



HIV impact on mother and child mortality in rural Tanzania

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HIV impact on mother and child mortality in rural Tanzania

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Abstract

Child mortality in Tanzania rose from 137 per 1,000 in 1992-96 to 147 in 1995-99. HIV affects child mortality directly, due to mother to child transmission, and indirectly, because maternal illness and death has negative consequences for child health. A longitudinal community-based study in Kisesa ward, Mwanza region is used to show the contribution of HIV infection to child mortality. HIV status data of 4,273 mothers, from three rounds of serological testing (1994, 96 and 99) are linked to survival information for 6,049 children born between 1994 and 2001. Impacts of maternal survival and HIV status on child mortality are assessed using hazard analysis with time varying co-variates. 584 child deaths were recorded during 10,002 person-years of observation. Infant mortality among children of HIV positive mothers was 158 per 1,000 compared to 74 for children of HIV negative mothers. By age 5 child mortality risks were 265 and 135 respectively. 51 deaths were observed among women who gave birth, 14 of these were among the 149 mothers known to be HIV positive at parturition. Infant mortality among children whose mothers died was 257 compared to 87 amongst children of surviving mothers. Mortality risks for children whose mother died were as high in the year preceding the mother's death as in the first year of orphanhood. Statistical analysis showed that the effect of maternal death was independent of maternal HIV status, though numbers were too small to study interactions in children over age 3. After allowing for the effects of age, sex, twinning, birth interval, maternal education and residence, the child death hazard ratio for maternal HIV infection was 2.2 (1.6 – 3.1), the hazard ratio associated with maternal death was 4.6 (2.6 – 8.1). In a population in which HIV prevalence among pregnant women is 4.3%, the fraction of infant mortality attributable to maternal HIV infection is 8.1%.

Background

Past improvements in child mortality in sub-Saharan Africa have slowed dramatically in the 1990s, and in some cases have been reversed by the HIV epidemic. As the epidemic continues to spread the impact on child mortality is expected to be severe (Carael, Schwartlander and Zewdie, 1998; UNICEF, 2000). However, relatively few studies have examined child mortality classified by mother's HIV status – published studies using community-based data include two from Uganda: Nakiyingi et al., 2002; Sewankambo et al., 1994, and one from Malawi (Crampin et al. 2002). Studies based on cohorts selected from health facilities tend to lack a comparison group of children born to uninfected mothers (Lallemant et al., 1994; Marum; Tindyebwa and Gibb, 1997; Ryder et al., 1994; Taha et al., 1995). This is in contrast to the wealth of information on the effect of HIV on adult mortality, in which standard comparisons with the mortality of uninfected persons are presented (Leroy et al., 1995; Nunn et al., 1997; Sewankambo et al., 1994; Todd et al., 1997; Boerma et al., 2001).

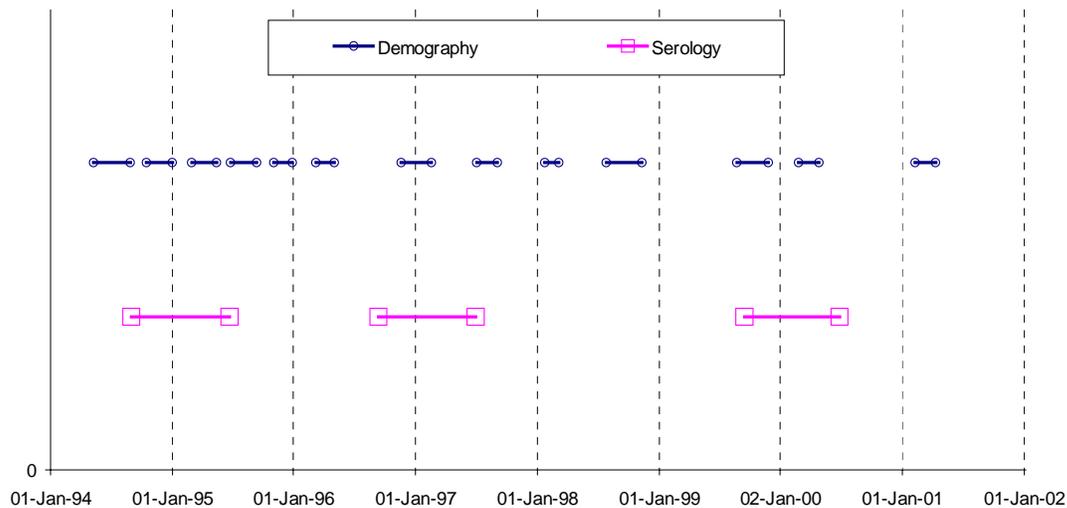
Although HIV affects child mortality directly through mother to child transmission, assessing the effect of HIV on child mortality runs into difficulties for a number of reasons. When measuring the HIV status of infants, results often show the existence of maternal antibodies which may be present in a child for up to 18 months even if the child has not become infected (European Collaborative Study, 1988). Information on cause of death for infants and children in relation to HIV is difficult to find. Establishing HIV as the cause of death is problematic, because it is difficult to distinguish from other causes of childhood death using the verbal autopsy methods, which have been used successfully in determining causes of death for adults (Dowell et al., 1993; Kamali et al., 1996; Urasa et al., 2001). This means that although longitudinal and clinic based studies collect evidence on child survival classified by maternal HIV status they are rarely able to express the results in terms of comparative mortality rates for infected and uninfected children.

Child mortality is also affected indirectly by maternal HIV infection as a mother's death has a negative impact on child health. Even if there has been no vertical transmission in-utero, or after birth during breastfeeding, the HIV status of the mother can still have an affect on the child's mortality. The risk of an HIV positive mother dying is higher than that for an HIV negative mother, therefore an uninfected child with an infected mother is more likely to be orphaned. In general, studies find that orphans experience higher mortality rates than children brought up by their own mothers (Bledsoe, Ewbank and Isiugo Abanihe 1988; Taha et al. 1996). Maternal mortality, here defined as mortality of mothers of young children, introduces reporting bias into estimates of child mortality based on retrospective reports by mothers. Most estimates of child mortality in sub-Saharan Africa are based on analysis of birth history data collected in household sample surveys, such as the DHS. Only surviving mothers are questioned in these surveys, and if the children of dead mothers experience higher mortality than children of living mothers, this will cause an overall underestimate of child mortality in the population (Ward and Zaba, 1999).

The UNICEF study of child mortality in HIV affected populations aims to provide accurate estimates of the mortality differentials between the children of HIV infected mothers and the children of healthy mothers, allowing for the effects of varying levels of maternal mortality. The TANESA project in the Mwanza region of Northern Tanzania, which established an observational cohort study in Kisesa ward in 1994, has been an integral part of this study. With accurate linkage of mother and child records, based on seven years of demographic monitoring and three serological surveys, the relationships between the HIV status of mothers, their mortality and the mortality of their children can be studied in detail. This paper describes the results of analysing these relationships and estimates the proportion of infant and child mortality attributable to HIV.

Methods

Figure 1 Fieldwork rounds, Kisesa, 1994-2001



Fieldwork

The study covers one ward in the Magu district, containing six villages and a semi-urban roadside settlement. The ward has a population of about 26,000 inhabitants of which around 95% are Sukuma, the largest ethnic group in Tanzania. The majority of the residents are involved in farming with some small scale trade of agricultural produce. The cohort study involves three major research activities: demographic surveillance, epidemiological sero-surveys and antenatal clinic surveillance. A more detailed description of this study is given elsewhere (Boerma et al., 1999).

A demographic surveillance system has been in place since 1994 and by the end of 2001, thirteen demographic rounds (including the baseline) had been completed. All households are visited each round and information is collected on residence and survival status of all household members, on pregnancy of women of reproductive ages and on new arrivals (migrants and new-borns).

The epidemiological sero-surveys form the second major research activity in the cohort. Between 1994 and 2000, three rounds of epidemiological sero-surveys were conducted in 1994/95, 1996/97 and 1999/2000. All individuals aged 15-44, 15-46 and 15+ were eligible to participate in the first, second and third rounds respectively. Participation in the surveys was 5,783 individuals (first survey), 6,392 (second survey) and 7,438 for the third round. In all three rounds, participants were interviewed using standardised questionnaires (in the Swahili language). The questionnaire measured variables such as socio-demographic characteristics, births history, marital history, family planning, sexual behaviour, STDs, HIV/AIDS awareness and risk perception.

Participants provided blood samples for HIV screening in all the three surveys. In the first survey, venous blood was used, but in the second and third surveys a filter paper (dry blood spot) method was used to improve participation. For a description of sample collection and testing strategies see Mwaluko et al. 2002. All participants were given study numbers and no names were used at

any stage of the serological surveys. Briefly, the testing algorithm was based on two independent ELISA assays; Vironostika HIV-MIXT (Organon, Boxtel, the Netherlands) and Enzygnost HIV1/HIV2 (Behring, Marburg, Germany). Only samples with two positive ELISA tests were considered HIV positive.

Data entry was done using Dbase IV (Borland International., Scotts Valley, California) and a double entry system was used for quality control. The clean data files were merged and analysed using Stata version VII (Stata Corporation, College Station, Texas, USA).

Statistical procedures

Life table survivorship probabilities and cumulated risk of dying were summarised at single years of age based on the exact values of the Kaplan-Meier survival function. Separate life tables were also constructed for sub-populations of children, classified by key attributes, such as mother's HIV status at the birth of the child, and her current survival status. By cumulating child-years of exposure in each category it was possible to calculate mortality rates (and hence derive mortality risks) for both fixed characteristics (such as sex of the child) and time variant characteristics (such as current calendar year). For fixed characteristics, exposure time starts from birth for all children, and finishes at exit from the study (i.e. at death, or at time of leaving the study area, or when censored at the last observational round). For time variant characteristics, exposure time may start at different ages, and may finish when the child ceases to be classified in a particular category, rather than at exit from observation.

Piecewise exponential hazards models are used as the basis of the statistical analyses. This means that the forces of mortality are assumed constant and independent for any segment of time in which the independent (risk factor) variables do not change. Life table functions are expressed as risks or probabilities, but the hazard ratios are based on central mortality rates calculated for the segments of time when the risk variables assume their specified values. Although both uni-variate and multi-variate results are presented, the effects of some of the risk variables can only be fully understood when the confounding effects of others have been allowed for, the most important confounder being the age of the child.

Initially, mother's HIV status at birth of the child was classified in six categories:

- pre-negative – children born to mothers who subsequently had a negative HIV test
- post-negative – births to mothers who were not subsequently tested, but whose last test before the birth was negative
- sero-converters – children born in the time interval between a mother having a negative HIV test and a subsequent positive test
- pre-positive – children born to mothers who had not had a HIV test previously, but who subsequently tested positive
- post-positive – children born to a mother who had previously had a positive HIV test
- never tested – children whose births were recorded in the demographic surveillance system, but whose mothers never attended the sero-survey clinics.

For analytical purposes these were re-grouped into just three categories:

- negative – pre-negative, post-negative and sero-converters born in the first half of the inter-test interval
- positive – pre-positive, post-positive and sero-converters born in the second half of the inter-test interval
- never tested

Clearly, it is only the pre-negative and post-positive mothers about whose HIV status we can be certain, there is some ambiguity in the other categories. However, HIV sero-conversion is a sufficiently rare event (estimated at an average of 1.2% per year over the duration of the study (Isingo et al., 2002) to justify allocating births to post-negative and pre-positive mothers to the negative and positive categories respectively. Allocating the sero-converters according to the

timing of the birth relative to the test dates was judged to be better than omitting them from the analysis, since this would have weakened the power of the analysis with respect to other variables.

Maternal survival is a time varying risk factor with respect to child survival, and each period of a child's life was initially classified in four categories:

- mother alive – the whole of the period of observation of the child of a mother who survived to the end of the study, the time between the child's birth and a year before the mother's death for children of mothers who died
- mother terminally ill – the year before a mother's death
- mother recently died – the year after a mother's death
- mother died long ago – from one year after a mother's death to the end of the period of observation of the child

This classification was used because experience in other studies (Zaba, 2002) has shown that the year preceding the death of a mother is a critical period for children. Mothers who are terminally ill may be unable to care adequately for their children, breastfeeding may be discontinued and family life may be severely disrupted if the mother is taken away for treatment. Negative impacts such as these may also occur soon after the mother's death, but if the child survives the mother by a year the risks associated with the family crisis are generally reduced, as long-term coping measures are implemented. For analytical purposes, mothers' survival was re-grouped into just two categories:

- alive / died long ago
- terminally ill / recently dead

The grouping together of the two critical periods is justified by uncertainty over dating of events (in many cases just the month of death is reported), and by the relatively small numbers involved which would make for wide confidence intervals in ungrouped estimates.

As well as furnishing information on mother's survival and HIV status, the study was able to supply data on other factors previously identified in the literature as potential risk factors for child mortality: whether the mother was co-resident with the child, whether the mother was a teenager, whether the child was a singleton or one of twins, the sex of the child, the length of the preceding birth interval and the mother's education (Mosley and Chen, 1984). Calendar years for exposure and death are grouped into two segments – from 1994 to 97, and from 1998 to 2001, roughly corresponding to the period before the second serological survey and the period after that – to allow for secular mortality trends.

Calendar year, mother's age and co-residence are time variant characteristics, the others are fixed at birth. Maternal education is classified according to whether she reported five years or less completed schooling (including those with no schooling) or more than five years, which would include those who had completed primary school, and all those with some secondary education. Preceding birth interval is only defined for second and higher order births, and for these births an interval is classified as short if it is less than 18 months long.

Results

Survival data were obtained for 6,049 births to 4,273 mothers between 1994 and 2001, furnishing a total of 10,002 child-years of observation. At the end of the study period 584 (10%) children had died, 1,787 (30%) had left the study area and 3,679 (60%) were alive and living in Kisesa at the 13th round of the demographic survey. A total of 51 mothers died, between them, these mothers had given birth to 72 children in the study period.

A total of 2,284 mothers (67%) had had at least one HIV test, as a result 4,487 births (75%) could be classified by maternal HIV status at birth. Of the 4,264 births classified as occurring to HIV negative mothers, 3,185 were born prior to the mother's HIV test; 1,052 were born after the last negative test; and 27 were births occurring early in a sero-conversion interval. The 223 births classified as occurring to HIV positive mothers consisted of 123 births to mothers who had already tested positive; 84 to women who had not yet been tested but subsequently tested positive; and 16 born late in a sero-conversion interval. The average length of the 43 sero-conversion intervals in which births occurred was 3.3 years. Children born in a sero-conversion interval who were classified as born to a HIV negative mother were born on average 0.8 years after the last negative test, those classified as born to HIV positive mothers were born, on average, 2.5 years after the negative test.

Patterns of maternal and child mortality

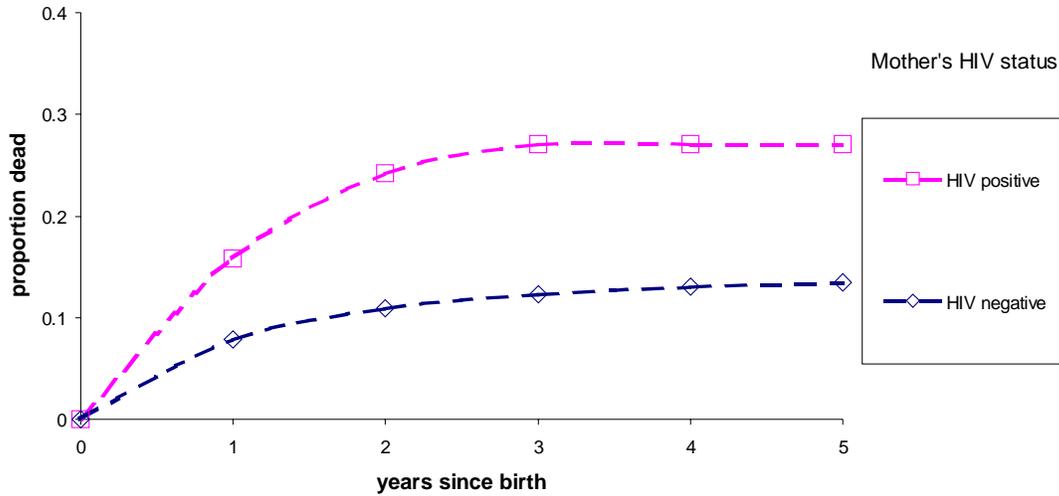
Overall infant mortality for children of HIV positive mothers is 158 per 1,000 (95% confidence limits 112 – 221) compared to 79 per 1,000 (70 – 88) for those of HIV negative mothers, child mortality risk (by age 5) is 270 (201 – 358) and 138 (121 – 150) per 1,000 respectively for children of HIV positive and negative mothers.

A total of 51 deaths occurred among women who gave birth in the study period, these women had borne a total of 72 children during the study. Children who experience the death or terminal illness of their mother whilst they themselves are infants have extremely high mortality. Infant mortality for these children is 386 (232 – 595) per 1,000, compared to an infant mortality of 257 (170 – 378) among all children whose mother died at any other time during the study period, and 83 (76 – 91) for children whose mothers survived to the end of the study. Child mortality risk for children whose mothers died at any time was 350 (246 – 482) compared to 141 (128 – 155) amongst children of surviving mothers.

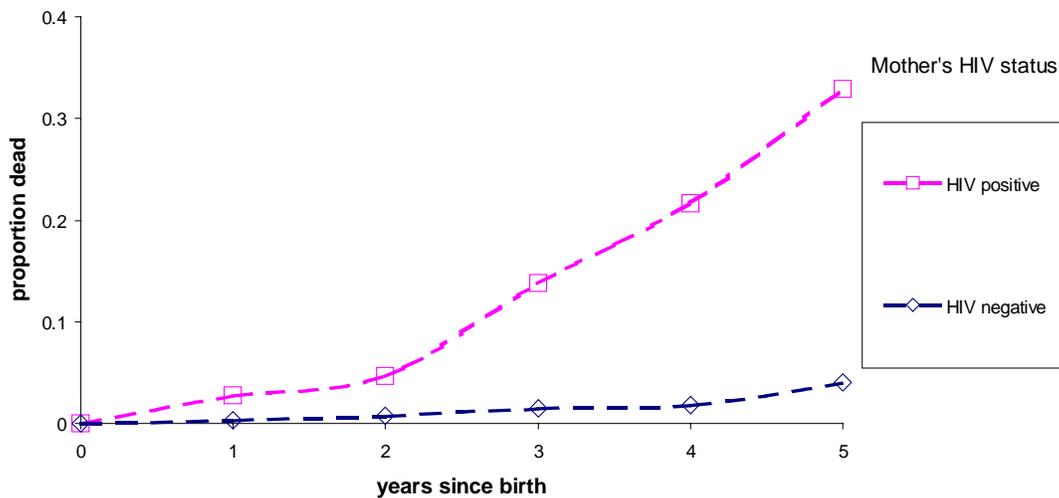
The life table cumulated probabilities of dying for children, classified by mother's HIV status are shown in figure 2(a), for comparison with the cumulated mortality risk for mothers following the birth of a child in figure 2(b). It is clear from these diagrams, that the mortality risks for mothers follow a very different pattern to that of the children. Child mortality risks decline rapidly after the first two years, so that cumulated mortality levels off. For mothers, mortality increases with age, causing the cumulated mortality curve to curve upwards. For HIV positive mothers mortality risks begin to accelerate rapidly about two years after they give birth. Before this time they are already significantly higher than the risks for HIV negative mothers (cumulated risk ratio in the first two years is 6.2), but after this time the disparity grows much wider (cumulated risk ratio for years 2 to 5 is 12.9). The shape and scale of these curves explains why mothers – even those who are HIV positive – are much more likely to outlive their children in the first few years after birth. It is only after 5 years that the cumulated mortality of HIV positive mothers, 329 per 1,000 (157 – 604) begins to approach that of their children.

Figure 2 Cumulated proportions of mothers and children dead by time since birth

(a) Children classified by mother's HIV status at birth



(b) Mothers, classified by HIV status



The joint survival of mother-child pairs is illustrated in Figure 3, which also shows how this is influenced by maternal HIV status. The unit of observation in this figure is the child: each child features once, mothers may be represented more than once if they had multiple births in the study period. Child death is much more common than maternal death, so we see much higher proportions of mother child pairs where the child is dead and the mother alive for both HIV negative (9.2%) and HIV positive (15.7%) mother-child pairs, than instances where the mother has died, leaving behind an orphan child who has survived to the end of the study (0.8% and 4.0% for HIV negative and HIV positive mothers respectively).

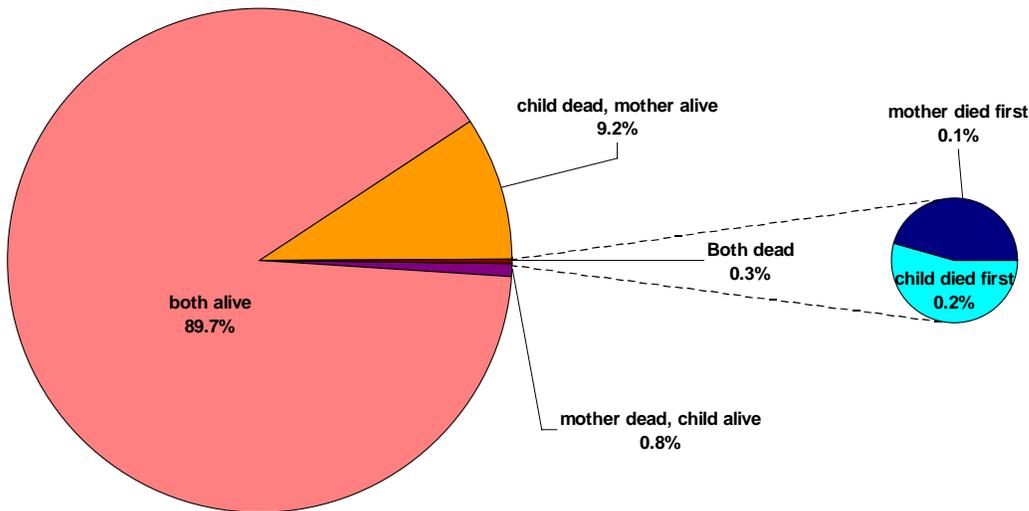
By the end of the study, 49 of the 3,679 surviving children were orphans. Of these, 34 had been born to mothers who were HIV negative at birth, 9 to HIV positive mothers, and 6 were born to

mothers who were never tested. The proportion of mother child pairs in which both had died was almost 10 times as high for the HIV positive (2.7%) as for the HIV negative (0.3%). In both cases this was much higher than would have been expected if maternal and child death had been independent events – expected proportions would be approximately 0.6% for HIV positive mother child pairs, 0.07% for HIV negative. Where both mother and child died, it was more common for the child to die first: 6 of 13 dead children of HIV negative mothers who died experienced a brief period of orphanhood before death, only 1 of the 6 dead children of dead HIV positive mothers was already an orphan at the time of death.

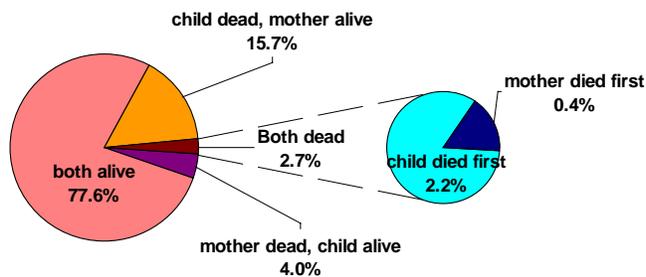
Maternal death and HIV infection have a cumulative, re-enforcing effect on child mortality. The risk of dying by age 5 for the child of an uninfected mother who survives to the end of the study is 133 per 1,000 (119 – 148), for an uninfected mother who dies child mortality is 300 per 1,000 (185 – 464). This is slightly higher than that for the child of a surviving infected mother: 248 (178 – 339), whereas children of HIV positive mothers who died before the end of the study have a child mortality risk of 460 per 1,000 (234 – 759).

Figure 3 Joint survival of mother-child pairs by HIV status of mother at birth

HIV negative mothers: 4130 children



HIV positive mothers: 214 children



Maternal mortality and reporting bias in retrospective surveys

A demographic surveillance system captures full information about child mortality, unlike cross-sectional surveys that interview surviving mothers and use their retrospective birth history reports for estimating child mortality. Such retrospective estimates of child mortality will be biased by the omission of reports about children of dead mothers. Table 1 shows the extent of such biases, for HIV positive and negative mothers respectively. For infant mortality the biases are negligible, under 2% for both HIV positive and HIV negative mothers, since relatively few mothers die within a year of giving birth. However, with respect to child mortality there is a larger bias for HIV positive women – an 8.3% undercount, since 5 years after the birth of a child nearly one-third of HIV positive women will have died. Even so, this may not have a large impact on the overall estimate of child mortality, if HIV positive mothers form a minority of the population. In Kisesa, the average prevalence amongst women who gave birth between 1994 and 2001 and for whom HIV status could be ascertained, was 4.3%, so that the overall underestimate of child mortality based on retrospective birth histories would have amounted to just 2.3%.

Table 1 Biases in mortality estimates based on birth histories from surviving mothers

		Mother's HIV status		All mothers
		HIV positive	HIV negative	
Infant mortality				
	All births	0.158	0.079	0.086
	Births to surviving mothers	0.156	0.077	0.084
	% under-estimate	1.2%	1.8%	1.6%
Child mortality				
	All births	0.270	0.135	0.144
	Births to surviving mothers	0.248	0.133	0.141
	% under-estimate	8.3%	1.7%	2.3%

Risk factor analysis for child mortality

Child mortality risks due to HIV and maternal survival can be put in the context of other important risk factors. Table 2 shows the number of children ever exposed and the person-years exposure for each risk factor. Note that for fixed characteristics, numbers exposed in each category add up to the total number of births, but for time-variant characteristics the number exposed is larger than the total births, since children typically move between categories over the course of their lifetimes. Person-years of exposure always adds to 10,002 subject only to rounding to integer values. This table also shows the number of deaths occurring for each category of risk factor, the resulting crude death rate, and the rate ratio, comparing the crude rate for a particular category to the crude rate observed in the reference category for each classification.

The age pattern of mortality displays the familiar pattern of rapid decline from infancy, when the central death rate is 100 per 1,000, to relatively low values, under 20 per 1,000, after age 2. The usual sex differential is observed, with girls having a statistically significant 20% mortality advantage over boys. Twins are severely disadvantaged, experiencing twice the mortality risks of singleton births.

Table 2 Simple hazard analysis for child survival

	Children ever at risk	Child- years lived	Deaths	Death rate	Rate ratio	RR 95% confidence limits	
Total in survey	6049	10002	584	0.058			
Age of child							
0	6049	4519	449	0.100			
1	3336	2529	90	0.036	0.36	0.29	0.45
2	1937	1565	26	0.017	0.17	0.12	0.26
3	1200	914	8	0.010	0.10	0.05	0.19
4+	647	473	6	0.015	0.15	0.07	0.31
Sex of child							
male	3010	4984	321	0.064			
female	3039	5018	263	0.052	0.81	0.69	0.96
Multiple birth							
singleton	5852	9695	549	0.057			
twin	197	306	35	0.114	2.02	1.43	2.84
Previous birth interval							
18 months or longer	2979	4533	288	0.064			
less than 18 months	398	676	61	0.090	1.42	1.08	1.87
not known	1622	2718	138	0.051	0.80	0.65	0.98
first births	1050	2076	97	0.047	0.74	0.58	0.93
Calendar year							
1994-1997	3013	5226	310	0.060			
1998-2001	5075	4775	273	0.057	0.96	0.82	1.13
Age of mother							
20 and over	5435	8998	509	0.057			
teenager	1048	1004	75	0.075	1.32	1.04	1.68
Mother's education							
less than 5 years	2036	3904	236	0.060			
5 years or more	2700	4870	244	0.050	0.83	0.69	0.99
not reported	1313	1227	103	0.085	1.40	1.11	1.77
Mother's co-residence							
present	5984	9681	577	0.060			
absent	275	321	7	0.022	0.37	0.17	0.77
Mother's survival							
living or died long ago	6033	9948	570	0.057			
terminally ill or recently dead	60	53	13	0.242	4.22	2.44	7.32
Mother's HIV status							
negative	4264	8035	407	0.051			
positive	223	328	41	0.125	2.47	1.79	3.40
never tested	1562	1639	136	0.083	1.64	1.35	1.99

Children born after a short birth interval (less than 18 months) have 40% higher mortality than those born after a longer interval. Information on preceding birth interval information is not available for two categories of children – first births, and higher order births that were the first ones observed for a particular mother in the study period, but from whom information on the date of the preceding birth was not obtained during questions in the interviews accompanying the sero-surveys. The latter category probably consists in the main of children born after long intervals, since retrospective reporting of short open birth intervals is usually more complete than reporting of long intervals. The apparent protective effect of first births (25% lower mortality risk than children born after a long birth interval) is an unusual finding, as first births are concentrated among young mothers, and generally have higher mortality than higher order births. Mother's HIV status could be a confounding factor in this result, since in populations with little contraceptive use, women giving birth for the first time would have been sexually active for a shorter period (and thus run lower risks of HIV) than women who had experienced several pregnancies.

No significant time trends in child mortality are apparent from this crude analysis, but child's age is a likely confounder in this case, since the exposure in the second half of the study period will include a higher proportion of children at older ages. The age of the mother has a strong effect, with a 30% excess mortality associated with having a teenage mother. However, there will be some confounding effects of child's age in this case also, since children of teenage mothers will be younger, on average, than children of older women.

Mother's education is associated with a small mortality differential, with children of more educated mothers having 17% lower mortality than children of mothers with less than 5 years schooling. Children whose mother's education is not stated appear to have significantly higher mortality risks, but there may be some confounding here, since these women are more mobile – they entered the study population after the baseline survey, but did not stay long enough to attend one of the sero-surveys at which educational attainment was measured. Surprisingly, mother's absence appears to confer mortality advantages on the child, but this is almost certainly due to confounding by age, since young children are rarely left behind if their mother goes away.

The survival of the mother has a dramatic impact on child mortality, with children who live through the year before or after the death of their mother experiencing mortality rates that are four times higher than normal. Since a large proportion of mothers who die may be HIV infected, a multiple regression approach is needed to allow for confounding due to vertical transmission of HIV by mothers at an advanced stage of HIV infection.

Children of HIV positive mothers face 2.5 times the risk of dying compared to children of uninfected mothers, with children of mothers who have not been tested facing an intermediate risk level. Not all the excess mortality of these children is due to vertical transmission of HIV, since the uninfected children of HIV positive mothers will also be exposed to increased mortality risks associated with maternal illness and death, and they face a higher risk of experiencing a maternal death than children of uninfected mothers.

A life table analysis allows for the effects of child's age, but to allow for all the other possible confounding effects that the factors listed in Table 2 may have on each other, a competing hazards analysis is needed. This is shown in Table 3. Two multiple regression models are presented: model A includes all the factors and categories used in Table 2, model B is a more efficient representation, presenting significant effects only, and re-grouping the classifications to include those categories with similar relative risks in one group whenever logically possible. Model B aims to maximise the log likelihood function whilst making an allowance for the degrees of freedom used in specifying the hazard factors.

Three risk factors have been omitted from model B that appear in model A. The direction of the effect of calendar year changed when the confounding effect of age of child was allowed for compared to the simple hazard analysis shown in Table 2, possibly suggesting a slight upward

trend in mortality over time, but this did not reach statistical significance. Age of mother lost significance when age of child was allowed for, but the direction of the effect remained the same. Finally co-residence of mother and child loses statistical significance, as expected, when age of child is controlled for, but does not emerge as a detrimental factor.

Age and sex retain the same effects when treated as part of the competing risk models in Table 3, as they had in the simple hazard analysis of Table 2. The differences in age specific mortality hazards after age 2 are not significant, and in model B we partition age into just three groups, 0 (infancy), 1 and 2+. Girls retain a 20% mortality advantage over boys when all other factors are allowed for. The hazard ratio associated with being a twin is reduced when other effects are allowed for, but the excess of 65% remains highly significant. The mortality disadvantage of children of uneducated mothers is more apparent when other risk factors are allowed for, and the unexpected effect of unknown educational status disappears when we control for participation in the sero-surveys. The disadvantage of being born after a short birth interval remains when other risk factors are controlled, but loses statistical significance, unless mothers with unknown birth interval length are grouped with those who have longer birth intervals (model B). The protective effect of being a first birth is no longer apparent when maternal age and HIV status are controlled for.

Finally, when the effects of maternal mortality and HIV status are both assessed in the same model, the effect of HIV status is somewhat attenuated (from a hazard ratio of 2.5 in the simple analysis in Table 2, to a ratio of 2.2 in the multivariate analysis). The maternal mortality effect is strengthened, with the hazard ratio rising from 4.2 in the simple analysis, to 4.7 in the competing risk models in Table 3. However, these small changes lie well within the 95% confidence limits of the rate ratios estimated in the simple analysis.

Tests for inter-action between age of child, maternal HIV infection and maternal survival were carried out, but inter-action terms did not assume statistical significance, jointly or separately. We can therefore conclude that within the constraints imposed by the size of the data set, maternal HIV infection and survival act independently on mortality in early childhood.

Table 3 Competing hazard analysis for child survival

	Model A			Model B				
	Hazard ratio	confidence limits		Hazard ratio	confidence limits			
Age of child								
	0							
	1	0.37	0.29 0.46	} 0.36	0.29	0.46		
	2	0.18	0.12 0.26		} 0.15	0.11	0.20	
	3	0.10	0.05 0.19			} 0.11	0.07	0.20
	4	0.15	0.07 0.33					
Sex of child								
	male							
	female	0.80	0.68 0.94	0.80	0.68	0.95		
Multiple birth								
	singleton							
	twin	1.66	1.13 2.42	1.65	1.13	2.40		
Previous birth interval								
	18 months or longer							
	less than 18 months	1.28	0.94 1.74	} 1.40	1.04	1.88		
	not known	0.72	0.56 0.93		} 1.17			
	first births	0.91	0.70 1.17					
Calendar year								
	1994-1997							
	1998-2001	1.12	0.94 1.33					
Age of mother								
	20 and over							
	teenager	1.03	0.78 1.35					
Mother's education								
	less than 5 years			} 1.30	1.09	1.54		
	5 years or more	0.78	0.50 1.19		} 0.93			
	not reported	0.78	0.65 0.93					
Mother's co-residence								
	present							
	absent	0.89	0.42 1.90					
Mother's survival								
	living or died long ago							
	terminally ill or recently dead	4.65	2.65 8.17	4.67	2.67	8.19		
Mother's HIV status								
	negative							
	positive	2.23	1.60 3.09	2.20	1.59	3.05		
	never tested	1.71	1.18 2.50	1.48	1.20	1.83		

Discussion

The average prevalence of HIV infection among women giving birth in Kisesa ward between 1994 and 2001 was 4.3%. If we assume that in the absence of HIV all children in Kisesa ward would have experienced the same mortality rates that currently pertain amongst the children of HIV negative mothers, then the proportion of current infant mortality attributable to HIV is 8.1%. A slightly smaller fraction of child mortality, 6.3%, is attributable to maternal HIV infection. Both the direct causes (transmission of the virus from mother to child) and indirect causes (the effects of maternal mortality on child survival) play an important role.

The observed effects of HIV are much lower than in the Masaka cohort in southwest Uganda, where the fraction of child mortality attributable to maternal HIV infection was 14% and the prevalence of HIV among women giving birth is 7.3% (Nakiyingi et al., 2002). The Kisesa cohort has a shorter follow-up time than the Masaka study: under age 2 the Kisesa study accumulated 7,050 person years of child observation compared to 5,900 person-years in Masaka. Between the ages 2 and 5 the Kisesa study observed under 3,000 person-years whereas the Masaka study observed a further 5,260 person-years. Infant mortality among children of HIV positive mothers in the Kisesa cohort, at 158 per 1,000 was considerably lower than the 225 per 1,000 observed in Masaka. From age two, mortality risks for children of HIV positive mothers in the two studies were broadly similar: probability of dying by age two in Kisesa is about 250 per 1,000, compared with 277 in Masaka. However, infant and child mortality risks for children of healthy mothers are higher in Kisesa. Infant mortality for children of HIV negative mothers in Kisesa is 74 per 1,000 compared to 58 per 1,000 in Masaka, probabilities of dying by age 5 are 130 and 102 per 1,000 for Kisesa and Masaka respectively. In both studies survival of infected mothers followed similar patterns, with 27% dead within 4 years of giving birth.

Most risk factors for child mortality were similar in the two studies: the pattern of declining mortality risks with age of the child; males experiencing higher risks than females, an increased risk associated with being one of twins and a decreased risk associated with maternal education. However the effects of maternal absence differed – in Masaka this had a significant negative impact on child survival (Nakiyingi et al., 2002).

Some of the results of the competing hazards analysis do not conform to expectations based on previous studies of child mortality in populations not affected by HIV. It is surprising that neither first order births nor births to teenage mothers emerged as having significantly higher mortality, as commonly found elsewhere (Zaba and David, 1996). The proportion never tested among teenage mothers (36%) was considerably higher than the proportion never tested of older mothers (24%). This is probably because many teenage mothers were new arrivals, moving into the study area on marriage. As teenagers, they would have been sexually active for a shorter time than the older mothers, and thus would have had a lower exposure to risk of HIV infection, and this may be a strong enough effect to cancel out some of the excess risks usually associated with teenage motherhood.

Collecting child mortality information from a continuous demographic surveillance system rather than using retrospective birth history reports means that there is no bias due to reliance on reports obtained only from surviving mothers. In this study with an average prevalence of 4.3% amongst women who gave birth between 1994 and 2001, the overall underestimate of child mortality based on retrospective birth histories would have amounted to just 2.3%. We would expect a much larger bias in populations with higher HIV prevalence and lower pre-existing infant and child mortality levels.

Tracing the joint survival of mother child pairs shows that it is more common for the child to die before the mother: by the end of the study 9.2% of HIV negative and 15.7% of HIV positive mother-child pairs were observed with the mother still alive but the child dead; compared to 0.8%

and 4.0% respectively in which a maternal orphan survived to the end of the study. Mortality patterns of mothers and children after birth are very different with high mortality rates for children falling rapidly, and low mortality rates for mothers increasing slowly. This helps explain why mothers are more likely to outlive their children. Only five years after birth do the cumulated mortality rates of HIV positive mothers begin to approach those of their children.

Because of the limited duration of the study (maximum possible years of observation of a child born into the study population is seven), we can only study the youngest age group of orphans, those under five. The total number of orphans under five in Kisesa at the end of the study period is somewhat higher than the 49 orphaned births recorded as surviving to the end of study. The survival analysis includes only those born in the study population, not those who were born elsewhere and came to Kisesa with mothers who subsequently died, nor those who came into the study area as orphans. It is not possible to measure the extent of orphanhood amongst in-migrating children, as information about their mothers is incomplete. It is also likely that some maternal deaths (and thus incidences of orphanhood) may have been missed due to the mother's experience being censored as a result of out-migration. Overall, in this population where 4.3% of mothers were HIV positive at the time of birth, about 21% of the surviving orphans (9 of the 43 whose mothers were tested) were born to HIV positive mothers. Since other analyses suggest that HIV is more common in mobile adults (Isingo et al., 2002), it is likely that the true proportion of orphans under five living in the ward whose mothers were HIV positive is somewhat higher than 21%. HIV positive childbearing women have ten-fold higher annual mortality rates than their HIV negative counterparts (36.3 per 1,000 compared to 3.4), but because of their lower fertility (Hunter et al., 2002), and the very high mortality of their young children, the number of non-AIDS orphans considerably exceeds the number of AIDS orphans at ages under five.

HIV is having a significant impact on child mortality in this rural community, with infant and child mortality nearly 10% higher than would be expected if all children had the mortality of those born to HIV negative mothers. This impact will rise with the increasing HIV prevalence and incidence that have been observed in the study area (Mwaluko et al., 2002). As the epidemic matures, and the proportion of HIV infected women with longer duration since infection rises, we are also likely to see increasing levels of mortality among childbearing women in this community. This will further exacerbate mortality levels amongst their children, and increase the proportion who become orphans. Urassa et al. (1997) showed that in the initial stages of the epidemic, the community was coping reasonably well with the burden of looking after increasing numbers of orphans. For instance, there was no evidence of discrimination against these children in terms of schooling. It is to be hoped that the community can continue to cope with the expected increasing impacts. Further work is needed to assess the community response to the expected increasing impact of AIDS in rural communities such as Kisesa.

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