Increased mortality risk for motherless children aged less than 5 years: a systematic review and meta-analysis

Lana Clara Chikhungu[[1]](#footnote-1)\*, Marie-Louise Newell[[2]](#footnote-2), Nigel Rollins[[3]](#footnote-3)

# Abstract

**Background:** It is unclear whether the association between maternal and infant survival seen in the context of HIV applies to the general population.

**Objective:** To investigate the relationship between maternal survival and mortality of children <5 years outside the HIV context.

**Methods:** A systematic review of literature published between January 1990 and November 2016 (3079 papers identified, 156 abstracts screened, 23 full texts) reporting mother’s vital status and mortality of children less than five years of age. Eight studies were included in a qualitative analysis and four in a meta-analysis using a random effects model. Summary estimates of the odds of dying by maternal survival were obtained and statistical heterogeneity estimated. Quality of included studies was assessed using the ROBINS –I Tool and quality of the body evidence was assessed using GRADE.

**Findings:** Children < 5 years whose mother had died were 4.09 times (95% confidence interval, CI: 2.40, 6.98) more likely to die than those of surviving mothers (I2= 83%). Due to heterogeneity, further pooled estimates were not possible. The odds of dying ranged from 1.40 (95% CI 0.47,4.21) to 2.92 (95% CI 1.21,7.04) in two-four year olds, 6.1 (95% CI 2.27,16.77) to 33.78 (95% CI 24.21,47.14) in infants <one year and 4.39 (95% CI 3.34, 5.78 ) to 52.46 (95% CI 20.48,131.79) in infants <six months.

**Conclusion:** The loss of a mother was associated with increased mortality among children, especially when maternal death occurred in the first year post delivery.

# Introduction

Although the number of child deaths globally has declined substantially since 1990, child mortality remains a global health challenge, especially in resource-limited settings; 17,000 children die every day, the majority in sub-Saharan Africa and Southern Asia [1]. Socio-economic factors are central to a child’s survival as they are associated with maternal and environmental factors, nutritional status and injury [2]. The leading causes of under-five mortality are respiratory infections, diarrhoea, prematurity, low birth weight and neonatal infections [1].

In 2013, globally, 2% of mortality amongst children less than 5 years of age was attributed to HIV infection in the child [3] . However, with the successful roll-out of prevention of mother-to-child transmission (PMTCT) programmes, fewer infants and children are becoming infected with HIV each year [4], and attention is turning to the health and survival of the large numbers of children born to HIV-infected mothers who are themselves not HIV-infected. Increased mortality compared to children not exposed to HIV has been reported in this population [5, 6] which could be associated with sub-optimal infant feeding (possibly to prevent mother-to child transmission) or as a consequence of mothers dying or being unwell [7-10] and maternal HIV status [5, 10-12]. One review examined the effect of parental death on child survival in all settings and found that the death of a mother significantly increased the risk of death of her children especially during the early years [13]. However, the review did not stratify outcomes by the HIV status of parents which may be an important confounder of outcomes among children.

To understand the association between maternal death and the risk of mortality in HIV-exposed uninfected children, we conducted a systematic review to estimate the risk of death among children in the general population according to maternal vital status. No prior systematic reviews limited to this population were identified. The findings of the review will help inform whether the increased mortality risks reported among HIV-exposed children following maternal death is exceptionally due to HIV or might be attributable to loss of maternal care; this would be important in light of the expanding use of ART to delay HIV disease progression and improve survival among mothers living with HIV.

**Methods**

We conducted a systematic review based on the following Population, Intervention, Comparison and Outcome (PICO) framework: In populations not affected by HIV (P), does the loss of a mother (I) compared to the mother surviving (C) increase the risk of death (O) in infants/children aged under the age of five years[14].

The review included both experimental and observational studies i.e. randomised controlled studies, cohorts, cross sectional and longitudinal studies in which the study participants were mothers and children aged less than 5 years from the general population, excluding studies that recruited mothers living with HIV. Death and illness of the mother were considered as separate exposures. The primary outcome was death in children aged less than five years of age. The time interval between maternal and child death was a secondary outcome measure. Studies were excluded if they did not provide estimates of mortality for children under the age of five, if the focus was on death of the mother from pregnancy-related causes, or if the population of interest was HIV-infected children.

English language publications between January 1990 to November 2016 were searched from the following databases: PubMed, Medline, Web of Knowledge, Delphis and CINAHL. We also searched the website of the International Union for the Scientific Study of Population 2013 conference, the main population-based science international conference for relevant articles. An “all text” search was undertaken with search terms as provided in the footnote of Figure 1. Reference lists of identified articles were also searched. Titles and abstracts were carefully examined for relevance to the review by LC and MLN. Through discussion between the two authors, eight articles were included in the qualitative analysis, of which four were also included in the meta-analysis. There were no disagreements between the two reviewers.

We used the ROBINS I tool to assess the quality of the included studies (Supplementary Table 1) [15]. We were guided by the AMSTAR tool in the development of the review and in the preparation of the final manuscript[16].

Statistical analysis

Data on maternal and child deaths in publications were captured and summarised using Review Manager Software version 5.3. Odds ratios and standard errors were extracted from studies, or computed from raw data for each of the studies included in the analysis. Studies with a similar measure of effect, study design and children’s age groups were pooled. Random effects analysis models [17] were used to obtain summary estimates of the odds of dying for children with 95% confidence intervals that are presented as forest plots (Fig 2). Heterogeneity was assessed by the observed value of I2 with a level of between 50% to 90% taken as indicative of considerable heterogeneity [18]. We conducted a sensitivity analysis by assessing each study’s contribution to the heterogeneity score and made a decision to include or exclude studies dependent on a study’s contribution to the heterogeneity score as well as risk of bias. A narrative qualitative analysis was adopted in the analysis of studies that could not be summarised through a meta-analysis. The quality of the body of evidence was assessed using GRADE and summarised in evidence profiles [19]. It was not appropriate to use funnel plots to explore the potential for publication bias due to the small number of studies [20]; however, since the deaths of mothers and children occur naturally the potential for publication bias would have been limited.

Ethics statement

The study was exempted from ethics review as all data had been previously published.

# Results

The search of databases identified 3,060 articles; an additional 19 articles were identified from secondary bibliographical searches giving a total of 3,079 articles. The PRISMA flow chart is shown in Figure 1. In total, 23 abstracts were assessed for eligibility by two authors together (LC and MLN), of which 15 articles were subsequently excluded (Supplementary Table 2, including reasons for exclusion). All eight studies identified were observational, four reported data from demographic surveillance sites, three reported population or civil registration data, and one study that provided data from a randomised control study was considered observational because it was not randomised based on the outcome interest. The four studies included in the meta analysis were all cohorts. Data extracted from the eight studies are presented in Supplementary Table 3, which also includes information on background maternal and child mortality rates obtained from the WHO Global Health Observatory website, where available [21].

The Grade evidence profiles are presented in Supplementary Table 4. All studies started with low quality of evidence due to being observational by design. The studies by Sear et al. 2002 and Reher et al. 2003 were further downgraded to very low quality due to the potential for selection bias since data from birth and death registers may have missed children that were not registered or those that died before they could be registered. The results of assessment of the risk of bias of the studies using the ROBINS I tool is presented in Supplementary Table 5. All studies were given a medium risk of bias because although they provided sound evidence for a non-randomised study, they could not be considered comparable to a well-performed randomised trial. These observational studies could not be assessed on selection of participants, departures from intended interventions and missing data aspects as death of the mother was not an intervention as would be the case in randomised trials.

## Risk of dying for children whose mother died compared to children whose mother survived

Due to differences in ages of children studied, measures of effect and study design, only four studies could be included in the pooled analysis of the odds of dying for children aged less than five years [22-25]. The results of the meta-analysis are presented in Figure 2.

The overall risk of dying before age five years in children whose mothers had died was four times higher than in children whose mothers survived, odds ratio (OR) 4.09 (95% confidence interval, CI: 2.40, 6.98) (Figure 2). However, there was considerable statistical heterogeneity (I2 = 83%) between the four studies. A sensitivity analysis indicated that removing the Ronsmans et al. 2010 study from the meta analysis reduced heterogeneity considerably (I2 = 26%) and in an analysis of the remaining three studies the risk of dying before five years of age in children whose mothers had died was three times that of children whose mothers survived, OR 3.16 (95% CI: 2.27, 4.38). However, since there was no difference in the risk of bias across the four studies we decided not to exclude the Ronsmans et al. 2010 study from the meta analysis.

It was not possible to undertake a meta-analysis by age sub-groups (two to four years, one to two years, less than one year and less than six months) due to differences in study design. Individual study estimates are presented in Table 1. In Becher et al. (2004), among children aged two to four years, the estimated odds of dying of those whose mothers had died was three times higher than for children whose mothers survived, OR 2.92 (95% CI: 1.21, 7.04); however, in the study by Sear et al. (2002), there was no statistically different risk (OR 1.34 (95% CI: 0.58, 3.14)). In the one study that provided data regarding children aged between one and two years of age (Sear et al. (2002), the odds of dying for children whose mothers had died was five times higher than for children whose mothers survived (OR 5.21, 95% CI : 1.58,17.21). There was considerable variation in the estimated odds of dying by maternal survival status among infants aged less than one year in the two studies included in the analysis: Sear et al. (2002) provided an estimate of 6.17 (95% CI: 2.27, 16.77) while Ronsmans et al. (2010) reported an estimate of 33.78 (95% CI :22.21, 47.14). Only one study, Reher et al. (2003) reported the risk of death among infants 6-11 months of age. In this report, infants aged between six and 11 months were twice as likely to die if their mothers died compared to if their mothers were alive, OR, 2.27 (95% CI: 1.56, 3.29). Considerable variation in the estimated odds of dying by maternal vital status was also evident for infants less than six months of age, with an estimated risk for infants whose mother had died compared to those whose mother survived of 4.39 (95% CI: 3.34, 5.78) in Reher et al. (2003), 36.23 (95% CI 24.97, 52.58) in Ronsmans et al. (2010) and 52.46 (95% CI 20.88, 131.19) in Katz et al. (2003).

## The risk of dying by timing of maternal death for children aged under the age of five

The association between risk of child death and timing of maternal death was addressed in only three of the eight studies [22, 26, 27]. Narrative synthesis of these three studies indicated that the risk of dying was increased nearer to the timing of the mother’s death.

The study by Beekink *et al.* (1999), based on data from the Dutch provincial town of Woerden between 1850 and 1930, reported that the relative risk of dying for children whose mothers died compared to those whose mother survived was increased within six months of maternal death (relative risk 4.16, t value 5.45). The risk of death for children beyond six months of the mother’s death was not significantly different from that of children with surviving mothers (relative risk 1.28, t value 0.63) [26].

Clark *et al.* (2013), using data from a rural, South African demographic surveillance site collected between 1994 and 2008, reported that the probability of a child dying started to increase in the period six to eleven months prior to the mother’s death and increased markedly during the two months immediately before the month of her death, adjusted odds ratio 7.1, (95% CI 3.7, 12.7). The odds of child death were highest in the month of her death, OR 12.6, (95% CI 6.2, and 25.3). The odds ratios in this study were adjusted for child and mother characteristics. There was no significant difference in the odds ratio of death amongst children whose mother died six months or more before the child’s death and those of children whose mothers were alive, odds ratio 1.59, 95% confidence interval (0.61, 4.15) [27].

Similar findings were reported from Guinea Bissau [22]. In urban Bissau, the mortality rate ratio for children whose mothers had died compared to children whose mothers were still alive was 3.09, (95% CI 1.27, 7.49) in the period 0-5 months after the death of the mother, but no longer significantly different after that period 1.77, 95% confidence interval (0.61, 5.11). In rural areas, the mortality rate ratio in the period 0 to 5 months after a mother’s death was 5.93 (95% CI 3.44,10.26) and 2.56 (95% CI 1.29,5.09) if the death of the mother was more than six months ago.

# Discussion

Our systematic review of the literature found only eight papers suitable for inclusion in the analysis. Findings relating to four studies consistently demonstrated that children aged less than five years were at an increased risk of death when their mothers died [22-25]. This pattern was also reflected in the sub–age group narrative analysis, although pooled estimates were not possible due to differences in study design [23, 25, 28-30]. Mortality risks were especially increased for infants less than six months of age. For children aged more than one year, the increased likelihood of dying when their mothers died were statistically significant among children 1-2 years of age but not in older children, 2-4 years of age. Results from three studies strongly indicated that children were more likely to die around the time of a maternal death [22, 24, 31] than in the periods 6 months or more after the mother’s death.

The increased risk of death for children in the first six months of life reported in the three studies identified may reflect the particular vulnerability of infants in this period [32] and explain why sickness in the mothers in the first six months postpartum may have such serious consequences [33]. Mothers who are ill may not be able to provide adequate care to their children, including optimal breastfeeding, jeopardising the nutritional and health status of children [33-36]. Premature weaning may occur and this is associated with higher mortality rates, especially for younger infants [7, 22, 34, 37]. In settings where infant survival is highly dependent on continued breastfeeding, this may partly explain reports that the loss of a father may not increase the risk of child dying to the same extent as the loss of the mother [26, 38]. Even though adoption and remarriage may protect children, the quality of childcare received by such children may be lower than that received when mothers are living [32, 39-41].

We were unable to search EMBASE due to access restrictions, and only searched the main population based 2013 International Union for the Scientific Study of Population conference for grey literature, however our search of PubMed, CINAHL, Delphis and Web of Knowledge and further searches of reference lists from the articles that we obtained as well as abstracts from the large, international and relevant conference were comprehensive and it is unlikely that we will have missed an important publication.

There was considerable variation in child mortality risks across the studies reviewed; this could reflect differences in background infant and child mortality rates related to socio-economic, demographic and environmental factors and may also reflect different health and social support systems. The quality of data may also have been variable. Civil registration data in developing countries is often incomplete and may not capture deaths as well as data from demographic surveillance sites resulting in apparently higher mortality rates in such studies than from civil registration data. Similarly, historical data such as from church registers in developed countries are likely to have missed deaths that occurred before children were registered for baptism and may thus have underreported early deaths. Methodological approaches may also account for some differences. The study by Sear *et al.* (2002) in the Gambia used multilevel modelling to obtain the median odds of dying within households whilst other studies modelled the odds of dying at the individual level. The quality of the data from included studies also ranged from low to very low. However, despite these variations across studies, the estimates of increased risk following maternal death were consistent and all in the same direction, even if statistical significance was not always reached due to limited sample sizes.

# Conclusions

Children with deceased mothers have reduced survival than children whose mothers survive at least to their fifth birthday. Their vulnerability is highest in infancy, especially the first six months of life and the risks decrease as they get older. Provisioning by health systems and communities for child care and the nutritional needs for infants who have lost their mothers may improve their survival chances. Remarriage and adoption could also increase children’s survival probability if they happen in the first six months after the mother’s death although care received by children of deceased mothers may be lower than that received by children with living mothers.

**Declaration of interests**

NR is a WHO employee. MLN and LC received funding from the WHO specifically for the systematic review.

**Acknowledgements**

The authors would like to acknowledge the financial support provided by the World Health Organisation, which enabled this study to be conducted.

The opinions expressed by the authors in this publication do not represent the views or positions of the World Health Organization or other affiliated institutions.

**References**

1. UNICEF-World-Bank-WHO. **Levels and trends in child mortality : Estimates developed by the UN Inter-agency Group for Child Mortality Estimation**. 2014

2. Mosley WH & Chen LC. **An analytical Framework for the Study of Child Survival in Developing Countries**. *Population and Development Review* 1984; **10**(Supplement: Child Survival: Strategies for Research)**:**25-45.

3. WHO. **Causes of deaths among children under 5 years, 2015**. 2015. Geneva, Switzerland: WHO <http://www.who.int/gho/child_health/mortality/causes/en/> (accessed 15th March 2016).

4. UNAIDS. **THE GAP REPORT**. 2014. Geneva, Switzerland: UNAIDS <http://www.unaids.org/en/resources/campaigns/2014/2014gapreport/gapreport> (accessed 15th March 2016).

5. Brahmbhatt H, Kigozi G, Wabwire-Mangen F, Serwadda D, Lutalo T, Nalugoda F, Sewankambo N, Kiddugavu M, Wawer M & Gray R. **Mortality in HIV infected children and uninfected children of HIV infected and uninfected mothers in rural Uganda**. *Journal of Acquired Immune Deficiency Syndrome* 2006; **41:**504-508.

6. Marinda E, Humphrey J, Illif PJ, Mutasa K, Nathoo K, Piwoz EG, Moulton LH, Salama P & Ward B. **Child mortality according to maternal and infant HIV status in Zimbabwe**. *The Paediatric Infectious Disease Journal* 2007; **26**(6).

7. Kuhn L, Aldrovandi GM, Sinkala M, Kankasa C, Semrau K, Mwiya M, Kasonde P, Scott N, Vwalika C, Walter J, Bulterys M, Tsai W-Y & Thea DM. **Effects of Early, Abrupt Weaning on HIV-free Survival of Children in Zambia**. *New England Journal of Medicine* 2008; **359**(2)**:**130-141.

8. Rollins NC, Ndirangu J, Bland RM, Coutsoudis A, Coovadia HM & Newell M. **Exclusive Breastfeeding, Diarrhoeal Morbidity and All-Cause Mortality in Infants of HIV-Infected and HIV Uninfected Mothers: An Intervention Cohort Study in KwaZulu Natal, South Africa**. *PLoS One* 2013; **8**(12).

9. Kuhn L, Sinkala M, Semrau K, Kankasa C, Kasonde P, Mwiya M, Hu CC, Tsai WY, Thea DM & Aldrovandi GM. **Elevations in mortality associated with weaning persist into the second year of life among uninfected children born to HIV-infected mothers**. *Clin Infect Dis* 2010; **50**(3)**:**437-444.

10. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P & Dabis F. **Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis**. *Lancet* 2004; **364**(9441)**:**1236-1243.

11. Chatterjee A, Bosch RJ, Hunter DJ, Fataki MR, Msamanga GI & Fawzi WW. **Maternal Disease Stage and Child Undernutrition in Relation to Mortality Among Children Born to HIV-Infected Women in Tanzania**. *JAIDS Journal of Acquired Immune Deficiency Syndromes* 2007; **46**(5)**:**599-606 510.1097/QAI.1090b1013e31815a35703.

12. Marinda E, Humphrey JH, Iliff PJ, Mutasa K, Nathoo KJ, Piwoz EG, Moulton LH, Salama P & Ward BJ. **Child mortality according to maternal and infant HIV status in Zimbabwe**. *Pediatr Infect Dis J* 2007; **26**(6)**:**519-526.

13. Atrash HK. **PARENTS' DEATH AND ITS IMPLICATIONS FOR CHILD SURVIVAL**. *Revista Brasileira de Crescimento e Desenvolvimento Humano* 2011; **21**(3)**:**759-770.

14. NCCMT. **Defining your question: PICO and PS.** 2012. Hamilton, ON: McMaster University. <http://www.nccmt.ca/resources/search/138> (accessed 15th December 2015).

15. Sterne JAC, Higgins JPT & Reeves BC. **A Cochrane Risk of Bias Assessment Tool for Non Randomised Studies of interventions (ACROBAT\_NRSI) Version 1.0.0**. 2014 Available from <http://www.riskofbias.info> accessed 20th September 2016.

16. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, Henry DA & Boers M. **AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews**. *J Clin Epidemiol* 2009; **62**(10)**:**1013-1020.

17. Borestein M, Hedges LV, Higgins JPT & Rothstein HR. **Introduction to meta-analysis**. 2009. West Sussex, UK: Wiley

18. Higgins J, Green S & (editors). **Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 2008** 2008 [www.cochrane-handbook.org](http://www.cochrane-handbook.org ) [Updated September 2009, accessed 15th December 2015].

19. Guyatt G, Andrew D, Gunn E, Kunz R, Falck-Ytter Y & Schunemann HJ. **GRADE: What is "quality of evidence" and why is it important to clinicians?** *BMJ* 2008; **336**(7651)**:**995-998.

20. Mavridis D & Salanti G. **How to assess publication bias: funnel plot, trim-and-fill method and selection models**. *Evidence Based Mental Health* 2014; **17**(1)**:**30.

21. WHO. **Global Health Observatory (GHO) data, country statistics**. 2016: WHO <http://www.who.int/gho/countries/en/> (accessed 4th May 2016).

22. Masmas TN, Jensen H, da Silva D, Høj L, Sandström A & Aaby P. **Survival among motherless children in rural and urban areas in Guinea-Bissau**. *Acta Pædiatrica* 2004; **93**(1)**:**99-105.

23. Ronsmans C, Chowdhury ME, Dasgupta SK, Ahmed A & Koblinsky M. **Effect of parent's death on child survival in rural Bangladesh: a cohort study**. *Lancet* 2010; **375**(9730)**:**2024-2031.

24. Clark SJ, Kahn K, Houle B, Arteche A, Collinson MA, Tollman SM & Stein A. **Young children's probability of dying before and after their mother's death: a rural South African population-based surveillance study**. *PLoS Med* 2013; **10**(3)**:**e1001409.

25. Becher H, Müller O, Jahn A, Gbangou A, Kynast-Wolf G & Kouyaté B. **Risk factors of infant and child mortality in rural Burkina Faso**. *Bulletin of the World Health Organization* 2004; **82:**265-273.

26. Beekink E, van Poppel F & Liefbroer AC. **Surviving the loss of the parent in a nineteenth-century Dutch provincial town**. *J Soc Hist* 1999; **32**(3)**:**641-670.

27. CLARK SJ, KAHN K, HOULE B, ARTECHE A, COLLINSON MA, TOLLMAN SM & STEIN A. **Young children's probability of dying before and after their mother's death: a rural South African population-based surveillance study**. *PLoS Med,* 2013.

28. Sear R, Steele F, McGregor I & Mace R. **The effects of kin on child mortality in rural Gambia**. *Demography* 2002; **39**(1)**:**43-63.

29. Reher DS & González-Quiñones F. **Do parents really matter? Child health and development in Spain during the demographic transition**. *Population Studies* 2003; **57**(1)**:**63-75.

30. Katz J, West Jr KP, Khatry SK, Christian P, LeClerq SC, Pradhan EK & Shrestha SR. **Risk factors for early infant mortality in Sarlahi district, Nepal**. *Bulletin of the World Health Organization* 2003; **81:**717-725.

31. Beekink E, van Poppel F & Liefbroer AC. **Surviving the loss of the Parent in a Nineteenth-Century Dutch Provincial Town**. *J Soc Hist* 1999; **32**(3)**:**641-669.

32. Razzaque A, Hossain A & DaVanzo J. **Effect of Maternal Mortality on Survival of Under-five Children**. *Asian Population Studies* 2014; **10**(1)**:**60-74.

33. Nuruddin R, Kin LM, Hadden WC & Azam I. **Maternal chronic ill health negatively affects child survival in a poor rural population of Pakistan**. *World Health Popul* 2007; **9**(3)**:**27-35.

34. Rollins NC, Ndirangu J, Bland RM, Coutsoudis A, Coovadia HM & Louise Newell M-L. **Exclusive Breastfeeding, Diarrhoeal Morbidity and All-Cause Mortality in Infants of HIV-Infected and HIV Uninfected Mothers: An Intervention Cohort Study in KwaZulu Natal, South Africa**. *PLoS One* 2013; **8**(12).

35. Cutts FT, Dos Santos C, Novoa A, David P, Macassa G & Soares AC. **Child and maternal mortality during a period of conflict in Beira City, Mozambique**. *Int J Epidemiol* 1996; **25**(2)**:**349-356.

36. Van den Broeck J, Eeckels R & Massa G. **Maternal determinants of child survival in a rural African community**. *Int J Epidemiol* 1996; **25**(5)**:**998-1004.

37. Shapiro RL, Kitch D, Ogwu A, Hughes MD, Lockman S, Powis K, Souda S, Moffat C, Moyo S, McIntosh K, van Widenfelt E, Zwerski S, Mazhani L, Makhema J & Essex M. **HIV transmission and 24-month survival in a randomized trial of HAART to prevent MTCT during pregnancy and breastfeeding in Botswana**. *Aids* 2013; **27**(12)**:**1911-1920.

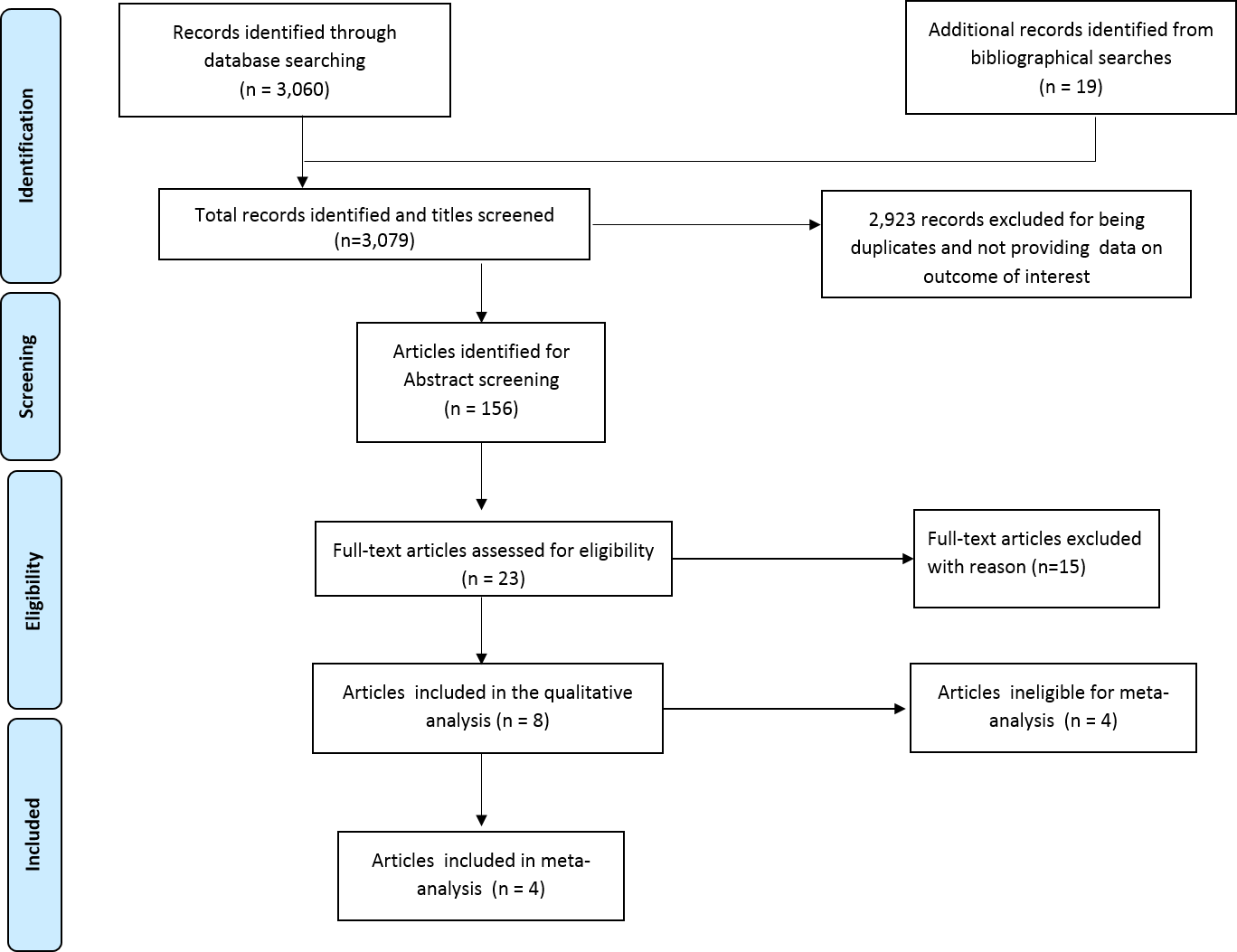
38. Rostila M & Saarela JM. **Time Does Not Heal All Wounds: Mortality Following the Death of a Parent**. *Journal of Marriage and Family* 2011; **73**(1)**:**236-249.

39. Anderson FW, Morton SU, Naik S & Gebrian B. **Maternal mortality and the consequences on infant and child survival in rural Haiti**. *Matern Child Health J* 2007; **11**(4)**:**395-401.

40. Al-Adili N, Shaheen M, Bergstrom S & Johansson A. **Survival, family conditions and nutritional status of motherless orphans in the West Bank, Palestine**. *Scandinavian Journal of Public Health* 2008; **36**(3)**:**292-297.

41. Willfuhr KP & Gagnon A. **Are stepparents always evil? Parental death, remarriage, and child survival in demographically saturated Krummhorn (1720-1859) and expanding Quebec (1670-1750)**. *Biodemography Soc Biol* 2013; **59**(2)**:**191-211.

## Figure 1 PRISMA Flow diagram



## Search terms in PubMed

(((((((((("maternal mortality"[All Fields] OR "maternal death"[All Fields]) OR "maternal survival"[All Fields]) OR (("mothers"[MeSH Terms] OR "mothers"[All Fields] OR "maternal"[All Fields]) AND vital[All Fields] AND status[All Fields])) OR "mother\* death"[All Fields]) OR "mother\* survival"[All Fields]) OR "parental death"[All Fields]) OR "parental survival"[All Fields]) OR "parent's death"[All Fields]) OR (parent's[All Fields] AND ("mortality"[Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms]))) AND ((("child mortality"[All Fields] OR "under-five mortality"[All Fields]) OR "child death"[All Fields]) OR "infant death"[All Fields]) OR "infant survival"[All Fields]) OR "child survival"[All Fields] NOT ("hiv"[MeSH Terms] OR "hiv"[All Fields]) AND ("1990/01/01"[PDAT] : "2016/11/30"[PDAT])

Figure 2 Odds of dying for children under the age of five years by mother’s survival status.

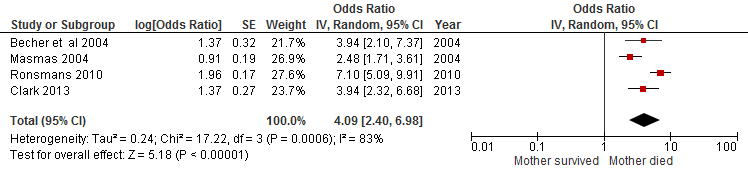


Table 1 Odds of dying for children whose mother died compared to children whose mother survived ( Children of various age groups)

|  |  |  |  |
| --- | --- | --- | --- |
| **Study ID** | **Study design and context** | **Children's age group** | **Odds Ratio (95% CI)** |
| Becher et al. 2004 | Cohort, 1992 to 1999 Burkina Faso | Two to four years old | 2.92 ( 1.21,7.04) |
| Sear et al. 2002 | Birth and Death registers 1950 to 1974 | Two to four years old | 1.40 (0.47,4.21) |
|  |  |  |  |
| Sear et al. 2002 | Birth and Death registers  1950 to 1974 | One to two years old | 5.21(1.58,17.21) |
|  |  |  |  |
| Sear et al. 2002 | Birth and Death registers  1950 to 1974 | Less than one year | 6.17(2.27,16.77) |
| Ronsmans et al. 2010 | Cohort, 1982 to 2005, Matlab, Bangladesh | Less than one year | 33.78 (24.21,47.14) |
| Reher et al. 2003 | Birth/Death registers,  1870 to 1950, Spain | Six to eleven months | 2.27 (1.56, 3.29) |
| Reher et al. 2003 | Birth/Death registers  1870 to 1950, Spain | Less than six months | 4.39 (3.34,5.78) |
| Ronsmans et al. 2010 | Cohort , 1982 to 2005 Matlab, Bangladesh | Less than six months | 36.23 (24.97,52.58) |
| Katz et al. 2003 | Randomised Control Trial\* 1994 to 1997,Nepal | Less than six months | 52.46 (20.88,131.79) |

\* In the study by Katz et al. (2003), participants were randomised to receive or not to receive a nutritional supplement

Supplementary Table 1 Risk of bias judgement based on the ROBINS-I Tool

|  |  |
| --- | --- |
| **Domain** | **Description\*** |
| Confounding | **Low risk:** If the study is comparable to a well performed randomised trial.  **Moderate risk:** if all known critically important confounding domains have been appropriately measured and adjusted for.  **Serious Risk:** At least one known critically important domain not measured or adjusted for.  **Critical Risk**: Confounding inherently not controllable.  **No information:** No information on whether confounding might be present. |
| Selection of Participants into the study | Selection bias occurs when the selection of participants occurs to both the intervention and outcome.  **Low risk**: All participants who would have been eligible for the target trial were included.  **Moderate Risk:** Selection into the study was related to intervention and outcome.  **Serious risk:** Selection into the study was related to intervention and outcome.  **Critical risk:** Selection into the study was strongly related to intervention and outcome.  **No information:** No information about the selection of cases and controls. |
| Measurement of Interventions | **Low risk:** Intervention status is well defined and based solely on information collected at the time of intervention.  **Moderate risk:** Intervention is well defined but some aspects of the assignments of intervention status were determined retrospectively  **Critical risk:** An extremely high amount of misclassification of intervention status e.g. because of unusually strong recall biases  **No information:** No information of intervention or no explanation of the source of information about intervention status |
| Departures from intended interventions | **Low risk**: No bias expected if both interventions and comparator are implemented over a short time period and subsequent interventions are part of the routine medical care.  **Moderate risk:** Bias due to departure from the intended intervention is expected and switches, co-interventions and some problems with intervention fidelity are appropriately measured and adjusted for in the analyses  **Serious risk:** Switches in treatment, co –interventions or problems with implementing fidelity are apparent and are not adjusted for in the analyses.  **Critical risk:** Substantial departures from the intended intervention are present and are not adjusted for in the analysis.  **No information:** No information is reported on whether there departure from the intended intervention. |
| Missing data | **Low risk:** Data were reasonably or proportions and reasons of missing participant were similar across intervention groups.  **Moderate risk:** Proportions of missing participants differ across intervention or reasons for missingness differ minimally across interventions  **Serious risk:** Proportions of missing participants differ substantially across interventions or reasons for missingness differ substantially across interventions  **Critical risk:** There were critical differences between interventions in participants with missing data that were not or could not be addressed through appropriate analysis  **No information:** No information is reported about missing data or the potential for data to be missing |
| Measurement Outcomes | **Low risk:** The methods of outcome assessment were comparable across interventions groups and the outcome measure was unlikely to be influenced by knowledge of the intervention received by participants and any error in measuring the outcome is unrelated to intervention status.  **Moderate risk:** The methods of outcome were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants and any error in measuring the outcome is only minimally related to intervention status.  **Serious risk:** The methods of outcome assessment were not comparable across intervention groups or the outcome measure was subjective  **Critical risk:** The methods of outcome assessment were so different that they cannot reasonably be compared across intervention groups  **No Information:** No information is reported about the methods of outcome assessment |
| Selection of the reported result | **Low risk:** There is clear evidence that all reported results correspond to all intended outcomes, analyses and sub-cohorts  **Moderate risk:** The outcome measure and analyses are consistent with an a priori plan, or are clearly defined and internally and externally consistent and there is no indication of selection of the reported analysis from any multiple analysis and there is no indication of selection of the cohort or sub group analysis and reporting on the basis of the results.  **Serious risk:** Outcome measurement or analyses are internally or externally inconsistent or there is a high risk of selective reporting from among multiple analysis or the cohort or subgroup is selected from a larger study for analysis and appears to be reported on the basis of the results.  **Critical risk:** There is evidence or strong suspicion of selective reporting of results and the unreported results are likely to be substantially different from the reported results.  **No Information:** There is too little information to make a judgement for example if only an abstract is available for the study. |
| Overall | **Low risk: of bias** The study is comparable to a well performed randomised trial  **Moderate risk of bias:** The study provides sound evidence for a non-randomised study but cannot be considered comparable to a well-performed randomised trial  **Serious risk of bias:** The study has some important problems  **Critical risk of bias:** the study is too problematic to provide any useful evidence and should not be included in any synthesis |

\*Detailed description of each domain is Available from http://www.riskofbias.info

Supplementary Table 2 Studies excluded from the analysis

|  |  |  |
| --- | --- | --- |
| No. | Reference | Reason for Exclusion |
| 1. | ANDERSON,F.W., MORTON,S.U., NAIK, S., GEBRIAN, B: Maternal mortality and the consequences on infant and child survival in rural Haiti. *Maternal and child health journal* 2007, 11(4):395-401. | Low numbers  Children’s ages (months)were different between the two comparison groups |
| 2. | AL-ADILI, N., SHAHEEN, M., BERGSTROM, S. & JOHANSSON, A. 2008. Survival, family conditions and nutritional status of motherless orphans in the West Bank, Palestine. Scandinavian Journal of Public Health, 36, 292-297. | The study does not provide a comparison group, therefore its only good to include in the discussion |
| 3. | ATRASH, H. K. 2011. PARENTS' DEATH AND ITS IMPLICATIONS FOR CHILD SURVIVAL. Revista Brasileira de Crescimento e Desenvolvimento Humano, 21, 759-770 | This article is a literature review of various studies on the impact of maternal death on child survival. It is not used for analysis but it is included in the discussion. |
| 4. | CUTTS, F. T., DOS SANTOS, C., NOVOA, A., DAVID, P., MACASSA, G. & SOARES, A. C. 1996. Child and maternal mortality during a period of conflict in Beira City, Mozambique. Int J Epidemiol, 25, 349-56. | The exposure of interest in the study was mother’s illness and not mother’s death |
| 5. | Finlay JE, Moucheraud C, Goshev S, Levira F, Mrema S, Canning D, Masanja H, Yamin AE: The Effects of Maternal Mortality on Infant and Child Survival in Rural Tanzania: A Cohort Study. *Matern Child Health J* 2015, 19(11):2393-2402. | Focus was on comparing infant and child survival in children whose mothers died from maternal and non-maternal causes |
| 6. | LI, J., VESTERGAARD, M., CNATTINGIUS, S., GISSLER, M., BECH, B. H., OBEL, C. & OLSEN, J. 2014. Mortality after parental death in childhood: a nationwide cohort study from three Nordic countries. PLoS Med, 11, e1001679. | The study does not focus on under-fives. It includes mortality of children aged over 5 years |
| 7. | Moucheraud C, Worku A, Molla M, Finlay JE, Leaning J, Yamin A: Consequences of maternal mortality on infant and child survival: a 25-year longitudinal analysis in Butajira Ethiopia (1987-2011). *Reprod Health* 2015, 12 Suppl 1:S4. | Focus was on estimating infant and child survival in children whose mothers died from maternal causes |
| 8. | NURUDDIN, R., KIN, L. M., HADDEN, W. C. & AZAM, I. 2007. Maternal chronic ill health negatively affects child survival in a poor rural population of Pakistan. World Health Popul, 9, 27-35. | The exposure of interest is child death. It assesses maternal mortality amongst mothers whose children had died. |
| 9. | PAVARD, S., GAGNON, A., DESJARDINS, B. & HEYER, E. 2005. Mother's death and child survival: the case of early Quebec. *J Biosoc Sci,* 37**,** 209-27. | This study analyses mortality between the ages of 28 days and 15. There was no disaggregation by age. |
| 10. | RAZZAQUE, A., HOSSAIN, A. & DAVANZO, J. 2014. Effect of Maternal Mortality on Survival of Under-five Children. Asian Population Studies, 10, 60-74. | The interest of the study was to investigate differences in mortality between children that were adopted and those that stayed at home |
| 11. | STRONG, M. 1992. The health of adults in the developing world: A view from Bangladesh *Health Transition Review,* 2, 215-224. | Includes mortality for children up to the age of 10. There was no disaggregation by age. |
| 12. | Sear R, Mace R: Who keeps children alive? A review of the effects of kin on child survival. *Evolution and Human Behavior* 2008, 29(1):1-1y8. | This article is a literature review of various studies on the effects of kin of child survival. |
| 13. | SEAR, R., MACE, R. & MCGREGOR, I. A. 2000. Maternal grandmothers improve nutritional status and survival of children in rural Gambia. *Proceedings Yoyal Society of London,* 267. | The sample used in this study was part of the sample used in Sear et al. 2002 which is included in the analysis. |
| 14. | VAN DEN BROECK, J., EECKELS, R. & MASSA, G. 1996. Maternal determinants of child survival in a rural African community. *Int J Epidemiol,* 25**,** 998-1004. | The article compares mortality by mother’s chronic illness and not between children whose mother died and those whose mother survived. The article is good for inclusion in the discussion section. |
| 15. | WILLFUHR, K. P. & GAGNON, A. 2013. Are stepparents always evil? Parental death, remarriage, and child survival in demographically saturated Krummhorn (1720-1859) and expanding Quebec (1670-1750). *Biodemography Soc Biol,* 59**,** 191-211. | Includes mortality for children up to the age of 15. There was no disaggregation by age. |

Supplementary Table 3: Data extracted from studies included in the meta-analysis

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **General information of the study (Study ID, title, authors)** | **Study design** | **Methodological limitations** | **Main results re association between child and maternal survival** | **Associated factors** | **Type of estimate** |
| **Becher *et al.* 2004**  Risk factors of infant and child mortality in rural Burkina Faso  \*The under-five mortality rate in Burkina Faso were 202 in 1990, 194.4 in 1995 and 185.7 in 2000 per 1000 live births  \*The maternal mortality ratio was 727 in 1990, 636 in 1995 and 547 in 2000 per 100000 live births | Demographic surveillance site, children were followed from 1992 to 1999 | Did not control for correlation between variables i.e. birth order and age of the mother at birth | **Main findings:**  *10122 live births*  *1340 deaths*  9396 mothers were alive at the end of follow up and 42 died  86.8% of children with living mothers and 64.3% children whose mothers had died were alive  Death of the mother and being a twin were the strongest risk factors for mortality  Amongst 18 children whose mother died within the first year of life, 9 died within the follow up period  Rate ratio for increased mortality for infants who lost their mother was 15.6 (7.61-31.8)  For children (1 to 5 yrs.) 5.35 (1.69-16.9)  **Conclusion:** findings supported the multi-causation of childhood deaths in west Africa during the 1990s and supported the overall trend of decreasing childhood mortality in these populations | Study controlled for socio-demographic factors e.g. distance to health facility, birth order, age the mother, ethnic group, sex, season of birth, time to the birth of the next sibling, vital status of the older sibling | **Mortality rate ratio**  **Other estimates from raw data** :  Mortality rate for  all children whose  mother died (0 to 5 years) = 15/42 (0.36) 36%  Mortality for children whose mothers were alive = 1238/9396 = 0.13 (13%)  **In the first year of life**  M Rate for children without mothers = 9/18 (0.5) 50%?  M rate for children with mothers = Not given  **In the 2nd to 5th years of life**  M Rate for children without mothers = 6/24 9(0.25) 25%? |
| **Beekink, *et al* 1999**  Surviving the loss of the Parent in a Nineteenth-Century Dutch Provincial Town | Data from population registers covering the period 1850 to 1930  A total of 3936 live born children were studied | No raw estimates showing  numbers or rates of mortality | In the second half of the nineteenth century almost 29% of the live born children did not reach the end of the first year of life. Age five was not reached by almost 38% of the children born during the period 1850-1899.  Children aged 0 to 12 months Compared with children that had a complete family, the relative risk of dying for children with a deceased mother was 2.42 (t value 4.01)  Relative risk for child death by duration since the mother died  Compared with children that had a complete family, children whose mother was deceased <6 months ago had a relative risk of dying of 4.16 (t value 5.45)  Whilst children whose mother was deceased more than 6 months ago had a relative risk of 1.28(t value 0.63)  Among children aged less than six months  Relative risk of a child dying was 2.46 (t value 6.09)  Among children aged 6 months or more  Relative risk of a child dying if the mother was deceased <6 months ago was 1.92( t value 1.28) and if the mother was deceased >6 months ago was 1.30 (t value 0.67) | Study controlled for sex, birth year, parity, age of mother at birth, age of the mother squared, signature of the bride, religion, social group, regional origin of spouses, child experienced epidemic, family situation of child | **Relative risk** of dying for children aged 0 to 12 months |
| **Clark *et al.* 2013**  Young children’s probability of dying before and after their mother’s death: a rural South African Population based surveillance study | Socio-demographic surveillance system for children aged 0 to 5 years between 1 January 1994 and 31 December 2008 | Diagnosis of AIDS death by verbal autopsy rather than serostatus, lack of knowledge when a very ill mother will die, lack of information on child nutrition and care  Used discrete time survival analysis methods | Total number of children followed 4,584  1,244 children died  (180/950 mother died)  (1,064/40634 mother was alive)  There were 950 mother deaths out of which 259 were AIDS/TB related in a population of 24,860 mothers  **Amongst all children**  The odds of dying for children whose mother  died from a cause other than AIDS/TB  was 3.93(2.3,6.7) p value <0.001 compared to children with living mothers  The probability of child death began to rise 6-11 months prior to the mother’s death and increased markedly during the 2 months immediately before the month of her death OR 7.1 (3.9,12.7)  In the month of her death OR 12.6(6.2,25.3) and  2 months after death 7.0(3.2,15.6)  Infants aged 0-6 months were more likely to die than children aged 2 to 5 years  Conclusion: Young children in lower income settings are more likely to die not only after their mother’s death but also in the months before | Controlled for period before and after mother’s death, sex of child, child’s age, time period, mother’s cause of death and interaction between time period and mother’s cause of death | **Odds** of dying amongst children aged 0 to 5 years with deceased mothers compared to mothers who died of HIV/AIDS and those with mothers |
| **Katz *et al.* 2003**  Risk factors for early infant mortality in Sarlahi district Nepal  \*The Infant Mortality Rate for Nepal was 76.8 in 1995 and 59.6 in 2000 per 1000 live births  \*The maternal mortality ratio was 660 in 1995 and 548 in 2000 per 100000 live births | Randomised community trial assessing the impact of a weekly nutritional supplement for all women of child bearing age on maternal and infant health and survival  15,469 live born infants were followed over the period 1994- 1997  Vital status available for 14323 infants, a total of 409 infants died in the first week of life, 237 between 8 and 28 days and 294 between 4 and 24 weeks | Some possible confounders were not controlled for e.g. health status of women, quantities of alcohol, tobacco | *15469 live births*  *2086 deaths*  Cumulative mortality up to 24 weeks of age was 65.6 per 1000 live births  The death rate was 13.5%  Maternal mortality was strongly associated with infant mortality at all ages, it increased the odds of death of an infant by 6.43 (2.35,17.56) in the first week of life, 11.73 (3.82, 36.00) from one to four weeks and 51.68 (20.26, 131.80) from 4 to 24 weeks of life | Risk factors included in the logistic regression were paternal and maternal education, history of prior miscarriages, stillbirths, prior deaths of live born children, parity, gestational age, mid-upper arm circumference measured during the second trimester, number of antenatal vaccinations, history of severe illness and vaginal bleeding in the last trimester | **Odds** of dying from 4 to 24 weeks  *Highlights vulnerability of the very young* |
| **Masmas *et al.* 2004**  Survival among motherless children in rural and urban areas in Guinea-Bissau  \*The under-five mortality rate was 229.3 in 1990, 194.4 in 1995 and 185.7 in 2000 (per 1000 live births)  \*The maternal mortality ratio was 907 in 1990, 780 in 1995 and 800 in 2000  ( per 100,000 live births) | Demographic Surveillance System  Data on women who died between 1990 and 1997  128 motherless children from the rural and 192 children from urban areas  807 controls | 32% of deaths were maternally related  Follow up only limited to 2 years | The mortality rate ratio between orphans and control children was 2.32 (1.11,4.84) in Bissau (city) and 4.16 (2.79,6.22) in rural areas  In rural areas twinning status modified the results slightly  The higher mortality rate among orphans compared with that for controls was not significantly different in the urban areas compared with the rural areas.  No significant difference in mortality between orphans and controls after two years  Conclusion: Premature weaning may be one of the major causes of the higher mortality rates observed among motherless children. | Controlled for various socio-demographic factors i.e. breastfeeding, age of child, gender, twinning status, mother’s age at death, ethnic group, socio-economic status, household background factors e.g. living with the father, father’s survival, polygamy, number of co-wives ranking of mothers among co wives, number of children | **Mortality rate ratio** |
| **Reher *et al.* 2003**  Do parents really matter? Child health and development in Spain during the demographic transition  Data for the period between 1870 to 1950  Infant mortality rate declined from 200 at the beginning of the century to 70 per 1000 live births in 1950 | Data from Aranjuez, Spain during the period 1870-1950,  N for surviving mothers = 17,845  Mothers died in child bearing= 2,650  Mother died when child was aged <24 months 481.  Mother died when child was aged <12 months 279 |  | Ratios of probabilities of death between children whose mother died and children whose mother survived:  0 months: childbearing 1.63,child <24 months 3.81, child<12 months 4.78  1-5 months : child bearing 1.69, child <24 months 3.74, child<12 months 4.47  6-11 months; child bearing 1.28, child <24 months 1.91, child<12 months 2.11  1 year: childbearing 1.44, child ,24 months 1.58 |  | **Ratios of probabilities of death** by age of child at the time of mother’s death : in child bearing , <12 months, <24 months |
| **Ronsmans *et al.* 2010**  Effect of parent’s death on child survival in rural Bangladesh  Mothers of 1385 children died before their children reached the age of ten years out of 144,858 mothers  \*Maternal mortality rates for Bangladesh were 569 in 1990, 479 in 1995, 399 in 2000 and 319 in 2005 (per 100,000 live births) | Data from population surveillance (1982 to 2005) in Matlab Bangladesh  144,861 live births and 14,868 children died by 10 years of age  Children were followed up for 120 months or until they died, migrated or censored in December 2005  (10% died over the ten year period) | The survival probabilities are cumulative and there are no estimates on survival probabilities of children by period before death | Greatest effect of mother’s death noticed in children aged 2 to 5 months: Rate ratio 25.05 95% CI (18.57,33.81)  For new births, the cumulative probability of survival at 5 months for children whose mother died was 35% whilst for children whose mother survived was 93%  For children that survived to 1 month the cumulative probability of survival at 11 months for children whose mother died was 49% and for children whose mother survived was 97% |  | **Cumulative probability of survival**  For children that survived up to the age of 6 months, cumulative probability of survival at the age of five for children whose mother survived was 0.96 whilst for those whose mother died was 0.69 |
| **Sear *et al.* 2002**  The effects of kin on child mortality in rural Gambia | Data collected by Sir Ian McGregor as part of a long term study between 1950 and 1980 in the district of West Kiang (the data came from four villages including the villages of Keneba and Manduar)  Data available for children from birth until they died or they were aged 5 or censored.  A total of 3,063 children aged 0 to 4 years lived in these villages during the period 1950 to 1974  Sample size reduced to 2,294 after those without a mother identity were removed, of whom 883 died before the age of five years. | Estimates are at household level and not individual | Of the 2,294 children that were followed, 883 died before the age of five  Odds of a child dying in infancy (0 -11 months) for children whose mother died were 6.2 times more than for children whose mother was alive  Odds of a child dying in toddler period (12-23 months) for children whose mother died were 5.2 times more than for children whose mother was alive | Full models included sex of child, year of birth, season of birth, village of birth, whether the child was twin, whether child was last born, birth order, length of preceding and succeeding birth intervals, mother’s age at birth, whether the subsequent sibling has different father, whether child had living elder brothers and sisters and number of wives the father has, paternal grandmother, paternal grandfather, maternal grandmother, maternal grandfather | **Odds of a child dying** in the infant period and toddler period  *Used multilevel discrete event history analysis* |

The source of the data is WHO Global Health Observatory data, country statistics : <http://www.who.int/gho/countries/en/>

Supplementary Table 4 Grade Evidence Profiles

**Question**: Risk of dying for children under the age five years by maternal survival status outside the HIV context

**Setting**: Bangladesh, Burkina Faso, Gambia, Guinea-Bissau, Nepal, Netherlands, Spain, South Africa

| **Quality assessment** | | | | | | | **Number of child deaths** | **Number of children followed** | **Effect** | **Quality** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Odds Ratio (95% CI)** |
| Odds of dying for children aged five years or less whose mothers died compared to those whose mother survived in cohort studies | | | | | | | | | | |
| 4 | observational studies 1 | not serious | not serious 2 | not serious | not serious | none | 32859 | 539973 | **OR 4.09** (2.40 to 6.98) | ⨁⨁◯◯ LOW |
| Odds of dying for children aged two to four years whose mother died compared to those whose mother survived in studies using registration data | | | | | | | | | | |
| 1 | observational studies 3 | serious 4 | not serious | not serious | not serious | none | 1505 | 3985 | **OR 1.40** (0.47 to 4.21) | ⨁◯◯◯ VERY LOW |
| Odds of dying for children aged two to four years whose mother died compared to those whose survived ( data from a demographic surveillance site) | | | | | | | | | | |
| 1 | observational studies 5 | not serious | not serious | not serious | not serious | none | 1340 | 10122 | **OR 2.92** (1.21 to 7.04) | ⨁⨁◯◯ LOW |
| Odds of dying for infants aged between one and two years whose mother died compared to those whose mother survived in studies using death registration data | | | | | | | | | | |
| 1 | observational studies 3 | serious 4 | not serious | not serious | not serious | none | 1505 | 3985 | **OR 5.21** (1.58 to 17.21) | ⨁◯◯◯ VERY LOW |
| Odds of dying for infants aged less one year whose mother died compared to those whose mother survived in study using death registration data | | | | | | | | | | |
| 1 | observational studies 3 | serious 4 | not serious | not serious | not serious | none | 1505 | 3985 | **OR 6.17** (2.27 to 16.77) | ⨁◯◯◯ VERY LOW |
| Odds of dying for infants aged less than one year whose mother died compared to those whose mother survived in a cohort study | | | | | | | | | | |
| 1 | observational studies 6 | not serious | not serious | not serious | not serious | none | 16176 | 402577 | **OR 33.78** (24.21 to 47.14) | ⨁⨁◯◯ LOW |
| Odds of dying for infants aged between 6 and 11 months whose mother died compared to those whose mother survived | | | | | | | | | | |
| 1 | observational studies 7 | serious 8 | not serious | not serious | not serious | none | NP9 | NP9 | **OR 2.27** (1.56 to 3.29) | ⨁◯◯◯ VERY LOW |
| Odds of dying for infants less than six months whose mother died compared those to whose mother survived in study using registration data | | | | | | | | | | |
| 1 | observational studies 7 | serious 8 | not serious | not serious | not serious | none | NP9 | NP9 | **OR 4.39** (3.34 to 5.79) | ⨁◯◯◯ VERY LOW |
| Odds of dying for infants aged less than six months whose mother died compared to those whose mothers survived in a cohort study | | | | | | | | | | |
| 1 | observational studies 6 | not serious | not serious | not serious | not serious | none | 137 | 253 | **OR 36.23** (24.97 to 52.58) | ⨁⨁◯◯ LOW |
| Odds of dying for infants aged less than six months whose mother died compared to those whose mother survived in a randomised control trial | | | | | | | | | | |
| 1 | observational studies 10 | not serious | not serious | not serious | not serious | none | 940 | 14323 | **OR 52.46** (20.88 to 131.79) | ⨁⨁◯◯ LOW |

1. The studies by Becher et al. 2004, Masmas et al. 2004, Ronsmans et al. 2010 and Clark et al, 2013 were based on data from demographic health surveillance sites.
2. Although heterogeneity was high the direction of effect was similar across the four studies.
3. The study by Sear et al. 2002 was based on deaths registers collected by Sir Ian McGregor between 1950 and 1974 in rural Gambia
4. Risk of bias. We downgraded once due to potential risk of selection bias since vital registration data may not accurately represent the number of deaths due to poor reporting in the study by Sear et al. 2002. Death reporting may not accurately represent the number of deaths taking place.
5. Study by Becher et al 2004 used data from a demographic surveillance site in Burkina Faso
6. The study by Ronsmans et al 2010 used demographic surveillance site data in Bangladesh.
7. The study by Reher et al. 2003 used data from civil registers in Aranjuez Spain between 1870 and 1950
8. Risk of bias. We downgraded once due to potential miss of deaths that occurred before birth registration in the study by Reher et al. 2003.
9. The study by Reher et al. 2003 had raw data on women who died by age of death and provided the probability of child survival by age group. No raw data on the number of child deaths and live births was given.
10. The study by Katz et al. 2003 was a randomised control trial in Nepal, but the randomisation was not based on the outcome of interest. The infant mortality in Nepal in 1999 was high (99 per 1000 live births). The extremely high odds of dying for infants without mothers compared to infants with mothers signifies the important role a mother plays in the first six months of life in populations with poor socio-economic conditions.

Supplementary Table 5: Assessment of Risk of Bias: ROBINS –I TOOL

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Confounding | Selection of  participants into the study\* | Measurement of  interventions | Departures  from intended interventions\* | Missing data\* | Measurement  outcomes | Selection of the  reported result | Overall |
| Becher et al. 2004 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Clark et al. 2013 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Katz et al. 2003 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Masmas et al. 2004 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Reher et al. 2003 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Ronsmans et al. 2010 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |
| Sear et al. 2002 | Medium risk | NA | Low risk | NA | NA | Low risk | Low risk | Medium risk |

\**The risk of bias assessment with respect to Selection of participants, Departures from intended interventions and Missing data* were not relevant to this study due to death of mother not being a typical intervention undertaken by non-randomised studies.

1. \* Corresponding author Dr Lana Clara Chikhungu,

   Park Building, School of Languages and Area Studies, University of Portsmouth, King Henry 1 Street, Portsmouth, PO1 2DZ.United Kingdom.

   Tel +44 (0) 2392846183, Email:lana.chikhungu@port.ac.uk

   2 Professor Marie-Louise Newell, Academic Unit of Health and Development and Global Health Research Institute, Faculty of Medicine, University of Southampton, Southampton, United Kingdom. Email: [M.Newell@soton.ac.uk](mailto:M.Newell@soton.ac.uk)

   3 Dr Nigel Rollins, Department of Maternal, Newborn, Child and Adolescent Health, World Health Organisation, Geneva, Switzerland. Email: [rollinsn@who.int](mailto:rollinsn@who.int) [↑](#footnote-ref-1)
2. [↑](#footnote-ref-2)
3. [↑](#footnote-ref-3)