INTRODUCTION

HIV has caused adult mortality rates to escalate rapidly in many countries of sub-Saharan Africa, and there is some indication that child mortality rates are also rising, possibly because of mother to child transmission. However, evidence for the causal role of HIV is relatively weak, for several reasons. First, background trends in child mortality from other causes may exacerbate or mask the deterioration in mortality due to HIV, making it difficult to detect changes attributable to HIV simply by monitoring time trends in overall child mortality. Secondly, methods of measuring child mortality that rely on retrospective reporting by mothers (either direct methods based on birth histories, or indirect methods using the Brass techniques) yield biased results in the presence of a strong correlation between the mortality of mothers and children. Finally, there are few community-based studies that measure the HIV status of infants and track their survival, because the persistence of maternal anti-bodies in the blood of infants makes the standard ELISA tests which are used for adults inappropriate for testing children. The alternative PCR tests that can detect the presence of the virus (as opposed to HIV antibodies) are very expensive and difficult to administer outside of a hospital setting.

This paper builds upon a series of investigations undertaken with funding from UNICEF to address these problems98 b6rtTj10.98 0 0 10.98 115.254froe8 b98 bqdt Tm(eld bine0 102yem)Tj10.98 0 0 10.4pret TE5pnu9 115.254froe

mortality, although they will be unrepresentative for the population as a whole. If available, these should be used to estimate the mortality of uninfected children in preference to projected rates from before the start of the epidemic.

Mortality of HIV negative children – projection method

Published time series of national mortality estimates usually include the probabilities of dying by age 1 (infant mortality) and age 5 (child mortality). In order to make sure that these values are applicable for uninfected children, estimates from before or very early on in the epidemic must be used and projected to the year required. Changes in the burden of disease over time can change not only the overall level of mortality in childhood, but also the relationship betw

mortality levels and trends are shown in table 2, together with infant and child mortality rates observed in these years. The points were chosen 10 years apart to obtain a reasonable estimate of the long term trend, with the later point corresponding to the latest year in which UNAIDS estimates suggest that prevalence in the general adult population was still below 1 per cent.

TABLE 2: PRE-EPIDEMIC INFANT AND CHILD MORTALITY RATES (PER THOUSAND LIVE BIRTHS)

Country	*year 1*	*IMR*	*CMR*	*year 2*	*IMR*	*CMR*
Botswana	1981	56	83	1991	38	53
Kenya	1977	64	105	1987	61	90
Uganda	1976	133	222	1986	98	177
Senegal	1978	113	279	1988	88	195
Zimbabwe	1976	55	92	1986	49	71
Malawi	1980	138	259	1990	135	234

Source: UN Population Division, 2002

Net and gross mortality of infected children – the Weibull model

Fewer HIV infected children will survive in a high mortality setting than in low mortality populations. A model pattern of "net" AIDS mortality has been constructed [Marston et al 2003], to represent the theoretical survival pattern observed if HIV related causes were the only ones operating for infected children. Age specific "net" mortality risks can be combined with mortality risks experienced by uninfected children to yield the "gross" overall mortality experienced by infected children.

It has been suggested [Spira et al, 1999; Peckham & Gibb, 1995; Kuhn et al, 1999] that HIV infected infants who acquired the infection in utero experience a more rapid progression through the disease stages leading to AIDS and death, than those acquiring the infection at parturition or during breastfeeding. The theoretical form of the survival curve for HIV mortality in paediatric infections embodying this frailty assump

Figure II. Trends in HIV prevalence

This can be expressed in terms of net mortality from HIV among infected children and mortality of uninfected children, by substituting the expression for $q_A(x)$ from equation 8 into equation 9 and simplifying, then substituting for h from equation (6):

$$\textit{Population Attributable Mortality} \quad \frac{h\ q_N(x)\quad h\ q_U(x)\ q_N(x)}{q_U(x)\quad h\ q_N(x)\quad h\ q_U(x)\ q_N(x)}$$

$$1\quad\frac{q_U(x)}{p\ \ v\ \ q_N(x)\ \ 1\quad q_U(x)}^{\ 1} \qquad \text{---(10)}$$

Results

The results below are presented graphically with reference to child mortality, cumulated to age 5, which captures more of the impact of HIV than infant mortality. Tables showing annual estimates of both infant and child mortality are provided in the appendix. Where an analysis of trends in infant mortality indicates substantial differences from the child mortality patterns this is noted in the explanatory text.

According to UN population division estimates, mortality in uninfected children was set to decline in all six countries, with the possible exception of Kenya, where it had been stagnating since the mid 1980s. Although the figure suggests that the steepest absolute decline was expected in Malawi, this is primarily a consequence of the historically very high child mortality rates in that country – the proportionate declines between 1990 and 2000 were in fact highest in Senegal and Zimbabwe. Infant mortality estimates showed a broadly similar pattern, except that Senegal was projected to have 20 per cent lower infant mortality among children born to uninfected mothers over the whole time period compared to Uganda – it is very high mortality among 1-4 year olds in Senegal that brings the estimates of child mortality for uninfected children in these two countries so close in figure III.

Figure III. Projected child mortality for uninfected children, 1990-2001

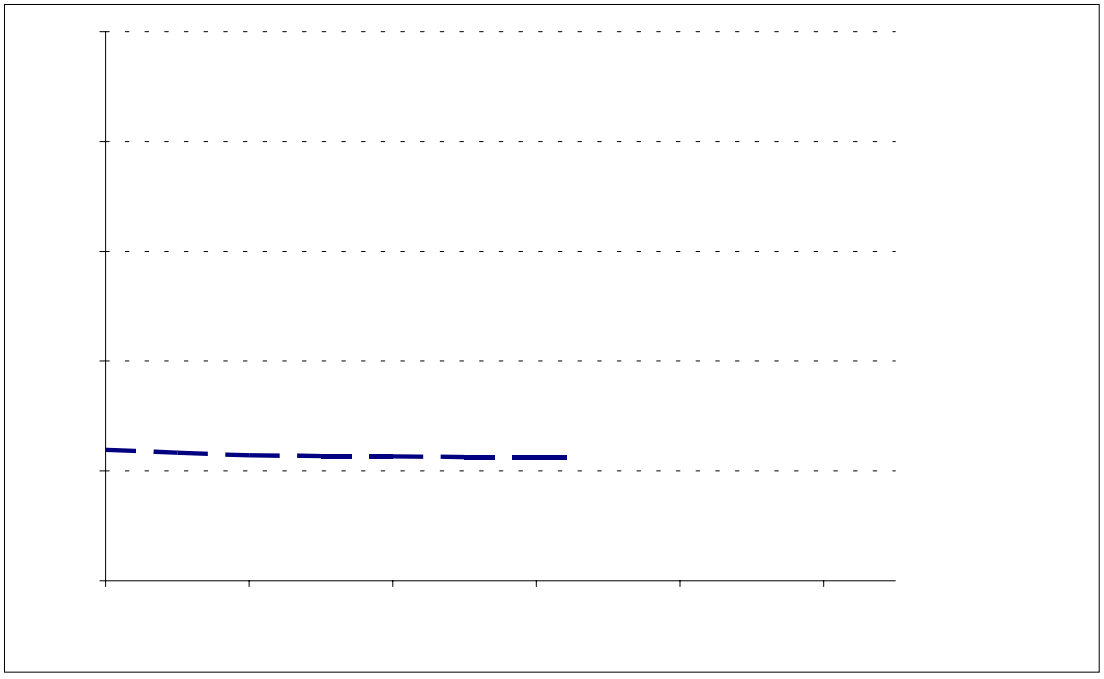


Figure IV. Estimated child mortality for infected children, 1990-2001

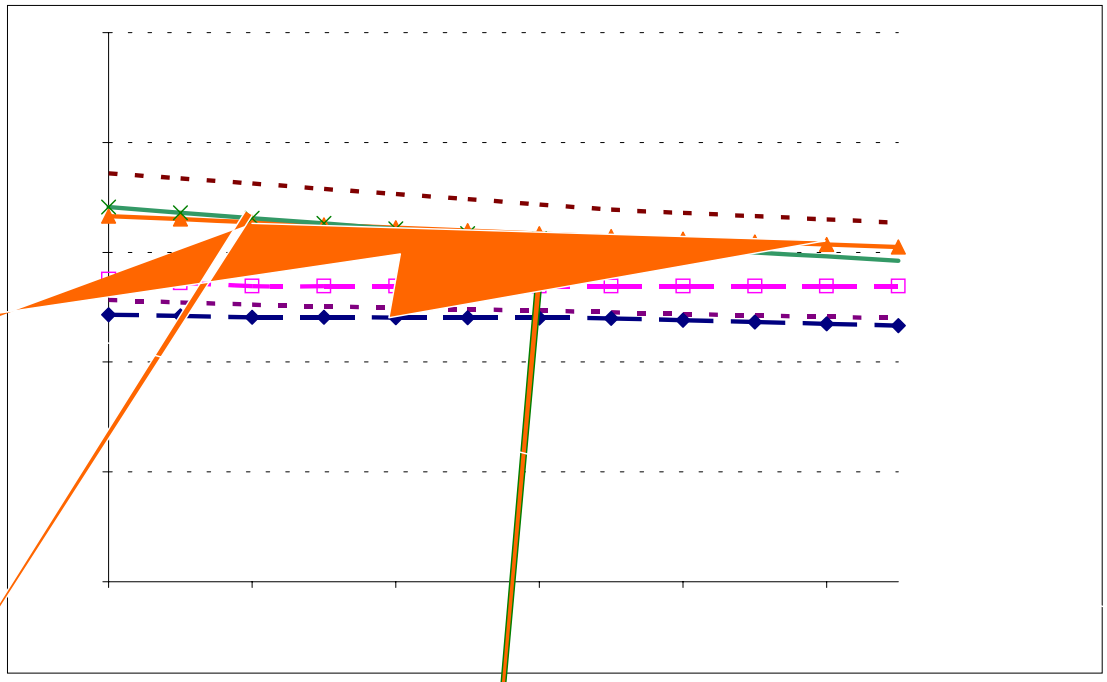
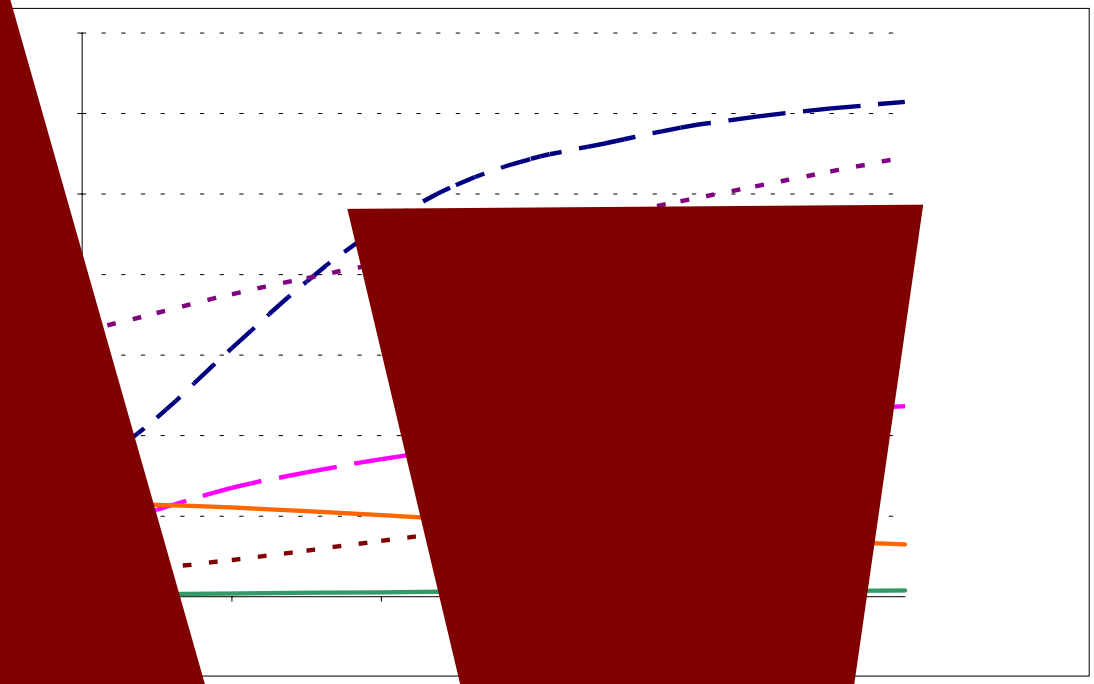


Figure V. Estimated child mortality for population as a whole, 1990-2001

Figure VI. HIV population attributable fraction of child mortality, 1990-2001



retain overall child mortality at a pre-HIV level of 150 per thousand would require background mortality to decline steadily: a fall of 2 per thousand in mortality of HIV negative children would offset the effect of an increase of 1 per cent in HIV prevalence, leaving overall mortality unchanged.

Net and Gross mortality of HIV infected children

Underlying the "cause deleted" formulation of equation (6) is the implicit assumption that for an infected child the risk of dying from HIV associated causes is independent of the risk of death from other causes, which may not be strictly true. When it comes to deriving the "gross" mortality of infected children from a knowledge of the "net" mortality curve and mortality of their uninfected peers this is a conservative assumption, since repeated challenges to the immune system are believed to hasten the progression of HIV-related illnesses, and these would be more frequent in an environment in which infectious diseases of childhood are common. Since the Weibull model net survival curve was derived using the same "independence" assumptions with a large collection of clinical and community sources this assumption is unlikely to bias the "gross" mortality estimate in one or other direction.

Vertical transmission of HIV and the proportion of children affected

We used an "average" value of 35 per cent for the proportion of children of HIV positive mothers who become infected. In fact this proportion varies between 25 per cent and 45 per cent in breastfeeding populations, and may fall as a result of PMTCT interventions. By exploring the effects of higher or lower levels

in the ANC. Since foetal losses associated with HIV generally occur early in the first trimester [Gray, 1997], whereas in Africa women tend to come for ANC in the second or even third trimester [Slaymaker, 2003], this should not affect the validity of our estimate.

Direct estimates of the mortality of HIV negative children based on the birth history reports of uninfected mothers identified in DHS+ surveys which measure adult HIV status could provide powerful evidence of background child mortality levels. Infected mother's birth histories collected in the same kind of survey might appear to provide a data source for estimating the mortality of infected children. However, deriving estimates of mortality of infected children from retrospective reports of infected mothers is not a straightforward procedure, since the proportion of infected children borne by these women is determined not just by the vertical transmission ratio, but also by the duration of time since the woman became infected: recently infected women will have borne most of their children prior to infection; women infected further back in the past (who will be relatively under-represented in the survey because of HIV related mortality) will have borne a higher proportion of their children after becoming infected. Recent modelling work by Artzrouni and Zaba [2002] suggests that the bias caused by the high correlation of mother and child mortality would lead to retrospective reports underestimating the true child mortality among infected mothers by around 8 per cent in mature epidemics, this is confirmed by observation in the Kisesa cohort study [Ng'Weshemi et al, 2003]. Estimates of the mortality of infected children that ignored this selection effect would be even more biased.

However even at quite high prevalence levels, Artzrouni and Zaba show that the bias in retrospectively reported overall child mortality rarely exceeds 5 per cent, provided that the estimates are based on births occurring in the five years immediat

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Brass, W. (1971). On the scale of Mortality in Brass, W. (ed)

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Under five mortality HIV positive children

Country	*1990*	*1991*	*1992*	*1993*	*1994*	*1995*	*1996*	*1997*	*1998*	*1999*	*2000*	*2001*
Botswana												