased manner (one site at a time) between July 1998 and February 2000. Household residence was defined on a *de jure* basis. A random sample of males aged 17-54 years and females aged 15-49 years resident within the study households was recruited into a longitudinal open cohort. First and second follow-up censuses and surveys were conducted in each of the same sites 3 years (July 2001 to February 2003) and 5 years (July 2003 to August 2005) after baseline, respectively. All baseline respondents and individuals who had previously been too young to participate but who now met the age criteria were considered eligible at each round of follow-up. Due to funding constraints, at the first follow-up, persons who had migrated into the study areas in the 3-year inter-survey period were only eligible for individual interview in the sites visited 5th to 12th in the phased enumeration. HIV serological testing was done on dried blood spot specimens using a highly sensitive and specific antibody dipstick assay (58). Written informed consent was sought as a condition of enrolment and continuation in the study. Prior ethical approval for the study was obtained from the Research Council of Zimbabwe - Number 02187 - and the Applied and Qualitative Research Ethics Committee in Oxford, United Kingdom - N97.039.

Following these procedures, 98%, 94% and 96% of the households identified in the survey areas at baseline and at first and second follow-up, respectively, were enumerated. Individual participation rates were 79%, 79% and 83% at baseline, first follow-up and second follow-up, respectively. Sixty-one per cent and 63% of those interviewed at baseline and first follow-up - and not known to have died subsequently - were re-interviewed at first and second follow-up, respectively. Out-migration was the principal reason for loss-to-follow-up – for example, at first follow-up, this reason was given directly by village guides or household respondents in 56% of cases and the individuals or their households could not be located in a further 42% of cases. Only 1% of baseline respondents and 2% of first follow-up respondents declined to participate in the next round of the survey. The participation and follow-up rates in the study were comparable to those obtained in similar surveys conducted in sub-Saharan Africa (29).

Data analysis. For the purposes of this study, households and their residents were recoded according to their location within the 3 principal socio-economic strata found in eastern Zimbabwe – small towns, large-scale tea, coffee and forestry estates and rural villages. Rural areas were defined as those characterised by subsistence farming and, for practical reasons, were taken to be those located more than 10 minutes walking distance from an urban centre or an estate compound. Households meeting this definition were treated as being located in rural villages.

Mortality. Sex- and age-specific mortality rates during each of two inter-survey periods, stratified by HIV infection status and location of residence at the start of the period, were calculated for the age-intervals 17-24 years, 25-39 years and 40-54 years, using data from the cohort of individuals enrolled at the start of the period. Weighted averages of the age-specific mortality rates for the two inter-survey periods were calculated to give estimates for the full study period (1998-2005), using the lengths of the inter-survey periods as weights.

Crude death rates for the full study period were calculated for each socio-economic stratum as weighted averages of the age-specific mortality rates using the proportion of all person-years exposed in each age-group as weights. Person-years of exposure were periods of residence within households located within the socio-economic stratum during the study period. These periods were calculated for each inter-survey period from data on dates of initial and follow-up household interview and dates of migration into/from household and/or death, where appropriate, and were then aggregated. For infant and early childhood mortality rates, we used indirect estimates derived from data on HIV prevalence in pregnant women (pregnant in the inter-survey periods) collected in the socio-economic stratum, an estimate of 30.7% for the probability of vertical transmission of HIV infection in Zimbabwe (59), and estimates for age-specific mortality from 0-1 years ($_1m_0$) and 1-4 years ($_4m_1$) of 0.429 and 0.132 for HIV-infected infants (14) and 0.056 and 0.007 for uninfected infants in sub-Saharan African populations (14). We assumed that no AIDS deaths occurred in the other age-intervals not covered in the individual cohort and estimated non-AIDS mortality for these ages using data from the longitudinal household census adjusted for under-reporting (18). Estimates for crude death rates in the absence of the HIV epidemic were based on the mortality experience of uninfected individuals.

Fertility. Standard procedures (60) were applied to calculate 5-year age-specific and total fertility rates for women aged 15-49 years in each socio-economic stratum using data on live births in the inter-survey periods. Separate estimates were derived and compared for women found to be infected with HIV and uninfected at follow-up. The estimates for uninfected women were taken to be indicative of fertility levels in the absence of the HIV epidemic and population-attributable change (PAC) in fertility was estimated using the formula PAC = {TFR in total population – TFR in HIV-negative population} / {TFR in HIV-negative population} (61). Crude birth rates were estimated from age-specific fertility rates and person-years of exposure within households in the same way as for crude death rates. Women who died were treated as lost to follow-up in the calculation of age-specific fertility rates by HIV-infection status. Other things being equal, this may have led to slight under-estimates of the impact of HIV on fertility and the rate of natural increase in the study populations.

Population structure and dependency ratios. Population pyramids were constructed to illustrate the differences in sex- and age-structure found between the different socio-economic strata using data from the third household census (2003-2005). The overall sex- and age-distributions for the 12 study sites combined at baseline and second follow-up were also compared with that for rural areas of Zimbabwe in

1987 (32) (i.e. prior to the impact of the HIV epidemic) and a mathematical model projection made in the mid-1990s (34, 62). Dependency ratios were calculated for the combined study population and for each of the socio-economic strata using the standard age-groups for dependents and economically-active individuals - {Number of individuals aged 0-14 years and 65 years and above} / {Number of individuals aged 15-64 years} – and compared with the equivalent ratio for 1987. Alternative dependency ratios, in which estimates for the numbers of HIV-infected adults in the economically-active age-groups incapacitated by AIDS – based on an average incubation period of 8 years and an average survival period with AIDS of 1 year – were added to the numerator and subtracted from the denominator, were also calculated and compared.

Rate of natural population increase. Estimates for the rate of natural increase for each socio-economic strata, in the presence and absence of the HIV epidemic, were obtained by taking the difference between the estimates of the crude birth rate and the crude death rate in each case.

Data analysis was done in Stata Version 9 (Stata Corporation, College Station, Texas, USA).

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

Figure legends

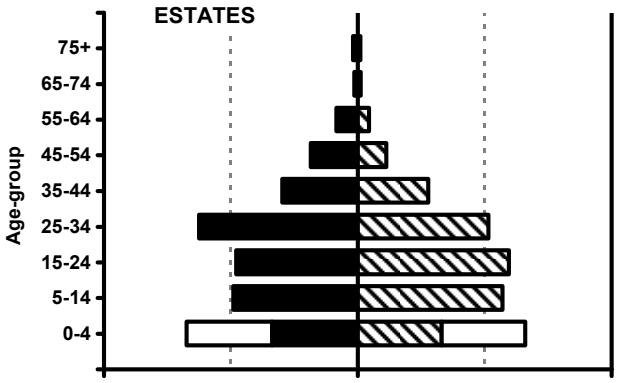
Figure 1 Sex- and age-structure of residents of: (a) towns, (b) estates, and (c) villages, Manicaland, Zimbabwe, 2003-2005. Open bars for ages 0-4 years show double the actual proportions to allow comparison with the 10-year intervals shown for other age-groups

Figure 2 Sex- and age-structure of combined study population in Manicaland, Zimbabwe: (a) 1998-2000; (b) 2003-2005. Histograms show empirical data for proportions of population in each sex- and age-group. Also shown, for comparison, the distribution of rural populations in Zimbabwe, as a whole, in 1987 (32) (shaded area); and mathematical model projections for the national rural population in 1999 (in graph (a)) and 2004 (graph (b)), in which HIV prevalence peaks at 25% in the late 1990s and the total fertility rate declines from 5.5 live births per woman in 1986 to 4.4 in 1992 and 3.5 in 1997 (solid line)

a


TOWNS
Males
Females
Age-group
75+
65-74
55-64
45-54
35-44
25-34
15-24
5-14
0-4

b


ESTATES
Age-group
75+
65-74
55-64
45-54
35-44
25-34
15-24
5-14
0-4

c


VILLAGES
Age-group
75+
65-74
55-64
45-54
35-44
25-34
15-24
5-14
0-4
20
0
20
Percentage distribution (both sexes combined)

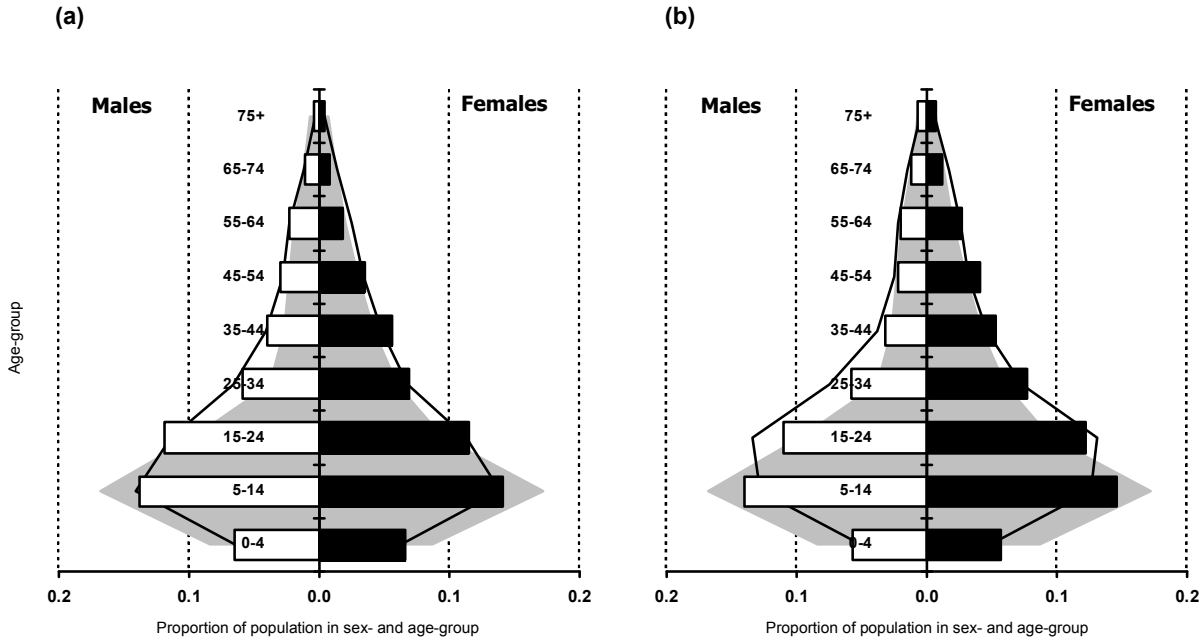

(a)
Males
Females
75+
65-74
55-64
45-54
35-44
25-34
15-24
5-14
0-4
Age-group
0.2
0.1
0.0
0.1
0.2
Proportion of population in sex- and age-group
(b)
Males
Females
75+
65-74
55-64
45-54
35-44
25-34
15-24
5-14
0-4
0.2
0.1
0.0
0.1
0.2
Proportion of population in sex- and age-group

Table 1. Adult mortality per thousand person years (PY) by HIV status and location, Manicaland, Zimbabwe, 1998-2005

Sex	Stratum	Age (years)	HIV prevalence* (%)	HIV-positive			HIV-negative			Proportion of deaths associated with HIV (%)	AR of HIV-associated mortality†
				Mortality	Deaths	PY	Mortality	Deaths	PY		
Males	Towns	15-24	8.3	27.8	1	36	2.5	1	395	50	45
		25-39	39.6	79.2	22	278	6.4	3	467	88	81
		40-54	37.7	71.5	8	112	14.6	4	275	67	53
		Total	26.9	72.8	31	426	7.0	8	1,137	79	72
	Estates	15-24	4.9	28.2	1	35	7.3	6	823	14	11
		25-39	29.7	44.4	19	428	2.2	3	1,342	86	82
		40-54	27.4	126.0	25	198	0.0	0	718	100	100
		Total	20.3	68.0	45	662	3.1	9	2,884	83	80
	Villages	15-24	2.5	14.3	1	70	6.8	20	2,939	5	2
		25-39	28.7	98.3	66	671	5.0	11	2,204	86	81
		40-54	28.8	152.3	52	342	7.2	8	1,113	87	83
		Total	14.8	109.9	119	1,083	6.2	39	6,255	75	71
Females	Towns	15-24	19.3	9.8	1	102	12.8	5	391	17	0
		25-39	57.2	55.1	22	399	2.5	1	408	96	91
		40-54	41.2	146.0	18	123	0.0	0	247	100	100
		Total	38.5	65.6	41	625	5.7	6	1,045	87	80
	Estates	15-24	14.8	27.7	2	72	4.9	3	610	40	33
		25-39	37.3	51.4	19	370	2.2	2	920	90	87
		40-54	19.0	69.0	8	116	2.2	1	465	89	86
		Total	24.6	52.0	29	558	3.0	6	1,995	83	78
	Villages	15-24	8.5	71.2	20	281	7.5	25	3,341	44	40
		25-39	31.8	81.6	105	1,287	4.0	18	4,463	85	81
		40-54	19.6	82.7	48	581	3.5	13	3,694	79	75
		Total	19.2	80.5	173	2,149	4.9	56	11,498	76	71

* Weighted average of HIV prevalence at baseline and two rounds of follow-up.

† AR, attributable risk = proportion of all deaths in the age-interval and location that could be averted in the absence of HIV. A value of 100% reflects the small sample size in the age-group.

Table 2. Total fertility rate by HIV status and location, Manicaland, Zimbabwe, 1998-2005

Stratum	All women	HIV-negative women	PAC*
Towns	3.01	3.51	-0.14
Estates	3.37	3.58	-0.06
Villages	3.56	3.79	-0.06

Total fertility rates for 15-49 year-olds based on births in the last 5 years and HIV infection status at follow-up

* PAC = population-attributable change in fertility = {fertility in total population - fertility in HIV-negative population} / {fertility in HIV-negative population}

Table 3. Crude birth rate (CBR), crude death rate (CDR) and population growth rate by socio-economic stratum in the presence and absence of HIV, Manicaland, Zimbabwe, 1998-2005

	HIV prevalence*		Observed			In the absence of HIV†		
Stratum	All ages	15-54 yrs	CBR	CDR	Rate of natural increase	CBR	CDR	Rate of natural increase
Towns	21.5%	32.8%	32.2	22.2	1.0%	36.7	7.4	2.9%
Estates	15.3%	22.2%	36.1	14.1	2.2%	37.8	4.5	3.3%
Villages	10.3%	17.3%	29.5	17.0	1.3%	30.9	8.2	2.3%

* Weighted average of HIV prevalence at baseline and two rounds of follow-up. HIV prevalence in children estimated from prevalence in pregnant women in the study communities, data on vertical transmission in Zimbabwe (60) and data on post-infection childhood survival (14)

† Based on fertility and mortality among uninfected individuals

Table 4. Intermediate and worst case estimates of HIV prevalence and rate of natural increase projected in mathematical models at a United Nations and World Health Organisation workshop held in December 1989

	Intermediate		Worst	
Model	HIV prevalence*	Rate of natural increase‡	HIV prevalence*	Rate of natural increase‡
Auvert	31.0	0.5%	55.0	-2.0%
Brouard	15.0	2.4%	55.0	-0.2%
Bulatao	39.5	2.5%	57.5	2.4%
Dietz	21.2	1.5%	43.9	-0.7%
IWG†	3.5	2.6%	42.4	-2.5%
Palloni	2.8	2.8%	30.3	0.0%

* HIV prevalence is defined across the whole population

† Interagency Working Group (45)

‡ The initial growth rate based on demographic inputs was 3.5% per annum

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