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Decline in early life mortality in a high HIV prevalence rural area of South Africa: evidence of HIV prevention or treatment impact?

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Abstract

Objective—We present early life mortality rates in a largely rural population with high antenatal HIV prevalence, and investigate temporal and spatial associations with a prevention of mother-to-child transmission (PMTCT) programme, an HIV treatment programme, and maternal HIV.

Design—A retrospective cohort analysis.

Methods—All births from January 2000 to January 2007 to women in the Africa Centre demographic surveillance were included. Under-two child mortality rates (U2MR) computed as deaths per 1000 live-births per year; factors associated with mortality risk assessed with Weibull regression. Availability of PMTCT (single-dose nevirapine; sdNVP) and antiretroviral therapy (ART) in a programme included in multivariable analysis.

Results—Eight hundred and forty-eight (6.2%) of 13 583 children under 2 years died. Deaths in under twos declined by 49% between 2001 and 2006, from 86.3 to 44.1 deaths per thousand live-births. Mortality was independently associated with birth season (adjusted hazard ratio 1.16, 95% confidence interval 1.02–1.33), maternal education (1.21, 1.02–1.43), maternal HIV (4.34, 3.11–6.04) and ART availability (0.46, 0.33–0.65). Children born at home (unlikely to have received sdNVP) had a 35% higher risk of dying than children born in a facility where sdNVP was available (1.35, 1.04–1.74). For 2005 births the availability of PMTCT and ART in public health programmes would have explained 8 and 31% of the decline in U2MR since 2000.

Conclusion—These findings confirm the importance of maternal survival, and highlight the importance of the PMTCT and especially maternal HIV treatment with direct benefits of improved survival of their young children.

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Keywords

Africa; ART; HIV; mortality; PMTCT; rural

Introduction

Vertically acquired HIV infection directly contributes to child mortality in high HIV prevalence areas [1,2], and maternal HIV infection and survival indirectly [3–6]. HIV impact is most pronounced in sub-Saharan Africa, with over 90% of all HIV-infected children, and HIV prevalence among women of childbearing age reaching 35% and above in Southern Africa [7–9]. Recent evidence suggests the achievement of Millenium Development Goal (MDG) 4 regarding reducing under-5 mortality by two-thirds is currently off-track in South Africa with a continued rise in child mortality rates, a trend attributed to the burden of HIV [10].

The effect of paediatric HIV infection on overall child mortality has been poorly quantified here, but without early identification of infection and appropriate treatment, about a third of vertically infected children will die before age 1 year, and half by 2 years [6,11]. Antiretroviral therapy (ART) substantially delays disease progression [12], but the impact of HIV treatment programmes on overall child mortality at population level remains unquantified.

Prevention of mother-to-child transmission (PMTCT), currently mostly through single-dose nevirapine (sdNVP) to HIV-infected mothers and their children, [13] can potentially affect child mortality through reducing numbers of vertically infected children. In South Africa, sdNVP reduced the risk of perinatal HIV transmission from an estimated 19% [14] to about 9% [15].

When HIV-infected women of childbearing age [16] proceed to have children, all their children, irrespective of their own HIV infection status, are at increased risk of dying, particularly in the first 2 years of life, both before and after maternal death [4,6,17]. Whether, on a population basis, deaths in infected mothers are prevented by ART, and whether this affects population child mortality rates remains unclear.

We investigated early life mortality in a largely rural population of KwaZulu-Natal, South Africa, where HIV prevalence in adults reaches 23% overall, and 50% among 25–29-year females [16,18,19]. We analysed temporal and spatial associations with roll-out of a PMTCT and HIV treatment programme, and maternal HIV to estimate the direct effect on mortality of a reduction in the number of vertically infected children, and an indirect treatment effect through the survival of their HIV-infected mothers.

Methods

The Africa Centre Demographic Surveillance Area (DSA), in the Umkhanyakude district of northern KwaZulu-Natal, covers 438km² and approximately 90 000 Zulu-speaking people in

11 000 households. Predominantly rural, with an urban township and informal peri-urban settlements, the principal sources of income are waged employment and state pensions [20].

Data came from the Africa Centre Demographic Information System (ACDIS), with, since 2000, twice yearly household visits. Questionnaires were administered to key household informants recording events including births, deaths, migrations and pregnancies. Fieldworkers have mapped all homesteads and facilities using differential global position systems [21]. Since 2000, overall fertility was steady in ACDIS at about three children per woman [22], with an average of 2200 live-births per year [23]. Further, since 2003, an annual population-based HIV surveillance, nested within ACDIS, documented the HIV status of consenting resident women aged 15–49 years and men aged 15–54 years [18]. The consent rate for mothers included in this surveillance was about 55% [20]. Written informed consent allowing use of data was obtained from all participants, and ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal.

The Hlabisa HIV Treatment and Care Programme, initiated in late 2004, is a partnership between the Department of Health and Africa Centre, providing free services at 17 local government primary healthcare clinics (PHCs) [24]. The number of women on treatment by the end of December 2008 was 4688 (68% of all adults on treatment), of whom 40% live in the DSA [25]. A PMTCT programme was introduced in 2001 and established at all clinics by the end of 2002 [26], sdNVP was provided to all HIV-infected women and their infants [27] with counselling on infant feeding options: HIV-uninfected women were counselled to exclusively breastfeed for the first 6 months of life, with sustained breastfeeding to at least 2 years. HIV-infected women were given the option of either replacement feeding or exclusive breast feeding for the first 6 months of life [28]. The sdNVP uptake among babies born to HIV-positive women in the district was estimated at 45% in 2007 [29]. At about the same time an intervention mother-to-child transmission cohort study, the Vertical Transmission Study (VTS), began enrolment in the five largest clinics in the area [30]. VTS women were supported to optimally feed their infants in line with international policies as described above [14,30].

All 13 583 children in ACDIS born between 1 January 2000 and 31 December 2006 (2 years before end of observation to allow at least 2 years of observation) were included.

Improved water and sanitation includes borehole and pipes for water, and ventilated-improved-pit latrines and flush for sanitation; all else were classified as unimproved. The household assets included items used for production or consumption, beds, bicycles, tables, telephones, television sets, sewing machines, block makers, wheelbarrows, tractors, cattle and other livestock. Birth season was classified as dry winter (April–September) and wet summer (October–March) [31]. History of foetal death was defined as a stillbirth or miscarriage prior to birth of index child, classified as yes or no [26]; previous child death was history of child death (age <5 years) prior to birth of index child, classified as yes or no. Maternal HIV status from surveillance was classified into known negative, known positive, never known, and ambiguous (unknown but HIV-negative before pregnancy, or unknown but positive after delivery) [4]. PMTCT availability, based on infant sdNVP, was classified as none (children born in a health facility pre-PMTCT availability), PMTCT only (children

born in hospital with sdNVP), PMTCT and VTS (children born in clinics with intensive feeding support and sdNVP) and children born at home (unlikely to have received sdNVP). ART availability was classified as: 'No ART' for children born before roll-out of the treatment programme, 'less than 2 years of ART' for those born within 2 years from roll-out of the HIV treatment programme and 'at least 2 years of ART' for those born 2 or more years later. By end 2007 less than 8% of people in the treatment programme were children; few were infants below age 2 years [32].

Geographic analysis

We used a geographical information system (GIS) to allocate each child to one of six PHC catchments within the study area [20]. The clinic catchments were derived using a GIS methodology described in detail elsewhere [33], which showed that 91% of households regularly used the most geographically accessible clinic. We then constructed thematic maps to investigate the spatiotemporal changes in under-two child mortality rates (U2MR; by clinic catchment).

Statistical methods

U2MR were based on deaths per 1000 live-births per year; survival time was estimated by the Kaplan–Meier method; Weibull regression was used to investigate simultaneously the effect of demographic, environmental and maternal factors on childhood survival rates [34,35]. The Cox proportional hazard model was inappropriate because the proportional-hazards assumption, based on Schoenfeld residuals, was violated when including the variables relating to PMTCT and ART [36]. For variables with missing data, we included 'unknown' as a category in the model to retain overall denominators. For each child, the observation time t was taken as the time from birth until death, the date of the second birthday, the end of observation period (31 December 2008) or date last seen, whichever came first. The 2-year age cut-off was chosen because mortality is highest in the first 2 years of life, reaching over 50% among HIV-infected, untreated children [6], and because effect of maternal survival is most acute in the early years [6]. Results for separate models for neonates, postneonates, and children aged 1–2 years are also reported. For neonatal mortality modelling, the observation time t was truncated at the 28th day of observation. For postneonates modelling, all children were included from their 28th day of observation to their first birthday; for the early childhood modelling, children were included from 1 year of age until the time of their second birthday. Multivariate models included all variables with a statistically significant association univariately. The goodness of fit of the final models was assessed using the likelihood-based Akaike information criteria (AIC) [37]. The estimated mortality rates by ART period were obtained from the predicted survivor function of the Weibull regression model. Predictions were calculated stratifying by the levels of the covariate (ART period) with respect to the reference value of the other covariates included in the model.

Further, taking 2005 as example, we modelled the potential contribution of PMTCT and the HIV treatment and care programmes to U2MR (Fig. 1). This model is based on the documented association between maternal survival and child mortality and accounts for the differentials in child survival by maternal HIV status [3–6]. Child mortality rates are then

adjusted based on the potential effects that PMTCT [38] and provision of ART treatment for both mother and child [12] would be expected to have had. Assumptions in this modelling: antenatal HIV prevalence of 40% [16], maternal mortality rates among HIV-infected and uninfected mothers of 45.3 and 5.9 per 1000, respectively [19], three-quarters reduction in early infant mortality due to early ART [12], and a quarter of children infected with HIV in the absence of PMTCT with sdNVP reducing peripartum transmission from about 20 to 14% (an approximately 5% reduction) [38,39].

We used Stata (Version 11.0, Stata Corporation, College Station, Texas, USA), which allows the analysis of continuous and time-dependent covariates.

Results

Eight hundred and forty-eight children died before 2 years of age from 13 583 live-births (Table 1). A substantial number of infants (10.6%) were born at home and therefore unlikely to have had sdNVP. Median age of mothers was 24 years (interquartile range 20–30); most had at least some primary education; the higher proportion of women with some primary education among mothers of children who died is likely to reflect the association between education and HIV infection [40]. HIV status was recorded within the surveillance for 7479 (55%) of mothers, of whom 702 (9.4%) were tested HIV-positive (note this is not an antenatal prevalence) before or during pregnancy and 4381 (58.6%) were tested HIV-negative during or after pregnancy. Of the 2396 (32%) women with ambiguous HIV status a substantial number are likely to have been HIV-positive during the index pregnancy in this high incidence setting.

Numbers of deaths under 2 years of age declined from a peak 152, in children born between 2001 and 2006, to 72 in 2006; the U2MR halved from a peak of 86.3 to 44.1 deaths per thousand live-births (Fig. 2). Crude mortality rates in neonatal and early childhood ages remained relatively stable; most of the decline in U2MR was in the postneonatal period. Between roll-out of the PMTCT programme (2001) and the HIV treatment programme (2004) U2MR declined by 36% from a peak of 86.3 to 55.3 deaths per thousand live-births, followed by a further 20% decline after HIV treatment roll-out (Fig. 2).

An estimated 5.4% of children would have died before age 2 years during the post-ART (2004–2007) compared to 8.6% during the pre-ART period (2000–2003) ($P = 0.001$) (Fig. 3).

Factors associated with under-2 mortality

Total exposure time for the 13 583 children was 22 288 years; mean follow-up was 1.6 years; there were 848 deaths (Table 1). Multiple births infants were more likely to have died, as were infants born in poorer households, those born at home, those with a maternal previous history of child death and those born when PMTCT and ART were not available (Table 1). In Weibull regression analysis the inclusion of PMTCT and ART variables did not affect the hazard for the other variables (data not shown). In multivariable analysis, first born children had a 27% significantly increased risk of dying, children born to mothers with at least primary education had a 21% significantly increased risk of dying, and a history of

previous child death increased more than three-fold the risk of dying for the index child (Table 2). Further, infants born at home had a 49% increased risk of dying before 2 years; those born in nonurban areas had a 67% increased risk of death than those born in urban areas, whereas twins had an 85% increased risk of dying.

Access to water, sanitation and electricity, household assets, and distance to the nearest health facility were not significantly associated with under-2 mortality. Children born in the wet summer months were 16% more likely to die than those born in the dry winter months. Children born to a mother with a positive HIV test result in surveillance were more than four times as likely to have died by age 2 years as children of mothers tested HIV-negative; the risk was also increased three-fold for infants born to mothers with an ambiguous or unknown HIV status.

The maternal death variable was not introduced in the models because its effect was captured by the ART period variable. We fitted models with ART period variable alone, maternal vital status alone and with both variables present. The AIC for the model with ART period alone was 8603.72, with maternal vital status alone 8626.36, and for both ART period and maternal vital status present 8693.18. The first model was marginally better with smaller value of AIC. We fitted interaction terms in the Weibull regression models, none were statistically significant.

Availability of PMTCT and ART in public health programmes and U2MR

In 2004, pre-ART, the effect of PMTCT on U2MR was evident in catchment areas of five clinics providing PMTCT and infant feeding counselling; the decline in mortality averaged 33% (range 19–51%) relative to baseline (2000) (Fig. 4). In 2006, 2 years into the maternal HIV treatment programme, a further decline in U2MR was observed in catchment areas of four clinics providing both ART and PMTCT, the decline rose to an average of 52% (range 26–70%) relative to 2000. The largest decline in absolute mortality was observed in areas with higher HIV prevalence.

In Weibull regression analysis, the effect of the PMTCT and ART programme on under-2 mortality was clear. Allowing all other variables, children born at home and unlikely to have received sdNVP had a 35% increased risk of dying than children born in a health facility where sdNVP was available. Children who accessed clinics where sdNVP with or without VTS operated were at lower mortality risk compared to the reference group, although this did not reach statistical significance. Children born within a 2-year period after implementation of the HIV treatment programme had an independent 34% reduced risk of dying before 2 years of age, whereas those born 2 years or more after the programme had a 54% reduced risk of dying.

Further analyses, with separate models for neonates, postneonates, and children aged 1–2 years, suggested that the PMTCT availability association applied mainly to the neonatal and postneonatal periods, whereas the ART availability refers mainly to the postneonatal period only (data not shown).

Taking the situation in 2005 only, as an example of the impact the PMTCT and ART programme could have had on U2MR, we estimated that the availability of PMTCT and ART in public health programmes would have explained 8 and 31% of the decline in U2MR from 2000, respectively (Fig. 1).

Discussion

We present U2MR among children born in a rural South African surveillance site between 2000 and 2006, and show relatively stable crude neonatal and 1–2 year mortality but significantly decreasing postneonatal mortality. Overall U2MR substantially declined from about 2001 onwards, despite continuing high HIV incidence and prevalence [18–20]. It is known that the contribution of HIV infection to child mortality, estimated from national data, is greater in countries with a lower pre-HIV mortality [8]. Thus, in a country like Botswana, with stable, relatively low, child mortality pre-HIV (60 per thousand in the late 1980s), but with antenatal HIV prevalence reaching over 35%, child mortality doubled in the 1990s. By contrast, in Malawi, where child mortality was nearly 250 per thousand before the epidemic, estimated child mortality levels continued to fall throughout the 1990s, although HIV prevalence reached nearly 15%. In Botswana, HIV-attributable mortality in 2000 was over 60%, in Malawi approximately 10% [8].

We show a 33% decline in U2MR following the introduction of a PMTCT programme, offering sdNVP with infant feeding counselling, and a further 52% decline after implementation of a maternal HIV treatment programme. Modelling the effect of these programmes, with informed, locally appropriate assumptions, we showed the decline in U2MR would partly be attributed to PMTCT (8%) but largely to the HIV treatment and care programme (31%). We previously estimated that the number of infants needing treatment, in 2007, in the Hlabisa sub-district would be 49 [41]. However, only two infants were on ART treatment, suggesting that less than 5% of infants requiring ART had initiated treatment; hence any treatment-associated U2MR decline in this population would largely be attributable to maternal rather than paediatric ART treatment. In Weibull regression analysis, assuming a constant risk which could increase or decrease monotonically over time [36], we find that availability of PMTCT reduced mortality risk by 15% compared to ART: less than 2 years and at least 2 after roll-out by 34 and 55%, respectively.

Vertically acquired HIV infection directly affects the risk of mortality [3,17]. The limited effect of PMTCT here needs to be considered in the light of available prophylaxis (sdNVP only), although with successful interventions in place, including antiretroviral prophylaxis, elective caesarean section and formula feeding, the rate of mother-to-child HIV transmission can be reduced to under 2% [38]; in most developing countries, successful interventions are still not widely accessible nor feasible [13], and the number of vertically infected children is unlikely to decrease substantially [9].

Risk factors for U2MR included those previously associated with mortality: multipregnancy [35], birth order [42], delivery location, area of birth [26,43] history of child death, maternal age [42], education [44] and HIV status [4,6]. A higher incidence of diarrhoea has been

observed in South Africa during the wet summer, which was associated with increased mortality for infants in our study [31].

Maternal survival is critical for the health of young children. Previous studies have shown that allowing for PMTCT and other variables, children born to HIV-infected, compared to HIV-uninfected, mothers were three times more likely to die; the year before and following a mother's death were particularly high risk [6,7,45]. sdNVP is estimated to reduce the transmission rates from about 20 to 14%, thus assuming a 20% HIV prevalence, sdNVP would potentially avoid infection in 1 out of 20 infants born to HIV-infected mothers, and could thus also prevent death associated with vertically acquired infection (however, these uninfected children would still be at risk of dying if their mother died). This would thus be unlikely to result in a dramatic reduction in mortality compared to maternal ART, which, by keeping infected mothers alive, has an effect on both the infected and uninfected children [46]. Therefore our finding of a decline in early child mortality is likely due to the impact of ART on adult health rather than of PMTCT.

We have no data directly linking receipt of PMTCT and ART to women and children; temporal associations were based on known availability of PMTCT and ART at PHC clinics. The lack of direct link to PMTCT [47] may have under-estimated the coverage of sdNVP, but our assumption that infants born at home would have been unlikely to have received sdNVP seems reasonable. We also have no HIV data on children. However, all children born to HIV-infected women, irrespective of their own HIV infections status, are at increased risk of dying particularly in the first 2 years of life [6], and few children under 2 years of age accessed the HIV treatment programme.

Conclusion

Even with a modestly functioning PMTCT and HIV treatment programme, benefits for survival of young children become quickly evident. With more comprehensive treatment coverage, and more effective PMTCT including zidovudine in addition to sdNVP (since March 2008), further significant reductions in early life mortality are expected. These findings are important for policy makers and service delivery and highlight the urgency in scaling-up HIV treatment and PMTCT programmes if MDG4 is to be realised.

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CMR: No PMTCT/ART = 47.3 deaths/1000; No PMTCT/No ART = 74.2 deaths/1000; PMTCT/No ART = 68.4; PMTCT/ART = 47.3; PMTCT in absence of ART = 8%; ART in presence of PMTCT = 31%; both present = 36%

Fig. 1. Modelling the contribution of PMTCT and the HIV treatment and care programmes to U2CMR

ART, antiretroviral treatment; CMR, child mortality rate; PMTCT, prevention of mother-to-child transmission.

Fig. 2.
Under-2 mortality rates per 1000 live-births in rural KwaZulu-Natal ($n = 13\,583$).

Fig. 3.
Estimated unadjusted mortality by antiretroviral therapy implementation.

Fig. 4. Temporal changes in U2MR by clinic catchment

The top row depicts absolute U2MR (per 1000 live-births), whereas the bottom row depicts the relative changes in U2MR per year with respect to the year 2000. Diagonal hatching denotes clinics offering PMTCT only and diamond hatching denotes clinics offering both PMTCT and ART. ART, antiretroviral therapy; PMTCT, prevention of mother-to-child transmission.

Table 1

Distribution of demographic variables and risk factors for mothers and their children, by survival status of child.

Characteristic	Live-birth Number (%) (n = 13583)	Alive Number (%) (n = 11946)	Dead Number (%) (n = 848)	P
Sex				
Male	6890 (50.7)	6045 (50.6)	454 (53.5)	0.099
Female	6693 (49.3)	5901 (49.4)	394 (46.5)	
Multipregnancy				
Singleton	12 961 (95.4)	11 438 (95.8)	791 (93.3)	<0.001
Twin/other	467 (3.4)	371 (3.1)	51 (6.0)	
Unknown	155 (1.2)	137 (1.1)	6 (0.7)	
Birth order				
First born	5629 (41.5)	4449 (37.2)	343 (40.5)	0.161
Second/third	5084 (37.4)	4915 (41.1)	342 (40.3)	
Fourth/later	2715 (20.0)	2445 (20.5)	157 (18.5)	
Unknown	155 (1.1)	137 (1.2)	6 (0.7)	
Delivery location				
Homestead	1439 (10.6)	1222 (10.2)	131 (15.5)	<0.001
Clinic	3461 (25.5)	3025 (25.3)	238 (28.0)	
Hospital	7393 (54.4)	6545 (54.8)	416 (49.1)	
Unknown	1, 290 (9.5)	1154 (9.7)	83 (7.4)	
Area of birth				
Rural	8701 (64.1)	7796 (65.3)	545 (64.2)	0.031
Peri-urban	4186 (29.9)	3581 (29.9)	277 (32.7)	
Urban	696 (5.1)	569 (4.8)	26 (3.1)	
Water and sanitation				
Unimproved	3615 (26.6)	3196 (26.8)	249 (29.4)	0.144
Improved	9728 (71.6)	8623 (72.2)	587 (69.2)	
Unknown	240 (1.8)	127 (1.0)	12 (1.4)	
Electricity				
No	6047 (44.5)	5402 (45.2)	384 (45.3)	0.287
Yes	7239 (53.3)	6371 (53.3)	446 (52.6)	
Unknown	297 (2.2)	173 (1.5)	18 (2.1)	
Household assets				
5	2406 (17.7)	2037 (17.1)	190 (22.4)	0.001
>5	10 840 (79.8)	9691 (81.1)	643 (75.8)	
Unknown	337 (2.5)	218 (1.8)	15 (1.8)	
Distance to health facility				
3km	7531 (55.4)	6546 (54.8)	457 (53.9)	0.609
>3 km	6052 (44.6)	5400 (45.2)	391 (46.1)	
Birth season				
April–September	7158 (52.7)	6305 (52.8)	422 (49.7)	

Characteristic	Live-birth Number (%) (n = 13583)	Alive Number (%) (n = 11946)	Dead Number (%) (n = 848)	P
October–March	6425 (47.3)	5641 (47.2)	426 (50.2)	0.089
Age of mother (years)				
<20	3145 (23.2)	2825 (23.6)	154 (18.2)	<0.001
20–30	6733 (49.5)	5829 (48.8)	471 (55.5)	
>30	3125 (23.0)	2780 (23.3)	193 (22.8)	
Unknown	580 (4.3)	512 (4.3)	30 (3.5)	
Maternal education				
At least primary	9745 (71.7)	2966 (24.8)	243 (28.7)	<0.001
Secondary and beyond	3371 (24.8)	8723 (73.0)	554 (65.3)	
Unknown	467 (3.5)	257 (2.2)	51 (6.0)	
Previous foetal death				
No	13 116 (96.6)	11 539 (96.6)	809 (95.4)	0.067
Yes	467 (3.4)	407 (3.4)	39 (4.6)	
Previous child death				
No	13 198 (97.2)	11 664 (97.6)	772 (91.1)	<0.001
Yes	385 (2.8)	282 (2.4)	6 (8.9)	
Maternal HIV status				
Known negative	4381 (32.3)	4182 (35.0)	117 (13.8)	<0.001
Known positive	702 (5.2)	613 (5.1)	59 (7.0)	
Ambiguous ^a	2396 (17.6)	2110 (17.7)	202 (23.8)	
Never known	6104 (44.9)	5041 (42.2)	470 (55.4)	
PMTCT				
No PMTCT	2441 (18.0)	2073 (17.4)	197 (23.2)	<0.001
Home delivery	1439 (10.6)	1222 (10.2)	131 (15.5)	
PMTCT only	6127 (45.1)	5483 (45.9)	311 (36.7)	
PMTCT and VTS	2286 (16.8)	2014 (16.8)	146 (17.2)	
Unknown	1291 (9.5)	1154 (9.7)	63 (7.4)	
ART period				
No ART	8248 (60.7)	7086 (59.3)	632 (74.5)	<0.001
<2 years of ART	3425 (25.2)	3045 (25.5)	177 (20.9)	
2 years of ART	1911 (14.1)	1815 (15.2)	39 (4.6)	

ART, antiretroviral therapy; PMTCT, prevention of mother-to-child transmission; VTS, Vertical Transmission Study. *P* denotes statistical differences between the children who were alive and those who died.

^a Ambiguous maternal HIV status = unknown but were negative before pregnancy or unknown but were positive beyond delivery.

Table 2

The risk of dying before age 2 years by maternal and infant characteristics and availability of PMTCT and ART programmes.

Characteristic	Infants (<2 years), <i>n</i> = 13583			
	Unadjusted hazard ratio (95% CI)	<i>P</i>	Adjusted hazard ratio (95% CI)	<i>P</i>
Sex				
Female	1.00		-	-
Male	1.13 (0.98–1.29)	0.087	-	-
Multipregnancy				
Singleton	1.00		1.00	
Twin/other	1.86 (1.40–2.47)	<0.001	1.85 (1.38–2.46)	<0.001
Unknown	0.61 (0.27–1.36)	0.229	0.28 (0.11–0.75)	0.011
Birth order				
Second/third	1.00 (0.69–1.00)		1.00	
First born	0.89 (0.77–1.04)	0.136	1.27 (1.07–1.51)	0.008
Fourth/later	0.82 (0.69–1.00)	0.052	0.81 (0.65–1.02)	0.074
Unknown	0.55	0.142	-	-
Delivery location				
Hospital	1.00		1.00	
Homestead	1.60 (1.32–1.95)	<0.001	1.49 (1.21–1.83)	<0.001
Clinic	1.21 (1.03–1.42)	0.018	1.10 (0.85–1.43)	0.506
Unknown	0.89 (0.69–1.17)	0.412	-	-
Area of birth				
Urban	1.00		1.00	
Rural	1.57 (1.06–2.33)	0.025	1.66 (1.10–2.49)	0.015
Peri-urban	1.68 (1.13–2.52)	0.011	1.67 (1.10–2.51)	0.015
Water and sanitation				
Improved	1.00		-	
Unimproved	1.07 (0.93–1.25)	0.339	-	-
Unknown	1.09 (0.61–1.92)	0.777	-	-
Electricity				
Yes	1.00		-	
No	0.99 (0.87–1.13)	0.934	-	-
Unknown	1.22 (0.76–1.96)	0.406	-	-
Household assets				
>5	1.00		1.00	
5	1.29 (1.09–1.52)	0.002	1.08 (0.91–1.28)	0.379
Unknown	0.89 (0.53–1.50)	0.686	0.61 (0.36–1.06)	0.078
Distance to health facility				
3 km	1.00		-	
>3 km	1.05 (0.92–1.19)	0.499	-	-
Birth season				

Characteristic	Infants (<2 years), <i>n</i> = 13583			
	Unadjusted hazard ratio (95% CI)	<i>P</i>	Adjusted hazard ratio (95% CI)	<i>P</i>
April–September	1.00		1.00	
October–March	1.13 (0.98–1.29)	0.084	1.16 (1.02–1.33)	0.028
Age of mother (years)				
<20	1.00		1.00	
20–30	1.46 (1.21–1.75)	<0.001	1.33 (1.09–1.63)	0.005
>30	1.26 (1.02–1.56)	0.032	1.39 (1.06–1.84)	0.017
Unknown	1.03 (0.70–1.54)	0.845	1.14 (0.72–1.79)	0.575
Maternal education				
Post primary	1.00		1.00	
At least primary	1.23 (1.06–1.44)	0.006	1.21 (1.02–1.43)	0.028
Unknown	2.22 (1.66–2.96)	<0.001	2.86 (2.07–3.95)	<0.001
Previous foetal death				
No	1.00		1.00	
Yes	1.40 (1.01–1.93)	0.040	1.39 (1.00–1.92)	0.045
Previous child death				
No	1.00		1.00	
Yes	3.89 (3.07–4.92)	<0.001	3.39 (2.64–4.36)	<0.001
Maternal HIV status				
Known negative	1.00		1.00	
Known positive	3.78 (2.76–5.17)	<0.001	4.34 (3.11–6.04)	<0.001
Ambiguous ^a	3.44 (2.73–4.31)	<0.001	3.26 (2.59–4.11)	<0.001
Never known	3.11 (2.53–3.81)	<0.001	2.95 (2.40–3.64)	<0.001
PMTCT				
No PMTCT	1.00		1.00	
Home delivery	1.19 (0.96–1.49)	0.112	1.35 (1.04–1.74)	0.024
PMTCT only	0.69 (0.57–0.82)	<0.001	0.85 (0.69–1.06)	0.163
PMTCT and VTS	0.86 (0.70–1.07)	0.190	0.94 (0.72–1.23)	0.670
Unknown	0.67 (0.51–0.89)	0.006	0.82 (0.59–1.13)	0.225
ART period				
No ART	1.00		1.00	
<2 years of ART	0.69 (0.58–0.81)	<0.001	0.66 (0.55–0.79)	<0.001
2 years of ART	0.49 (0.36–0.69)	<0.001	0.46 (0.33–0.65)	<0.001

ART, antiretroviral therapy; PMTCT, prevention of mother-to-child transmission; VTS, Vertical Transmission Study.

^a Ambiguous maternal HIV status = unknown but were negative before pregnancy or unknown but were positive beyond delivery.