# Measuring and correcting biased child mortality statistics in countries with generalized epidemics of HIV infection

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**Objective** Under Millennium Development Goal 4, countries are required to reduce child mortality by two-thirds between 1990 and 2015. In countries with generalized epidemics of human immunodeficiency virus (HIV) infection, standard statistics based on fertility history may misrepresent progress towards this target owing to the correlation between deaths among mothers and early childhood deaths from acquired immunodeficiency syndrome.

**Methods** To empirically estimate this bias, child mortality data and fertility history, including births to deceased women, were collected through prospective household surveys in eastern Zimbabwe during 1998–2005. A mathematical model was then used to investigate the determinants and temporal dynamics of the bias, first in Zimbabwe and then in other countries with different background mortality rates and HIV-related epidemic profiles.

**Findings** According to the empirical data, standard cross-sectional survey statistics underestimated true infant and under-5 mortality by 6.7% and 9.8%, respectively. These estimates were in agreement with the output from the model, in which the bias varied according to the magnitude and stage of the epidemic of HIV infection and background mortality rates. The bias was greater the longer the period elapsed before the survey and in later stages of the epidemic. Bias could substantially distort the measured effect of interventions to reduce non-HIV-related mortality and of programmes to prevent mother-to-child transmission, especially when trends are based on data from a single survey.

**Conclusion** The correlation between the HIV-related deaths of mothers and their children can bias survey estimates of early child mortality. A mathematical model with a user-friendly interface is available to correct for this bias when measuring progress towards Millennium Development Goal 4 in countries with generalized epidemics of HIV infection.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

# Introduction

Millennium Development Goal 4 (MDG4) calls for countries to reduce child mortality rates by two-thirds between 1990 and 2015.<sup>1,2</sup> There is concern that progress towards meeting this target in sub-Saharan African countries with generalized epidemics of human immunodeficiency virus (HIV) infection is being hampered directly by high levels of mother-to-child HIV transmission, and indirectly by illness and death among mothers with acquired immunodeficiency syndrome (AIDS), both of which undermine children's care.<sup>3–6</sup> According to the Joint United Nations Programme for HIV/AIDS (UNAIDS), in the 1990s HIV infection and AIDS accounted for more than 20% of the total risk of dying before the age of 5 years in seven countries.<sup>7</sup> However, the subsequent scale-up of antiretroviral therapy (ART) programmes and of national interventions to prevent mother-to-child HIV transmission <sup>8,9</sup> offers hope that HIV/AIDS control programmes can help meet the international goal.

To establish whether MDG4 is met, improved methods are being developed to measure trends in child mortality, which are usually assessed by interviewing mothers about the survival of their children.<sup>10–13</sup> In many countries there have been sustained declines in childhood mortality since 1950, but in some of the countries with severe epidemics of HIV infection, paediatric AIDS has generated increases in recent years.<sup>13</sup> Unfortunately, estimates of infant and under-5 mortality rates in countries experiencing generalized HIV epidemics are subject to important bias <sup>10,14</sup> that could lead to an incorrect assessment of their progress towards attaining MDG4. The bias stems from the fact that deaths occur most often in children born to women infected with HIV, who are less likely to be included in surveys because of illness or death. Little headway has been made in addressing this bias, whose magnitude is hard to estimate because it is determined by a set of inter-dependent relationships between fertility, mother's age, stage of HIV infection, the risk of motherto-child transmission and the survival of infected children. Such bias could be important in cross-country comparisons because it may vary according to the level of non-AIDS-related background mortality, as well as with the magnitude and stage of the epidemic of HIV infection. It could also confound trends analyses because its magnitude may change as the epidemic evolves, owing to changes in the age pattern of HIV infection, the number of women with advanced disease, and the uptake of services for the prevention of mother-to-child transmission and for the delivery of ART.

In this study we have tested the hypothesis that the correlation between death from HIV infection in mothers and their young children can cause a bias in child mortality rate estimates in excess of 5% (a level judged to introduce serious error).<sup>15</sup> To test this hypothesis we drew upon childhood mortality data from a prospective populationbased cohort study in Zimbabwe whose data covered both children born to women who were still living and children whose mothers had died. We developed a mathematical model to produce estimates of the bias in national surveys, first in Zimbabwe and then in other selected countries with different epidemic profiles of HIV infection and different baseline infant and childhood mortality rates. The model can be used to derive corrected infant and under-5 mortality rates and their trends for countries with generalized epidemics of HIV infection.

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(Submitted: 6 September 2009 – Revised version received: 6 March 2010 – Accepted: 9 March 2010 – Published online: 7 April 2010)

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# **Methods**

# **Data and analysis**

The data used in this analysis were taken from the Manicaland HIV/STD Prevention Study in eastern Zimbabwe. The detailed procedures followed in the study have been published elsewhere.<sup>16</sup> In brief, between July 1998 and February 2000 we conducted a baseline census of households in 12 locations in a phased manner (one site at a time) and recruited into an open cohort a random sample of adult household residents. We conducted a second and third round of censuses and surveys in the same sites 3 years and 5 years after baseline, respectively. At each round the questionnaires administered to members of the open cohort included sections on fertility history and child survival that resembled those included in the Demographic and Health Surveys (DHS).<sup>17</sup> At each survey round verbal autopsy interviews were conducted with the caregivers of cohort members who had died since the previous round.<sup>18</sup> During such interviews, data were collected on any births that had occurred between the date of the last round and the date on which the cohort member had died, as well as on any children who had died, both among those born since the last round or before it. Prior ethical approval for the study was obtained from the Research Council of Zimbabwe and the St Mary's Local Research Ethics Committee, London, United Kingdom of Great Britain and Northern Ireland.

In the three survey rounds, 98%, 94% and 96% of households and 80%, 81% and 87% of adult females participated, respectively. Of the women interviewed at baseline and first follow-up who were not known to have subsequently died, 60% and 65%, respectively, were re-interviewed in subsequent follow-up rounds. Outmigration was the main reason for loss to follow-up.<sup>19</sup>

Using the fertility history data collected in the third round of the survey, we estimated standard infant and under-5 mortality rates<sup>17</sup> for children born to surviving women aged 15–49 years. DHS analyses generate estimates covering 5-year periods before each survey date, but the Manicaland estimates covered the period 1998–2005 because of the phasing of the survey rounds. To measure the bias in the estimates attributable to the correlation between deaths among mothers and their young children, analogous calculations were performed for the children of deceased women using the verbal autopsy interview data from the second and third survey rounds. To obtain corrected infant and under-5 mortality rates, we combined the estimates for children born to surviving and deceased women and adjusted for the sampling of women in the open cohort and the loss to follow-up of women who had died. We assumed that women who died would have been lost to follow up, had they not died, for the same reasons that surviving women were lost to follow-up. The sensitivity of the results to this assumption was investigated. Further details are provided in Appendix A (available at: http://www1.imperial.ac.uk/medicine/ people/timothy.hallett/).

## Model and analysis

We created an individual-based stochastic model to simulate the mortality and fertility experience of cohorts of women born in rural Zimbabwe between 1920 and 2005 and the mortality experience of their children. Full details of the model are given in Appendix A. In brief, parametric probability distributions were used to describe the relationships between age, fertility, the risk of acquiring HIV infection, the time since HIV infection was acquired, HIV-related subfertility, AIDS-related mortality rates, and background mortality rates. The life-course experiences of women were simulated by drawing randomly from these distributions. The model puts out a data set analogous to one obtained in a cross-sectional survey of fertility histories. Model input settings for the rural Zimbabwe application were based on data from the Manicaland study and regional and national reports, and we performed a sensitivity analysis to explore the sensitivity of model outcomes to these assumptions (Appendix A).

Using data generated by the mathematical model, we produced three timeseries of infant and under-5 mortality measurements for Zimbabwe. The first, the uncorrected "DHS analogue", was created using standard DHS methods.<sup>17</sup> To test the validity of the model, we compared these estimates with reported national estimates for Zimbabwe from the 1988, 1994, 1999 and 2005 DHS surveys for the periods comprising 0-4 years, 5-9 years and 10-14 years before the survey dates.<sup>20-23</sup> The second or "DHS continuous" time series estimated mortality in a similar way, but estimates were calculated on a continuous basis (as if they had come from a very large number of closely-spaced surveys) and without censoring child survival

times. Finally, the "corrected" time series was calculated the same way as the DHS continuous time series, except that it also included reports for women who had died of AIDS before the survey.

The results from the DHS continuous and the corrected time series were compared, and the differences between them were taken as estimates of the extent to which underestimation of infant and under-5 mortality rates is expected to occur in standard statistics derived from cross-sectional surveys in rural Zimbabwe over the course of the epidemic of HIV infection. For further validation of the model, the expected differences in the late 1990s and early 2000s were compared with the empirical estimates from Manicaland.

We conducted a scenario-based sensitivity analysis to identify the main determinants of the extent of bias. The model was re-parameterized to compare estimates of the bias over time for six other countries in sub-Saharan Africa having epidemics of HIV infection of different intensity and different underlying infant mortality: Botswana, Côte d'Ivoire, Kenya, Lesotho, Namibia and Zambia. We used estimated rates of HIV infection based on UNAIDS prevalence data,<sup>24,25</sup> as well as mortality and fertility rates in the absence of HIV from DHS estimates for pre-AIDS periods. Finally, we used the model to estimate the impact of hypothetical interventions preventing mother-to-child transmission and delivering ART to adults on infant and under-5 mortality.

# Results

# **Bias in child mortality rates**

The empirical estimates of the underassessment in cross-sectional survey estimates of child mortality rates owing to the correlation between HIV-related deaths among mothers and their young children are summarized in Table 1. In round three of the Manicaland survey, complete fertility histories and child mortality data were collected for 6236 women aged 15-49 years. Such women reported a total of 3308 liveborns in the preceding 5 years. These data yielded uncorrected estimates of infant and under-5 mortality of 45.9 and 67.1 per 1000 live births, respectively. For children born to women who were HIV+ at round three, the infant and under-5 mortality rates were 85.7 and 135.3 per 1000, respectively. For children born to uninfected women, the corresponding rates were 32.3 and 46.3 per 1000.

#### Table 1. Empirical estimates<sup>a</sup> of infant and child mortality and their underassessment in cross-sectional surveys owing to the deaths of mothers from human immunodeficiency virus infection, Manicaland, Zimbabwe, 1998–2005

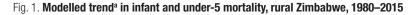
Parameter	Surviving mothers	Deceased mothers	All mothers	Underestimate <sup>b</sup> (%)
Infant mortality rate (per 1000 live births)	45.9	146.8	48.9	6.7
Under-5 mortality rate (per 1000 live births)	67.1	283.8	73.7	9.8
No. of births in the past 5 years <sup>c</sup>	5325	167	5 492	NA
No. of women aged 15–49 years, 2003–2005	10315	1 253	NA	NA

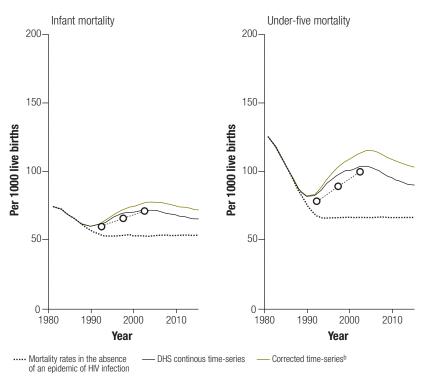
NA, not applicable.

<sup>a</sup> Based on a prospective cohort of women aged 15–49 years.

<sup>b</sup> The under-estimate is the difference between the mortality rates for children born to all mothers and for children born to surviving mothers, expressed as a percentage of the mortality rate among children born to surviving mothers.

° In the 5 years before the most recent survey round (conducted from July 2003 to August 2005).





--O-Uncorrected DHS analogue ratesc

DHS, Demographic and Health Survey; HIV, human immunodeficiency virus.

<sup>c</sup> The uncorrected DHS analogue rates that would be estimated in a 2005 cross-sectional survey for the periods 0–4, 5–9 and 10–14 years before the survey.

A total of 350 female members of the cohort who at round three would have turned between 15 and 49 years of age on their last birthday, were recorded as having died within the combined 5-year periods between surveys. Fertility histories were available from individual and verbal autopsy interviews for 322 (92%) of these women, who reportedly had 43 live births in the 5 years before the round three interviews and a further 80 live births in the preceding 5 years. These children experienced infant and under-5 mortality rates of 146.8 and 283.8 per 1000, respectively.

In total, 10 315 women aged 15–49 years were counted in the household census

in round three. If over the previous 5 years these women experienced birth rates similar to those among women whose fertility histories were obtained, they would have had a total of 5325 live births. Furthermore, if we assume that women who died between the first and third rounds of the survey were lost to follow-up (due to reasons other than death) at the same rates as women who survived, a total of 1253 women would have died during this period.

Again, if these deceased women experienced the same birth rates as the 322 women whose fertility histories were collected, they would have given birth to 167 children. If we then apply the infant and under-5 mortality rates observed in children born to surviving and deceased women to the estimated numbers of babies born to surviving and deceased women during the 5-year period between surveys, we obtain corrected estimates of infant and under-5 mortality rates of 48.9 and 73.7 per 1000, respectively. When the corrected and uncorrected rates are compared, it becomes clear the standard cross-sectional survey estimates for the 5-year period immediately before the survey underestimate the true levels of infant and under-5 mortality by 6.7% and 9.8%, respectively, of their observed values.

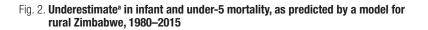
If we assume that the loss to follow-up (for reasons other than death) among the women who died was 20% greater than among those who survived, the corresponding estimated biases in infant and under-5 mortality rates would be 8.3% and 12.2%, respectively. If the loss to follow-up rate among the women who died were 20% lower instead, the estimated biases would be 5.6% and 8.3%, respectively.

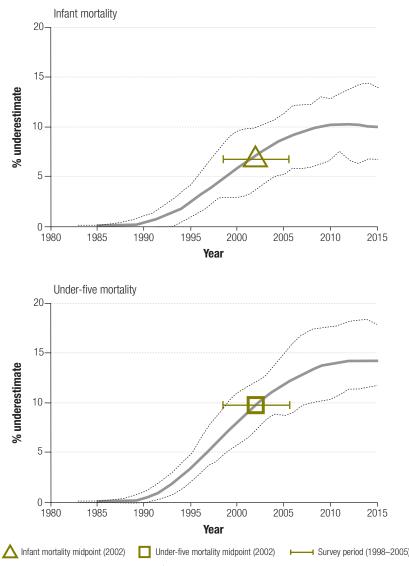
## **Bias over time**

The model, which was parameterized for rural Zimbabwe, generated a DHS analogue time-series that was in substantial qualitative agreement with national DHS survey data (Fig. C and Fig. D in Appendix A). The three mortality measures all show marked increases in mortality during 1990-2005, with the reductions during the 1980s largely being reversed (Fig. 1). Mortality rates were expected to decrease after 2005 due to declines in HIV infection prevalence in adults since 2000.<sup>26,27</sup> During the pre-AIDS era, the DHS analogue estimates for 0-4, 5-9 and 10-14 years before the survey were in line with the continuous measurements. However, the DHS analogue estimates from the 2005 survey for mortality over the periods 5-9 and 10-14 years before the survey were lower than the continuous measurement.

<sup>&</sup>lt;sup>a</sup> No intervention to prevent mother-to-child transmission is included.

<sup>&</sup>lt;sup>b</sup> The corrected time-series accounts for HIV-related deaths among women.





------ Range of outcomes from 200 simulations<sup>b</sup>

<sup>a</sup> No intervention to prevent mother-to-child transmission is included.

<sup>b</sup> The range of outcomes from 200 simulations using the same parameter distributions and indicating the uncertainty in the projections due to interperson variability and measurement errors in observational studies used to parameterize the model.

This pattern, reflected in the DHS data for Zimbabwe (Fig. C and Fig. D in Appendix A), reflects the fact that the women who were alive to report having children during these much earlier periods were typically women who were not infected then (since women infected at the time would have died before the survey).

The corrected time-series is substantially greater than the DHS analogue and the DHS continuous measurements. Fig. 2 shows the magnitude of the bias in rural Zimbabwe for 1980–2015 and the empirical results from Manicaland. The bias grew in the wake of the epidemic of HIV infection. The effect was minimal before the early 1990s but exceeded 5% by the late 1990s. The bias is greater for under-5 mortality than for infant mortality because mothers who gave birth further into the past are more likely to have died before the interview date. The empirical results for 1998-2005 agree strongly with model results, which show that the infant and under-5 mortality rates for this period were estimated by 7.1% (versus 6.7%) and 9.7% (versus 9.8%), respectively. The uncertainty in the estimates of bias yielded by the model encompasses the possible range of empirical estimates if one makes alternative assumptions about the relative loss to follow-up among women who survived and died.

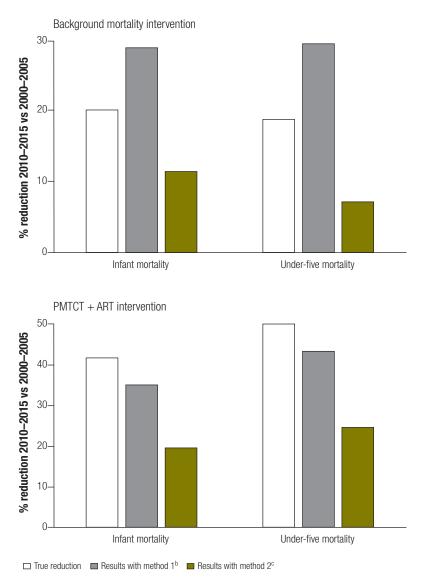
For the period from 2005 to 2009, the model predicted that infant mortality and under-5 mortality could be underestimated by as much as 9% and 13%, respectively. These multivariate sensitivity analysis results indicate that, over the same period, underestimates ranging from 3% to 17% for infant mortality, and from 4% to 23% for under-5 mortality, are supported by alternative model assumptions (Fig. E in Appendix A).

The lower the background childhood mortality rates, the greater the biases, since the fraction of HIV-related deaths among children would be higher. Higher fertility at older ages would also lead to greater biases because the women infected with HIV at older ages would also be giving birth. If fertility were to decline less steeply among HIV-infected women before the onset of AIDS, the bias would be greater as well because more children would be born to mothers likely to die within a short time. The bias also increases as the mother's disease progresses and the risk of mother-tochild transmission grows, since women in late stages of HIV infection, who are more likely to die, would be giving birth to more HIV-infected children.

We estimated the magnitude of the bias in 2005-2009 in six other African countries with generalized epidemics of HIV infection (Fig. F in Appendix A). Botswana and Lesotho, where the epidemic is intense and childhood mortality is relatively low, had the largest biases: 13% and 8% for under-5 mortality, respectively. In contrast, the bias was modest (< 2%) in Côte d'Ivoire, where the epidemic of HIV infection is smaller and background mortality is higher. Despite the fact that in 2005 the prevalence of HIV infection was similar in Namibia and Zambia, the bias in Namibia (6%) is greater than in Zambia (4%) and continues to increase, since background childhood mortality is higher in Zambia and the epidemic is more recent in Namibia.<sup>25</sup>

Trends in childhood mortality can be gleaned from fertility history data in two standard ways: by comparing standard (uncorrected) mortality estimates in successive surveys for the 5-year period before each survey date (method 1) and by comparing mortality estimates for successive periods using data from a single survey (method 2). The impact of interventions that reduce background childhood mortality may be overestimated by method 1, since the contribution of HIV to mortality is underrepresented in the uncorrected statistics (whereas the true reduction is accurately recorded in the estimates corrected for bias, (Fig. Ha in Appendix A and Fig. 3).

#### Fig. 3. Estimated impact<sup>a</sup> on infant and under-5 mortality of interventions to reduce background child mortality by 30% or prevent mother-to-child transmission (PMTCT) in Botswana



ART, antiretroviral therapy.

- <sup>a</sup> The bars show the reduction in mortality over 10 years (2010–2015 versus 2000–2005). The hypothetical interventions stipulate that, after 2005, all women will have access to therapy that will eliminate the risk of mother-to-child transmission, and that 50% of all the HIV+ women eligible will receive antiretroviral therapy.
- <sup>b</sup> A comparison of standard estimates of mortality for the period 0–4 years before each of two surveys in 2005 and 2015.
- $^{\rm c}$  A comparison of standard estimates of mortality for the periods 0–4 and 10–14 years before one survey in 2015.

On the other hand, the impact is underestimated by method 2 because estimates for periods closer to the survey date capture more of the deaths among children born to HIV-infected mothers, and this offsets the effect of actual reductions in background mortality.

The impact of interventions to prevent mother-to-child transmission and deliver ART to adults, which reduce HIV-related mortality among children, will be underestimated by standard mortality statistics (method 1 or 2), since HIV-related deaths are undercounted at baseline. In a model simulation of a hypothetical intervention in Botswana in which after 2005 all eligible women receive therapy that effectively eliminates the risk of mother-to-child transmission and 50% of all eligible adults receive treatment, infant and under-5 mortality would actually drop by 42% and 50% between the 2000–2005 and 2010–2015 periods, respectively (Fig. Ha in Appendix A and Fig. 3). However, applying method 1 (with the surveys conducted in 2005 and 2015) would yield reductions of only 35% and 43%. If, on the other hand, method 2 were used to infer the trend for the same period (comparing estimates for the periods 0–4 and 10–14 years before a survey in 2015), the actual change in mortality rates (Fig. Ha in Appendix A and Fig. 3) would not be captured at all, and reductions in infant and under-5 mortality of only 19% and 24% would be recorded, respectively.

# Discussion

We used direct empirical and mathematical modelling methods to measure and evaluate the extent of bias attributable to the correlation between AIDS-related deaths among women and their young children on early childhood mortality rates and trends derived by applying standard methods to data from retrospective fertility histories collected in household surveys. The data from Zimbabwe provide empirical evidence that this bias can be substantial, with underestimation of both infant and under-5 mortality exceeding 5% in a population in which the prevalence of HIV infection fell from 23% to 18% over the period 1998–2005,<sup>19</sup> when females died at a rate of 26 per 1000 (with 74% of the deaths being HIV-related)<sup>28</sup> and the uptake of interventions for preventing mother-tochild transmission and for delivering ART to adults was minimal.<sup>29</sup> The bias was greatest in the under-5 mortality rate - the statistic most commonly used to track progress towards MDG4. Using a specially-developed mathematical model, we demonstrated that the bias varies between countries depending on the scale and stage of the epidemic of HIV infection and on the level of background mortality. Furthermore, the estimated bias will typically be greater for periods further removed in time from the survey date. The model results also show that the bias generally increases during epidemics that are stable or increasing, and that this hampers comparisons between countries whose epidemics are in different stages. Reductions in background mortality may be either under- or overestimated, while the effect on mortality of programmes for preventing mother-tochild transmission, introduced in the early 2000s, will be substantially underestimated unless the bias is corrected for.

The existence of a bias in mortality estimates based on fertility histories was anticipated in earlier modelling work and in data from selected sentinel surveillance, <sup>14,30,31</sup> but the bias was expected to be modest and correction was deemed unnecessary. The reason may be that in those settings the epidemic of HIV infection was in an earlier phase at the time of the analysis. Ward & Zaba proposed an adjustment to the indirect "children surviving among children ever born" method for estimating child mortality to account for the correlation between the deaths of mothers and their children.<sup>15</sup> However, indirect methods require the use of an appropriate model life table to adjust the data for the age pattern of mortality in the general population, and estimates are difficult to locate in time.<sup>17</sup> Thus, the more direct approach based on fertility histories examined in this paper is usually preferred.<sup>17</sup> Estimates obtained using this method are given more weight in international procedures for assessing levels and trends in child mortality.<sup>10</sup>

The uncorrected infant and under-5 mortality estimates in the Manicaland cohort study are lower than the estimates obtained in the Zimbabwe Demographic and Health Survey 2005–2006,<sup>22</sup> possibly because the region is favoured with relatively good food supplies and better than average health-care services (e.g. private clinics on estates), and because the study sites were specifically selected to avoid including participants who belonged to religious groups that decline medical services such as childhood immunizations.<sup>32</sup> The mortality estimates for children born to women who died are based on small numbers owing, in part, to HIV-associated subfertility.<sup>33</sup> In addition, child deaths may have been underreported by verbal autopsy respondents. However, the response rate for the verbal autopsy interview was encouragingly high (92%). Assumptions were made in extrapolating from the samples of children born to deceased and surviving women to the whole population and in estimating loss-to-follow-up. However, the results show a reasonable level of internal and external consistency. The low birth rate among women who died compared to women who survived (54 per 1000 versus 106 per 1000) reflects severe sub-fertility at advanced stages of HIV infection.<sup>33</sup> The ratio of deceased (in the past 5 years) to surviving women in round 3 (1253 to 10 315) is consistent with measurements of female

adult mortality (26 per 1000 per annum) in this population,<sup>28</sup> and the estimates of mortality among children born to women who died are compatible with estimates from studies of mortality in HIV-infected children.<sup>34</sup> The increase in the participation rate of women in round 3 may reflect the slightly longer period spent in the study areas and therefore could have resulted in a higher participation rate among women who are more mobile. Although this trend, in itself, seems unlikely to have affected the results, it remains possible that if the women missed in the first two rounds of the survey had different HIV-associated death rates and/or fertility levels than those interviewed in these rounds, this could have affected the empirical estimates of bias in eastern Zimbabwe. The completeness of the birth history reports could not be fully assessed, and although the data presented are mostly from recent births (in the past 5 years), minimizing recall bias, it is possible that children who die when they are very young are selectively omitted in birth histories and that this may be more common among children born to HIV-infected women and particularly those who die between survey rounds.

The mathematical model entailed several simplifying assumptions (Appendix A) but was validated by comparison with observed mortality rates from national DHS surveys and direct empirical estimates of under-estimation calculated using the data from Manicaland. The correspondence between the model and DHS estimates of mortality, though in good qualitative agreement, is not exact (Fig. C and Fig. D in Appendix A) and this could partly reflect the quality of DHS data as well as uncertainties in key model parameters, in particular the assumed relationship between disease progression and fertility. It will be important to further validate the model with empirical estimates of bias in other settings. Although no other community based cohort study collects prospective data in exactly the same way that the Manicaland

study does, it will be possible to derive corresponding estimates in other studies by linking data from associated demographic surveillance systems and serosurveys.

Our findings show that standard infant and under-5 mortality statistics based on retrospective fertility histories need to be corrected for bias due to correlation between deaths among mothers and their young children in populations with generalized HIV epidemics. This will be particularly important when measuring trends, evaluating the impact of PMTCT programmes, or assessing progress towards MDG4. Increased access to antiretroviral therapy is expected to gradually reduce the bias - further obfuscating naive determination of trends - since mortality among HIV-infected mothers and their children will be lower (Fig. G in Appendix A). International procedures for measuring trends in child mortality<sup>10</sup> may need to be revised for high HIV prevalence settings; particularly so, because they are based, in part, on estimates for historical periods which are especially prone to bias. However, corrections should be made for estimates in all countries before international comparisons are drawn.

The model developed in this study is available as a stand-alone executable file that integrates with HIV incidence time-series outputs from UNAIDS' Epidemiological Projection Package<sup>35</sup> to provide estimates of early child mortality. All parameter settings for the model can be customized through a user-friendly interface in Microsoft Excel (Redmond, WA, United States of America).

## Acknowledgements

Timothy Hallett and Simon Gregson contributed equally to this work.

**Funding:** Funding for the study was provided by the Wellcome Trust.

**Competing interests:** None declared.

# ملخص

# قياس وتصويب الإحصاءات التحيزية لمعدلات وفيات الأطفال في البلدان التي يعم فيها وباء العدوى بفيروس العوز المناعي البشري (فيروس الأيدز )

الغرض وفقا للمرمى الرابع من المرامي الإنمائية للألفية، فإن البلدان مطالبة بخفض معدلات وفيات الأطفال بنحو الثلثين بين عامي 1990 و 2015. وفي البلدان التي يعم فيها وباء العدوى بفيروس الأيدز ، فإن الإحصاءات المعيارية المرتكزة على تاريخ الخصوبة قد تعطي انطباعا مغلوطا حول ما يُحرز من تقدم نحو هذا الغرض بسبب العلاقة ما بين وفاة الأمهات والوفاة المبكرة للطفل من جراء متلازمة العوز المناعى المكتسب أى الأيدز .

الطرق: ولإجراء تقديرات تجريبية حول هذا التحيز، جمعت المعطيات الخاصة بوفيات الأطفال وتاريخ الخصوبة متضمنة مواليد الأمهات المتوفيات،

من خلال المسوحات الاستباقية للعائلات والتي تمت خلال الفترة من 1998 وحتى 2005 في المناطق الشرقية من زيمبابوي. وقد استخدم في ذلك الوقت نموذج حسابي لتقصي المحددات والمحركات الوقتية لهذا التحيز، في زيمبابوي أولا ثم في سائر البلدان ذات الخلفية المتباينة من معدلات الوفيات والمرتسمات الوبائية المتعلقة بفيروس الأيدز .

**الموجودات** بناء على المعطيات التجريبية، فقد كانت الإحصاءات المعيارية للمسح المقطعي تقلل من الحجم الحقيقي لمعدلات وفيات الرضّع ومن هم دون الخامسة من العمر بنسب تراوحت بين %6.7 و%9.8 على التوالي. ولقد النتيجة إن الارتباط بين وفيات الأمهات وأطفالهن المتعلقة بفيروس الأيدز ، يمكن أن يؤدي إلى تحيّز تقديرات مسح الوفيات المبكرة للطفولة. ويتوافر الآن نموذج حسابي ذو واجهة سهلة الاستعمال لتصويب هذا النمط من التحيّز عند قياس التقدم المحرز نحو المرمى الرابع من المرامي الإنمائية للألفية في البلدان التي ينتشر فيها وباء العدوى بفيروس العوز المناعي البشري (فيروس الأدرز ).

توافقت هذه التقديرات مع نتائج النموذج والذي تباين فيه التحيز بحسب حجم وباء العدوى بفيروس الأيدز والمرحلة التي عر بها، وخلفيات معدلات الوفيات. وقد زاد التحيز مع طول الفترة التي انقضت قبل إجراء المسح ومع المراحل الأخيرة من الوباء. ويمكن لمثل هذا التحيز أن يعوق بصورة ملموسة من قياس تأثيرات المداخلات المعنية بخفض معدلات الوفيات التي لا تتعلق بفيروس الأيدز ، وكذلك برامج الوقاية من انتقال الفيروس من الأم إلى الطفل، ولاسيما عندما تكون الاتجاهات مبنية على معطيات منبثقة من مسح واحد فقط.

# Résumé

# Mesure et correction des erreurs de statistiques en termes de mortalité infantile dans les pays présentant une épidémie généralisée d'infection au VIH

**Objectif** En vertu de l'Objectif 4 du Millénaire pour le développement, les pays doivent réduire la mortalité infantile de deux tiers entre 1990 et 2015. Dans les pays enregistrant une épidémie généralisée du virus de l'immunodéficience humaine (VIH), les statistiques standard basées sur l'historique de la fertilité peuvent présenter de manière inexacte le progrès en ce sens, de par la corrélation entre les décès des mères et les décès des nouveau-nés liés au syndrome d'immunodéficience acquise. **Méthodes** Pour évaluer d'un point de vue empirique cette erreur, les données de mortalité infantile et l'historique de la fertilité, y compris les naissances chez des mères décédées, ont été recueillis en réalisant des enquêtes de ménage prospectives dans l'Est Zimbabwe entre 1998 et 2005. Un modèle mathématique a ensuite utilisé pour examiner les déterminants et la dynamique temporale de l'influence, d'abord au Zimbabwe, puis dans d'autres pays présentant des taux de mortalité et des profils épidémiques liés au VIH différents.

Résultats D'après les données empiriques, les statistiques des enquêtes croisées standard ont sous-estimé la vraie mortalité chez les nourrissons et les enfants de moins de 5 ans, de 6,7% et de 9,8% respectivement. Ces évaluations étaient en accord avec les résultats du modèle dans lequel l'influence variait en fonction de l'ampleur et du stade de l'épidémie de VIH et des taux de mortalité. L'influence était plus importante sur une période plus longue avant l'enquête et à des stades ultérieurs de l'épidémie. Cette influence peut considérablement déformer l'effet mesuré des interventions en vue de réduire la mortalité non liée au VIH et des programmes de prévention de la transmission mère-enfant, en particulier lorsque les tendances reposent sur les données d'une seule enquête.

**Conclusion** La corrélation entre les décès de mères et de leurs enfants liés au VIH peut influencer les évaluations des enquêtes sur la mortalité des nouveau-nés. Un modèle mathématique doté d'une interface conviviale est disponible pour corriger cette influence lors de la mesure des progrès vers l'Objectif 4 du Millénaire pour le développement dans les pays présentant une épidémie généralisée d'infection au VIH.

# Resumen

# Medición y corrección de los datos estadísticos sesgados sobre mortalidad infantil en países con epidemia generalizada de infección por VIH

**Objetivo** Según el Objetivo de Desarrollo del Milenio número 4, los países deben reducir la mortalidad infantil en dos tercios entre 1990 y 2015. En los países con epidemia generalizada de infección por el virus de inmunodeficiencia humana (VIH), los datos estadísticos estándar basados en el historial de embarazos pueden dar una idea equivocada del avance hacia la consecución de este objetivo como consecuencia de la correlación entre los fallecimientos de las madres y los fallecimientos en la primera infancia debidos al síndrome de inmunodeficiencia adquirida.

**Métodos** Para calcular empíricamente este sesgo, se recopilaron datos de mortalidad infantil y el historial de embarazos, incluyendo nacimientos en mujeres fallecidas, mediante encuestas prospectivas por hogares realizadas en Zimbabwe oriental durante 1998–2005. Luego, se utilizó un modelo matemático para investigar los factores determinantes y la dinámica temporal del sesgo, primero en Zimbabwe y, después, en otros países con tasas de mortalidad de fondo diferentes y perfiles epidémicos relacionados con el VIH.

Resultados Según los datos empíricos, los datos estadísticos de las encuestas transversales estándar subestimaron la verdadera

mortalidad en lactantes y niños menores de 5 años en un 6,7% y un 9,8%, respectivamente. Estos cálculos concordaban con los resultados del modelo, en el que el sesgo variaba en función de la magnitud y el estadio de la epidemia de la infección por VIH y las tasas de mortalidad de fondo. El sesgo era mayor cuanto más tiempo había transcurrido antes de la encuesta y en los últimos estadios de la epidemia. El sesgo podía distorsionar sustancialmente el efecto medido de las intervenciones para reducir la mortalidad no relacionada con el VIH y de los programas para prevenir la transmisión de la madre al niño, especialmente cuando las tendencias se basan en datos de una única encuesta.

**Conclusión** La correlación entre los fallecimientos relacionados con el VIH de las madres y de sus hijos puede ocasionar un sesgo en las estimaciones de la mortalidad en la primera infancia obtenidas a partir de las encuestas. Está disponible un modelo matemático con una interfaz fácil de usar para corregir este sesgo cuando se mide el progreso para la consecución del Objetivo de Desarrollo del Milenio número 4 en países con epidemia generalizada de infección por VIH.

# References

- United Nations General Assembly. United Nations Millennium Declaration (Resolution 55/2). New York: UN; 2000. Available from: http://www.un.org/ millennium/declaration/ares552e.htm [accessed 28 March 2010].
- 2. United Nations. *The Millennium Development Goals report 2005*. New York: UN; 2005.
- Adetunji J. Trends in under-5 mortality rates and the HIV/AIDS epidemic. Bull World Health Organ 2000;78:1200–6. PMID:11100615
- Timaeus IM. Impact of the HIV epidemic on mortality in sub-Saharan Africa: evidence from national surveys and censuses. *AIDS* 1998;12(Suppl 1):S15–27. doi:10.1097/00002030-199805000-00002 PMID:9677186
- Boerma JT, Nunn AJ, Whitworth JAG. Mortality impact of the AIDS epidemic: evidence from community studies in less developed countries. *AIDS* 1998;12(Suppl 1):S3–14. PMID:9677185
- Ahmad OB, Lopez AD, Inoue M. The decline in child mortality: a reappraisal. Bull World Health Organ 2000;78:1175–91. PMID:11100613
- Walker N, Schwartländer B, Bryce J. Meeting international goals in child survival and HIV/AIDS. *Lancet* 2002;360:284–9. doi:10.1016/S0140-6736(02)09550-8 PMID:12147371
- Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access. Geneva: World Health Organization; 2006.
- Progress on global access to HIV antiretroviral therapy: a report on "3 by 5" and beyond. Geneva: World Health Organization; 2006.
- United Nations Children's Fund, World Health Organization, The World Bank, United Nations Population Division. *Levels and trends of child mortality in* 2006: estimates developed by the Inter-agency Group for Child Mortality Estimation. New York: UNICEF, WHO, WB, UNPD; 2007.
- Bryce J, Daelmans B, Dwivedi A, Fauveau V, Lawn JE, Mason E et al.; Countdown Coverage Writing Group; Countdown to 2015 Core Group. Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet* 2008;371:1247–58. doi:10.1016/S0140-6736(08)60559-0 PMID:18406859
- Murray CJL, Laakso T, Shibuya K, Hill K, Lopez AD. Can we achieve Millennium Development Goal 4? New analysis of country trends and forecasts of under-5 mortality to 2015. *Lancet* 2007;370:1040–54. doi:10.1016/S0140-6736(07)61478-0 PMID:17889243
- Garenne M, Gakusi E. Health transitions in sub-Saharan Africa: overview of mortality trends in children under 5 years old (1950–2000). *Bull World Health Organ* 2006;84:470–8. doi:10.2471/BLT.05.029231 PMID:16799731
- Mahy M. Measuring child mortality in AIDS-affected countries. New York: United Nations Population Division, Department of Economic and Social Affairs; 2003. Available from: (http://www0.un.org/esa/population/ publications/adultmort/UNICEF\_Paper15.pdf [accessed 23 April 2009].
- Ward P, Zaba B. The effect of HIV on the estimation of child mortality using the children surviving/children ever born technique. *South Afr J Demogr* 2008;11.
- Gregson S, Garnett GP, Nyamukapa CA, Hallett TB, Lewis JJC, Mason PR et al. HIV decline associated with behavior change in eastern Zimbabwe. *Science* 2006;311:664–6. doi:10.1126/science.1121054 PMID:16456081
- 17. Rutstein SO, Rojas G. *Guide to DHS statistics*. Calverton: Demographic and Health Surveys and ORC Macro; 2006.
- Lopman BA, Barnabas RV, Boerma JT, Chawira G, Gaitskell K, Harrop T et al. Creating and validating an algorithm to measure AIDS mortality in the adult population using verbal autopsy. *PLoS Med* 2006;3:e312. doi:10.1371/ journal.pmed.0030312 PMID:16881730
- Gregson S, Nyamukapa CA, Lopman B, Mushati P, Garnett GP, Chandiwana SK et al. Critique of early models of the demographic impact of HIV/ AIDS in sub-Saharan Africa based on contemporary empirical data from Zimbabwe. *Proc Natl Acad Sci U S A* 2007;104:14586–91. doi:10.1073/ pnas.0611540104 PMID:17761795

- Zimbabwe Central Statistical Office. *Zimbabwe Demographic and Health* Survey, 1988. Harare: Zimbabwe Central Statistical Office and Macro International; 1989.
- Zimbabwe Central Statistical Office. *Zimbabwe Demographic and Health* Survey, 1999. Harare: Zimbabwe Central Statistical Office and Macro International; 2000.
- Zimbabwe Central Statistical Office. *Zimbabwe Demographic and Health* Survey, 2005-2006. Harare: Zimbabwe Central Statistical Office and Macro International; 2007.
- 23. Zimbabwe Central Statistical Office. *Zimbabwe Demographic and Health Survey*. Harare: CSO; 1994.
- Stover J, Johnson P, Zaba B, Zwahlen M, Dabis F, Ekpini RE. The Spectrum projection package: improvements in estimating mortality, ART needs, PMTCT impact and uncertainty bounds. *Sex Transm Infect* 2008;84(Suppl 1):i24–30. doi:10.1136/sti.2008.029868 PMID:18647862
- Joint United Nations Programme on HIV/AIDS. *Report on the global AIDS epidemic*. Geneva: UNAIDS; 2008. Available from: http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\_Global\_report.asp. [accessed 28 March 2010].
- Joint United Nations Programme on HIV/AIDS. *Evidence for HIV decline in Zimbabwe: a comprehensive review of the epidemiological data.* Geneva: Joint United Nations Programme on HIV/AIDS; 2005.
- Mahomva A, Greby S, Dube S, Mugurungi O, Hargrove J, Rosen D et al. HIV prevalence and trends from data in Zimbabwe, 1997–2004. *Sex Transm Infect* 2006;82(Suppl 1):i42–7. doi:10.1136/sti.2005.019174 PMID:16581759
- Smith J, Mushati P, Kurwa F, Mason PR, Gregson S, Lopman B. Changing patterns of adult mortality as the HIV epidemic matures in Manicaland, eastern Zimbabwe. *AIDS* 2007;21(Suppl 6):S81–6. doi:10.1097/01. aids.0000299414.60022.1b PMID:18032943
- Dube S, Boily M-C, Mugurungi O, Mahomva A, Chikhata F, Gregson S. Estimating vertically acquired HIV infections and the impact of the prevention of mother-to-child transmission program in Zimbabwe: insights from decision analysis models. *J Acquir Immune Defic Syndr* 2008;48:72–81. doi:10.1097/ QAI.0b013e31816bcdbb PMID:18317229
- Zaba B, Marston M, Floyd S. *The effect of HIV on child mortality trends* in sub-Saharan Africa. New York: United Nations Population Division, Department of Economic and Social Affairs; 2003. Available from: (http:// www0.un.org/esa/population/publications/adultmort/Zaba.pdf). [accessed 23 April 2009].
- Ng'weshemi J, Urassa M, Isingo R, Mwaluko G, Ngalula J, Boerma T et al. HIV impact on mother and child mortality in rural Tanzania. *J Acquir Immune Defic Syndr* 2003;33:393–404. PMID:12843752
- Daneel ML. Quest for belonging: introduction to a Study of African independent churches. Gweru: Mambo Press; 1987.
- Ross A, Van der Paal L, Lubega R, Mayanja BN, Shafer LA, Whitworth JAG. HIV-1 disease progression and fertility: the incidence of recognized pregnancy and pregnancy outcome in Uganda. *AIDS* 2004;18:799–804. doi:10.1097/00002030-200403260-00012 PMID:15075516
- Marston M, Zaba B, Salomon JA, Brahmbhatt H, Bagenda D. Estimating the net effect of HIV on child mortality in African populations affected by generalized HIV epidemics. *J Acquir Immune Defic Syndr* 2005;38:219–27. doi:10.1097/00126334-200502010-00015 PMID:15671809
- Brown T, Salomon JA, Alkema L, Raftery AE, Gouws E. Progress and challenges in modelling country-level HIV/AIDS epidemics: the UNAIDS Estimation and Projection Package 2007. *Sex Transm Infect* 2008;84(Suppl 1):i5–10. doi:10.1136/sti.2008.030437 PMID:18647867