Cofactors of neonatal mortality and hospitalization in western Kenya

Olivia Lang Schultes

Thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science

University of Washington

2023

Committee

Grace John-Stewart

Keshet Ronen

Program Authorized to Offer Degree:

Epidemiology

University of Washington

Abstract

Cofactors of neonatal mortality and hospitalization in western Kenya

Olivia Lang Schultes

Chair of the Supervisory Committee: Grace John-Stewart

Department of Epidemiology, Medicine, Global Health, and Pediatrics

Background: Although global neonatal mortality has been declining over the past several decades, it remains a major contributor to infant and childhood mortality rates. Determining the biological, psychosocial, and behavioral cofactors of neonatal mortality and hospitalization can help identify high-risk populations and behaviors associated with adverse neonatal health outcomes and will be relevant to research and programmatic interventions offering perinatal support.

Methods: The study cohort included 2451 maternal-infant pairs recruited from six clinics in western Kenya, who were control participants in the Mobile WACh NEO trial. Participants were enrolled during the third trimester of pregnancy and had follow-up visits at two and six weeks following delivery. Univariate and multivariate Cox regression models were used to test associations.

Results: Cumulative neonatal mortality was 15.1/1,000 live births, while cumulative neonatal hospitalization was 19.2/1,000 live births. Higher gestational age and birthweight were associated with decreased risk of mortality in multivariate models (Hazard Ratio [HR] = 0.83, 95% confidence interval [CI] 0.74, 0.93; HR = 0.41, 95% CI 0.20, 0.83), while male sex and primigravida were associated with increased mortality in univariate models (HR = 2.24, 95% CI 1.05, 4.76; HR = 1.95, 95% CI 1.02, 3.72). Lower maternal age was marginally associated with increased risk of mortality in the univariate model (HR = 0.94, 95% CI 0.88, 1.00). Higher gestational age and birthweight were associated with decreased risk of hospitalization in the multivariate models (HR = 0.81, 95% CI 0.73, 0.91; HR = 0.39, 95% CI 0.21, 0.72), while primigravida and higher maternal education were associated with increased risk of hospitalization in univariate models (HR=1.82, 95% CI 1.02, 3.22; HR=1.96, 95% CI 1.02, 3.78). Among

univariate models of infant care practices, appropriate cord care was associated with increased risk of neonatal mortality (HR = 3.505, 95% CI = 0.949, 12.946), while early initiation of breastfeeding was associated with a lower risk of hospitalization (HR = 0.160, 95% CI 0.04, 0.60).

Conclusion: Biological and social cofactors were associated with increased neonatal mortality and hospitalization, consistent with published literature. Our findings underscore the need for interventions to prevent preterm or low birthweight outcomes or to enhance care of these infants. Maternal education and breastfeeding practices are modifiable factors that may be addressed to improve neonatal outcomes. Associations between cord care practices and neonatal outcomes may have been due to infant illness at delivery. Lack of association between psychosocial factors and adverse infant outcomes suggests that structural factors may exert more influence than individual-level factors.

Background

Reducing neonatal morbidity and mortality has been a long-term focus of global health initiatives. In Eastern and Southern Africa, rates of neonatal mortality decreased from 43/1,000 live births in 1990 to 23/1,000 live births in 2021[1]. Less data is available on hospitalization rates in sub-Saharan Africa, and prior work has focused on hospital-based studies[2] or specific conditions[3,4]. A Tanzanian population-based study conducted from 2010-2014 found neonatal hospitalization rates of 78/10,000 and 102/10,000 neonate-months at two sites, respectively[5]. Understanding rates and cofactors of mortality and hospitalization among neonates[5] can direct interventions and guide allocation of healthcare resources.

Maternal psychosocial factors, such as social support, self-efficacy, and depression, have been linked to infant outcomes at and shortly after birth. Interventions to increase self-efficacy have resulted in increased breastfeeding rates[6] while social support and depression have been associated with preterm delivery and birthweight[7–10]. Social support and self-efficacy have also been associated with infant care practices such as exclusive breastfeeding, hygiene practices, and clinic visits[11]. In turn, infant biological characteristics, such as preterm delivery, low birthweight, and male sex are known risk factors for hospitalization[5,12] and mortality[12]. Similarly, infant care practices have been shown to reduce hospitalizations and mortality[13–16]. While some research has demonstrated associations between maternal psychosocial factors and more distal outcomes, such as infant cortisol reactivity[17] and febrile illness[9], less is known about the relationship between these factors and infant hospitalization and mortality. Previous evidence suggests that maternal depression may be associated with infant illness and hospitalization[18].

Identifying individual determinants of mortality and hospitalization is an important step toward reducing adverse neonatal outcomes. Innate factors, such as maternal age and marital status, may be used to identify high-risk populations while modifiable factors, such as parental self-efficacy or early initiation of breastfeeding, may help target support for a given community. This study investigates whether maternal demographic, obstetric, and psychosocial factors and infant biological and care factors are associated with neonatal hospitalization and mortality. The results will identify high-risk populations and behaviors associated with adverse neonatal health outcomes and will be relevant to research and programmatic interventions offering perinatal support.

Methods

Parent study design

This cohort study is nested within a non-blinded randomized control trial, Mobile WACh NEO, which evaluated a text message intervention's effect on the outcome of neonatal mortality[19]. The Mobile WACh intervention is a human-computer hybrid system that uses two-way SMS communication and patient tracking to provide consistent support to women and their infants during the peripartum period. Participants were randomly assigned to the intervention and control groups at a 1:1 ratio.

Participants were enrolled in the third trimester of pregnancy and continued follow-up through 6 weeks following delivery[19]. Recruitment took place between September 7, 2020 and June 30, 2022. Participants were recruited from antenatal care visits at six clinics in southeastern Kenya: Bondo Sub-County Referral Hospital (Siaya County), Rachuonyo County Hospital (Homa Bay County), Ahero Sub-District Hospital and Kisumu County Hospital (Kisumu County), and Mathare North Health Centre and Riruta Health Center (Nairobi County)[19]. These clinics are situated in urban and rural areas. Individuals were eligible for the randomized control trial if they were pregnant between 28 and 36 weeks gestation; 14 years of age or older; had daily access to a mobile phone on the Safaricom network; were willing to receive SMS messages; were able to read and respond to text messages in English, Kiswahili, or Luo, or had someone in their household who could help; and planned on living in the same area for at least 5 months postpartum. The last eligibility criterion was dropped on February 22, 2022.

Eligibility criteria

The study cohort was restricted to participants in the control arm of the parent trial because the text message intervention was designed to impact on neonatal hospitalization and mortality. Stillbirths were also excluded, as neonatal hospitalization and mortality rates are calculated among live births. The recorded narrative of all demises was reviewed by a neonatologist and an obstetrician to disaggregate stillbirths from early neonatal deaths. Discrepancies were discussed to determine a final classification for each demise. Participant-infant pairs who were lost to follow-up before delivery or who were missing information on infant vital status at delivery were excluded. Finally, only first-born neonates were included in the analysis to maintain independence between observations.

Data collection

Data for exposure variables were collected through participant interviews at enrollment, shortly following notification of delivery, and at study visits two and six weeks after delivery (Figure 1)[19]. Interviews were conducted over the phone or at the study clinic by trained study nurses. If a participant missed the 2- or 6-week study visit by 1 week, the study team conducted tracing by calling the participant's phone. If unsuccessful, they called additional contacts provided by the participant at enrollment or attempted to visit the participant's residence.

Data on death and hospitalization outcomes was collected via a severe adverse event (SAE) form, which was used to record locations, dates, symptoms, and outcomes[19]. SAE forms were filled out when participants reported infant hospitalization or death during the 2- or 6-week study visits. If a participant reported a hospitalization or death to the study team in between study visits, the participant was immediately contacted for additional information to complete the SAE form.

Weekly data quality checks were performed throughout data collection, and the data manager worked with study nurses to clarify and correct inconsistencies. Post-collection data cleaning was also conducted in collaboration with on-site study staff.

Outcome

The two outcomes evaluated were incidence of neonatal mortality and hospitalization, respectively. While participants were asked whether infants were hospitalized prior to death, date of hospital admission was not explicitly recorded in case of infant deaths. In these cases, manual review of the recorded SAE narrative was conducted to determine date of hospital admission. If an infant was hospitalized multiple times, only the first hospitalization was considered.

Exposures

We assessed five types of exposures: a) maternal demographic and socioeconomic, including age, partnership status, years of education, employment status, and household income/wealth; b) maternal obstetric, including number of prior pregnancies and facility delivery; c) maternal psychosocial, including

social support score, parental self-efficacy score, and depression score; d) infant biological, including gestational age at delivery and birthweight; and e) infant care practices, including appropriate cord care, appropriate thermal care, and early initiation of breastfeeding.

All maternal predictors except for facility delivery were collected through in-person participant surveys at enrollment; facility delivery was collected through a phone interview to the participant shortly after the study team was notified of delivery. Age and number of prior pregnancies were treated as continuous variables. Years of education was dichotomized between completed secondary education and did not complete secondary education, partner status was dichotomized between married or cohabitating with partner and other responses, employment status was dichotomized between any employment and other responses, and facility delivery was dichotomized between facility delivery and all other responses.

Maternal psychosocial scores were treated as both continuous and dichotomous measures, measured using the Medical Outcomes Study (MOS) Social Support Survey[20], the Karitane Parenting Confidence Scale (KPCS)[21], and the Edinburgh Postnatal Depression Scale (EPDS)[22], respectively. All scored variables have been validated several cultural contexts[23–31].

The MOS is a transformed mean score comprised of 19 items and ranges from 0 to 100, where higher scores represent higher levels of perceived social support. One item in the MOS was modified based on site staff recommendation to make the tool more culturally appropriate. The question “Do you have someone who hugs you” was changed to “Do you have someone who compliments you”, as hugging is not a common sign of affectionate support in Kenya and compliments would be a more culturally accepted sign of affection. In models where social support was treated as a binary predictor, individuals were coded as above or below the cohort median score (1 = above 81.5, 0 = below 81.5).

The KPCS is a summed score comprised of 15 items and ranges from 0 to 45, where higher scores represent higher levels of perceived parental self-efficacy. The clinical ranges for the KPCS are non-clinical range (40–45), mild clinical range (36–39), moderate clinical range (31–35), and severe clinical range (less than 31). Participants were classified as clinical or non-clinical (1 = mild, moderate, or severe clinical range, 0 = non-clinical range) in models where self-efficacy was treated as a binary predictor.

The EPDS is a summed score comprised of 10 items and ranges from 0 to 30, where higher scores indicate the presence of more depressive symptoms. Scores of 13 or greater are commonly used as clinical

thresholds indicating depression, and McCabe-Beane et al. have proposed the following ranges for EPDS: none or minimal depression (0–6), mild depression (7–13), moderate depression (14–19), and severe depression (19–30)[32]. In models where depression was treated as a binary predictor, participants were classified as moderate or severely depressed (13-30) or mild to no depression (0–12).

First trimester ultrasounds, considered the gold standard for estimating gestational age[33], are uncommon in the study area[34]. We followed the American College of Obstetricians and Gynecologists guidelines for determining gestational age using ultrasounds taken in the second and third trimester, respectively[33]. Specifically, participants' gestational age was calculated from ultrasounds prior to enrollment when available. When unavailable, gestational age was derived from the maternal and child health booklet, which came from the participants' last menstrual period or healthcare worker estimation. Some participants received ultrasounds between enrollment and delivery (in the third trimester), and this gestational age was used if the difference between the third-trimester ultrasound gestational age and the booklet gestational age was greater than 21 days. Gestational age was ultimately derived from an ultrasound for 16% of participants; last menstrual period or healthcare worker estimate were used to determine gestational age for the remaining participants. Birthweight was recorded in kilograms to the nearest decimal point from participants' maternal and child health booklet at the 2- or 6-week study visit. If the booklet was unavailable, participants reported infant birthweight. Infant sex was recorded during the 2- and 6-week study visits; if these variables were missing, infant sex recorded during the delivery report was used. Preterm delivery was defined as deliveries prior to 37 weeks of estimated gestational age, and infants weighing less than 2.5 kilograms were classified as low birthweight.

We defined appropriate cord care as no application of substances to the cord in accordance with WHO recommendations at study start[35]. During data collection, WHO released updated guidelines the including application of the antiseptic chlorhexidine as appropriate cord care when it replaces the application of harmful substances[36]; this aligns with the Kenya Ministry of Health recommendations[37]. Therefore, we added an additional question asking what type of antiseptics were applied. Approximately 30% of participants were asked this question. Appropriate thermal care was defined as delaying 1st infant bath for at least 24 hours following delivery, and early initiation of breastfeeding was defined as breastfeeding within 1 hour of delivery. Cord care and thermal care questions were asked at the 2-week visit or the 6-week visit

if the participant missed the 2-week visit. Early initiation of breastfeeding was only asked at the 2-week visit because we expected participant recall may be inaccurate six weeks after the event. This led to higher missingness in the early initiation of breastfeeding variable.

Data analysis

Cumulative incidence and incidence rate of neonatal hospitalization and mortality were calculated. For incidence rate, the time to event or censored outcome was calculated for each infant. Infants could be censored at loss to follow-up, 28 days of life, or death (for calculation of hospitalization incidence).

Calculated time to event or censorship was used as the outcome variable in the Cox proportional-hazards models. Univariate models were used to estimate hazard ratios (HRs) for each predictor-outcome pair. Predictors with a p-value of <0.1 were included in the multivariate model for each outcome.

Infants who are immediately hospitalized or die shortly after birth do not have the opportunity to receive infant care practices prior to the outcome event. Furthermore, healthcare workers are responsible for the care of infants hospitalized at birth, and therefore mother participants may have limited ability to perform infant care practices. Thus, for analyses which included infant care practices (cord care, thermal care, and early initiation of breastfeeding), infants with hospitalizations and deaths occurring during delivery hospitalizations were excluded. We used the SAE forms to distinguish hospitalizations due to normal delivery and hospitalizations due to illness. Study staff filled out SAE forms when a participant reported that an infant was held for a prolonged period after delivery due to a diagnosed condition. A manual review of the event narrative classified hospitalizations as a delivery hospitalization if the infant was hospitalized without discharge following delivery and as a post-delivery hospitalization if the infant was brought to the healthcare facility.

We implemented separate multivariate models for birthweight and estimated gestational age if both had $p<0.1$ in the univariate models due to collinearity. If infant care practices were significant at $p<0.1$ in the univariate models, we implemented one set of multivariate models without the infant care practices variable(s), including all outcome events, and another set of multivariate models with the infant care practices variable(s), excluding events during delivery hospitalization. The first set of models was intended to understand predictors of all deaths and hospitalizations, including those which occurred soon after birth.

They also provided more power to detect relationships since excluding events during delivery hospitalization reduced our sample size. The second set of models allowed us to specifically examine the role of infant care practices in neonatal mortality and hospitalizations. All analyses were conducted in R (version 4.2.2).

Ethical review

The parent study was reviewed and approved by University of Washington Institutional Review Board and Kenyatta National Hospital Ethical Review Committee. All participating women provided written informed consent.

Results

Study cohort

Of the 5,020 participants randomized in the parent trial, 7 were later discovered to have not been eligible at the time of enrollment and were not retained in analysis. Of these participants, 2508 were randomized to the control group and 2451 were included in the study cohort (Figure 2).

Among 2508 participants in the control arm, median age was 25 (interquartile range [IQR] 22, 29) and 1468 (60%) reported completing at least 12 years of education (Table 1). Two-thousand and four (82%) of participants were married or cohabitating with their partner, and 901 (37%) reported any type of employment. The median monthly household income was 106 US dollars (USD)[38] (IQR 71, 177), although 1035 (42%) of participants did not report household income.

Eight hundred and five (33%) of participants reported this was their first pregnancy, and 2,365 (98%) delivered in a healthcare facility. Rates of healthcare facility delivery were high across sites, ranging from 95% to 98% (data not shown). The median baseline MOS score was 82.9 out of 100 (IQR 65.8, 100), indicating high perceived levels of social support among the population. Similarly, the median KPCS score was 45 out of 45 (IQR 41, 45), indicating high levels of parental self-efficacy at enrollment. There was a higher rate of missingness (14%) for this construct because KPCS is a summed variable, meaning if a participant did not answer one item in the 15-question instrument the score was marked as missing. Median

baseline EPDS score was 1 out of 30 (IQR 0, 4), indicating low levels of depressive symptoms; prevalence of depressive scores at or above the standard clinical threshold of 13 was 3%.

The median gestational age at delivery was 39.6 weeks (IQR 38.1, 40.7), with 311 (13%) deliveries classified as preterm. The median birthweight was 3.2 kg (IQR 3.0, 3.5), with 126 (5%) deliveries classified as low birthweight. Forty-nine percent of live births were female. In follow-up visits, 2233 (95%) of participants reported appropriate thermal care, while 1402 (70%) reported early initiation of breastfeeding. Almost half of participants (n=1104 [46%]) reported no application of substances to the cord, and another 1037 (44%) reported applying antiseptics (Table A1). Among those who were asked about types of antiseptic use (n=307), 82% reported applying chlorhexidine, indicating high rates of chlorhexidine use among those who reported applying antiseptics.

Incidence of hospitalization and mortality

There were 38 neonatal deaths and 50 neonates who were hospitalized. Cumulative mortality was 15.1/1,000 live births, and cumulative hospitalization incidence was 19.2/1,000 live births. The mortality incidence rate was 0.70/1,000 infant-days, and the hospitalization incidence rate was 0.55/1,000 infant-days. Thirty-four (68%) of hospitalizations were delivery hospitalizations.

Kaplan-Meier plots show that over 50% of deaths occurred in the first two days of life, with mortality rates declining throughout the first 28 days of life (Figure 3). Similarly, over 50% of hospitalizations occurred on the first day of life, after which the rate of hospitalization declined.

Univariate models

In the univariate models, neonatal mortality was associated with being primigravida (Hazard Ratio [HR]=1.95, 95% confidence interval [CI] 1.02, 3.72) (Table 3, Figure A1). Gestational age and birthweight were inversely associated with mortality, with HRs of 0.82 (95% CI 0.73, 0.93) and 0.41 (95% CI 0.20, 0.84) for increases of one week in gestational age and one kilogram in birthweight, respectively. Infant sex was strongly associated with mortality, with male infants having a 2.02-fold higher risk (95% CI 1.02, 4.02) than female infants. Appropriate cord care had a marginally significant association with higher neonatal mortality with a large effect size, with those receiving appropriate cord care having a mortality hazard of 3.50 (95%

CI 0.95, 12.95) times that of infants who had substances applied to their cord. Maternal age was also marginally associated with neonatal mortality, with the neonates of younger mothers more likely to die compared to older mothers (HR = 0.94, 95% CI 0.88, 1.00).

Neonatal hospitalization was also associated with being primigravida (HR=1.82, 95% CI 1.02, 3.22) (Figure A2). Similarly, gestational age and birthweight were also inversely associated with hospitalization with hazard ratios of 0.83 (95% CI 0.75, 0.92) and 0.37 (95% CI 0.21, 0.68), respectively. Early initiation of breastfeeding was associated with lower risk of hospitalization, with neonates who received early initiation of breastfeeding having a 88.3% lower risk of hospitalization than neonates who did not receive early initiation of breastfeeding (95% CI 0.03, 0.42). Maternal education was also associated with hospitalization, with neonates whose mothers received 12 or more years of education more likely to be hospitalized (HR=1.96, 95% CI 1.02, 3.78) than those whose mothers received less education.

None of the continuous or binary maternal psychosocial factors were significantly associated with neonatal mortality or hospitalization. The models assessing associations of thermal care and mortality, thermal care and hospitalization, and facility delivery and hospitalization failed to converge.

We investigated the unexpected cord care results first by examining cord care as a categorical predictor which included the categories no substance applied (reference group), antiseptics, water, natural substance, and other substance. The categorical model failed to converge, as did a model with the simplified categories of no substances, antiseptics, and other substances. We then further reduced the categories to nothing and antiseptics, excluding participants who reported applying other substances to the cord; the findings were not significant (HR = 0.35, 95% CI 0.10, 1.30, p = 0.12). We then recoded participants who were asked the type of antiseptic and reported applying chlorhexidine as having given appropriate cord care and reran the models. The results were consistent with and more pronounced than the original results: the hazard ratio of mortality was 8.37-fold higher (95% CI 1.08, 64.85, p = 0.041) among those who applied either no substances or chlorhexidine versus those who applied other substances.

Multivariate models

Six predictors were eligible for inclusion in the multivariate mortality models: age, primigravida, gestational age, birthweight, sex, and appropriate cord care. The first two models included all neonatal deaths and did

not include appropriate cord care as a predictor; separate models were run adjusting for gestational age and birthweight to minimize collinearity. Increased birthweight was associated with decreased risk of mortality adjusting for maternal age, primigravida, and infant sex (HR = 0.41, 95% CI 0.20, 0.83), while increased gestational age was also associated with decreased risk of mortality adjusting for the same factors (HR = 0.83, 95% CI 0.74, 0.93) (Table 3). Male sex was significantly associated with increased risk of mortality in the birthweight model (HR = 2.24, 95% CI 1.05, 4.76) and marginally associated with mortality in the gestational age model (HR = 1.91, 95% CI 0.96, 3.81).

The second set of multivariate mortality models included appropriate cord care and excluded deaths that occurred during delivery hospitalization. In the gestational age model, appropriate cord care was marginally associated with increased mortality (HR = 3.48, 95% CI 0.94, 12.90), adjusting for maternal age, primigravida, gestational age, and infant sex. None of the other predictors were significantly associated with mortality. In the birthweight model, none of the predictors were significantly associated with neonatal mortality.

Five predictors were eligible for inclusion in the multivariate hospitalization model: education, primigravida, gestational age, birthweight, and early initiation of breastfeeding. As above, we ran two sets of models, first including all hospitalization events and then excluding delivery hospitalization events. In the first set of models, increased birthweight was associated with a decreased risk of hospitalization adjusting for primigravida and maternal education (HR = 0.39, 95% CI 0.21, 0.72), and increased gestational age was also associated with a decreased risk of hospitalization adjusting for the same factors (HR = 0.81, 95% CI 0.73, 0.91) (Table 4). Primigravida and maternal education were not significant in either mode. In the second set of models, infants with early initiation of breastfeeding had lower risk of hospitalization compared to those without early breastfeeding initiation in the model controlling for birthweight, primigravida, and maternal education (HR = 0.11, 95% CI 0.02, 0.49). There were similar findings in the gestational age model, where the HR for early initiation of breastfeeding was 0.16 (95% CI 0.04, 0.59). No other predictors in either model were significantly associated with hospitalization.

Discussion

In this study, we observed a cumulative firstborn neonatal mortality rate of 15.0 per 1000 live births, which was lower than the most recently published Kenyan Demographic Health Survey estimates of 21 neonatal deaths per 1000 live births from 2018 to 2022[39]. Neonatal mortality in Kenya declined from 33 deaths/1000 live births in 2003, and our data collected from 2020 to 2022 may indicate that neonatal deaths have continued to decline. Nationwide trends such as increases in antenatal care visits and deliveries attended by a skilled provider in Kenya may have contributed to this decline[39–41]. Our results also support prior research that approximately half of neonatal deaths occur within 48 hours of delivery[42]. Our observed rate of 19.2 neonatal hospitalizations per 1000 live births adds to the literature as there are few published estimates of neonatal hospitalization rates in sub-Saharan Africa. A prior study in western Kenya found a cumulative hospitalization rate of 9.7 hospitalizations per 1000 live births among a cohort of infants followed for nine months post-delivery[43]. The lower observed rate may represent differences in care-seeking between the two study areas, challenges of event recall for parents with young children, or difference in overall follow-up period. A centralized electronic medical records system could help improve data capture for neonatal hospitalizations and deaths in Kenya, although implementation challenges include integration with current paper-based record systems[44].

We observed associations between adverse neonatal outcomes and maternal primigravida status, maternal age, gestational age, birthweight, and infant sex. The risk of neonatal mortality was higher among infants born to women experiencing their first pregnancy[45], in part due to higher prevalence of low birthweight babies among younger mothers[46]. Maternal age was marginally associated with neonatal mortality in the univariate model, and this may reflect the U-shaped relationship between age and birthweight[46] which may not have been captured in a linear model. However, higher rates of neonatal hospitalization and mortality among mothers younger than 25 are evident in the Kaplan-Meier plots (Figure A1). Male neonates had two-fold higher risk of mortality compared to females, a trend that has been widely documented[47]. Delivery facilities can identify higher-risk infants based on maternal age and infant sex and should direct resources toward these populations. Infants born preterm had a 2.94-fold increased risk of mortality and a 2.98-fold risk of hospitalization. Overall, 13% of infants in our cohort were born preterm and 71% of deaths occurred in preterm infants. Preterm and low birthweight deliveries are closely linked, and in our cohort low

birthweight infants had a 4.43-fold increased risk of mortality and a 4.26-fold risk of hospitalization. Only 5% of infants were low birthweight, while 74% of deaths occurred in low birthweight infants. Preterm birth is the leading cause of global neonatal mortality[48], but progress has been made; healthcare interventions such as increased use of antenatal steroids, respiratory management, and surfactants have been linked to decreased rates of neonatal mortality among preterm infants[49]. A randomized control trial in Kenya and Uganda demonstrated that a delivery facility-level intervention containing a childbirth checklist, checklist implementation training, quality improvement plans, and data management to track progress led to a decrease in stillbirth or neonatal death among preterm and low birthweight babies[50]. Even farther upstream, interventions to improve access to antenatal care have been shown to reduce perinatal mortality and frequency of low birthweight infants, indicating that combined health system and community interventions should be a focus for improving neonatal outcomes[51].

Early initiation of breastfeeding was strongly protective against hospitalization in univariate and multivariate models. This is consistent with literature noting the marked benefits of early breastfeeding[52,53]. It is possible that infants born ill may have been unable to immediately latch[54] and, independently, were more likely to die or be hospitalized. To mitigate this potential confounder, we excluded infants born with severe illness by excluding hospitalizations that began at delivery. In this analysis the protective effect was retained. Thus, this association likely reflects a true relationship between early breastfeeding and decreased neonatal hospitalization. Among participants with data, 70% reported early initiation of breastfeeding. Given that most deliveries occurred in a healthcare facility, this indicates an opportunity for support and intervention. Hospital staff training programs can prepare healthcare workers to offer mothers emotional and practical breastfeeding support and have been shown to improve rates of early initiation of breastfeeding[55,56]. The WHO-led Baby-Friendly Hospital Initiative includes comprehensive recommendations for healthcare facilities to support infant feeding[57], and a meta-analysis found a dose-response relationship between the number of practices a mother is exposed to and positive breastfeeding outcomes[58]. Future interventions should focus on improving healthcare facility support for breastfeeding in the postpartum period.

Appropriate cord care was associated with increased risk of mortality in both univariate and multivariate models, although the relationship was not statistically significant. This effect is contrary to published data[59]. This may have been due to combining infants who received chlorhexidine or other antiseptics with those

who received other substances. However, none of our analyses found a strong protective effect of either no substances or chlorhexidine. It is possible that an undefined confounder led to the association between dry cord care and neonatal mortality. For example, infant illness at birth could potentially lead to both better cord care and increased risk of mortality. We attempted to control for this factor by excluding deaths occurring during delivery hospitalization. It is also possible that the small number of post-hospitalization delivery mortalities (n=15) influenced our results by chance. Two randomized control trials conducted in sub-Saharan Africa have found no difference in neonatal mortality rate between groups practicing dry cord care and those applying chlorhexidine[60,61], and Osrin and Colbourn suggested that the benefit of chlorhexidine is reduced in settings with high facility delivery rates and neonatal mortality rates of less than 30 / 1,000 live births[62]. Given that we did not start collecting data on type of antiseptics used until midway through the trial, we ultimately did not have enough data on chlorhexidine use to disaggregate its effects from the effects of no substance.

Maternal education was strongly associated with neonatal hospitalization in the univariate model, although the relationship was non-significant in the multivariate model. This supports prior findings that Kenyan mothers with higher levels of education are more likely to seek care in response to observed child illness[63,64] and neonatal danger signs[65]. Education could also be a proxy for access to healthcare, as women in urban areas tend to have higher education than those in rural settings[66]. Interestingly, education was not associated with mortality, which has been observed in other studies[41]. This could indicate that more educated participants disproportionately sought care for non-fatal conditions which were still serious enough to require hospitalization. The difference in hospitalization rates between mothers who had and had not completed secondary education suggests an opportunity to increase appropriate care-seeking. Interventions such as mHealth programs may approach this issue by meeting mothers' health education needs[67,68], while post-natal checklists administered by community health workers aim to increase contact with the healthcare system[69].

No significant relationship was observed between social support, parental self-efficacy, or depression and adverse neonatal outcomes. Baseline mean maternal psychosocial scores indicated high perceived levels of social support and parental self-efficacy and low levels of depressive symptoms, and the low variation in these characteristics could contribute to lack of observed associations. We were surprised by the low

proportion of participants with depression (3.2%) compared to prior research in the same study area[70–72]. We used a validated Kiswahili translation of the EPDS[73] and the study staff were retrained in administering the instrument halfway through data collection to ensure the data was being collected correctly; similar scores were observed before and after retraining. Although EPDS has been previously validated in the study area some studies have found that it demonstrates low sensitivity, suggesting EPDS may not be the optimal instrument for evaluating peripartum depression in this study population[71,74]. It is unclear why observed rates of depressive symptoms were lower than expected in this cohort.

There were extremely high rates of facility delivery (96.5%) and appropriate thermal care (91.1%), which led to unstable estimates in univariate models. Kenya has made great progress toward ensuring high rates of facility delivery. A national free maternal services policy introduced in 2013 eliminated delivery fees at public health facilities and was shown to increase facility-based deliveries[75]. Furthermore, the Kenyan Demographic Health Survey estimates that the percentage of deliveries attended by a skilled provider increased from 41% in 2003 to 89% in 2022[39]. Prior research in Kenya also found high rates of immediate drying after facility delivery, indicating that certain aspects of thermal care are commonly practiced[76].

The lack of predicted association between maternal psychosocial factors and adverse infant outcomes may indicate the importance of structural factors rather than individual-level factors. Access to care, quality of care, and population trust in healthcare services have been identified as barriers to lowering rates of infant morbidity and mortality[77]. The infant death narratives from this study's SAE forms echo these observations, as many describe appropriate care-seeking by mothers but difficulties accessing adequate care. When not all factors are within the mothers' control, individual-level interventions to improve neonatal morbidity and mortality can only go so far. The increase in facility deliveries following national policy change shows that structural change can be an effective tool to improve neonatal health outcomes[75]. This success could be leveraged to further improve infant outcomes by increasing beneficial infant care practices such as early initiation of breastfeeding. To reduce rates of neonatal morbidity and mortality, multifaceted policy- and community-level changes must improve access and quality of care by focusing on the most at-risk populations, including mothers who are pregnant for the first time and those who have received less education.

Our study has strengths and limitations. This was a large multi-site study with extremely high retention (99.3%) enabling robust analyses of cofactors of neonatal mortality and hospitalization. We confirmed the large impact of preterm birth on neonatal outcomes and examined several relevant psychosocial and care-associated variables. Limitations of the study include suboptimal estimation of gestational age in the cohort, as most women did not receive first trimester ultrasounds. Birthweight was recorded from participants' maternal and child health booklet or participant report. Because birthweight was recorded to the nearest 10^{th} of a kilogram, infants weighing between 2.45 and 2.49 kgs may have been misclassified as normal weight. Despite potential misclassification, we still observed strong significant relationships between both predictors and mortality and hospitalization in univariate models. The observed associations may be biased toward the null and true associations may be stronger than here observed.

Despite the size of this cohort, low rates of hospitalization and mortality may have limited statistical power in our analyses, particularly in the multivariate models. Population-based studies may provide an advantage through larger sample size, but in areas without broad coverage of electronic medical records cohort studies are often the best data source for epidemiologic studies. Additionally, we could not confirm all hospitalizations and deaths with medical records. This could result in missed hospitalization or mortality events or inaccurate recall of the events. However, given the high retention it is unlikely we missed many outcomes. In addition, participants or a close contact of the participant were contacted immediately after the event to complete the SAE form, reducing the risk of inaccurate recall.

The incidence of neonatal mortality observed in this study is consistent with a continued decline of neonatal deaths in Kenya. We also present incidence of neonatal hospitalization among a community cohort, which may be used by healthcare practitioners to allocate healthcare resources. Maternal primigravida status, gestational age, birthweight, and infant sex were associated with neonatal mortality, while maternal education, primigravida status, gestational age, and birthweight were associated with neonatal hospitalization. Observed associations between appropriate cord care and mortality and early initiation of breastfeeding and hospitalization may have been confounded by infant illness at birth. In particular, deeper investigation into the role of chlorhexidine application on neonatal mortality is warranted. Healthcare facility- and systems-level interventions should be implemented to reduce neonatal mortality among high risk groups.

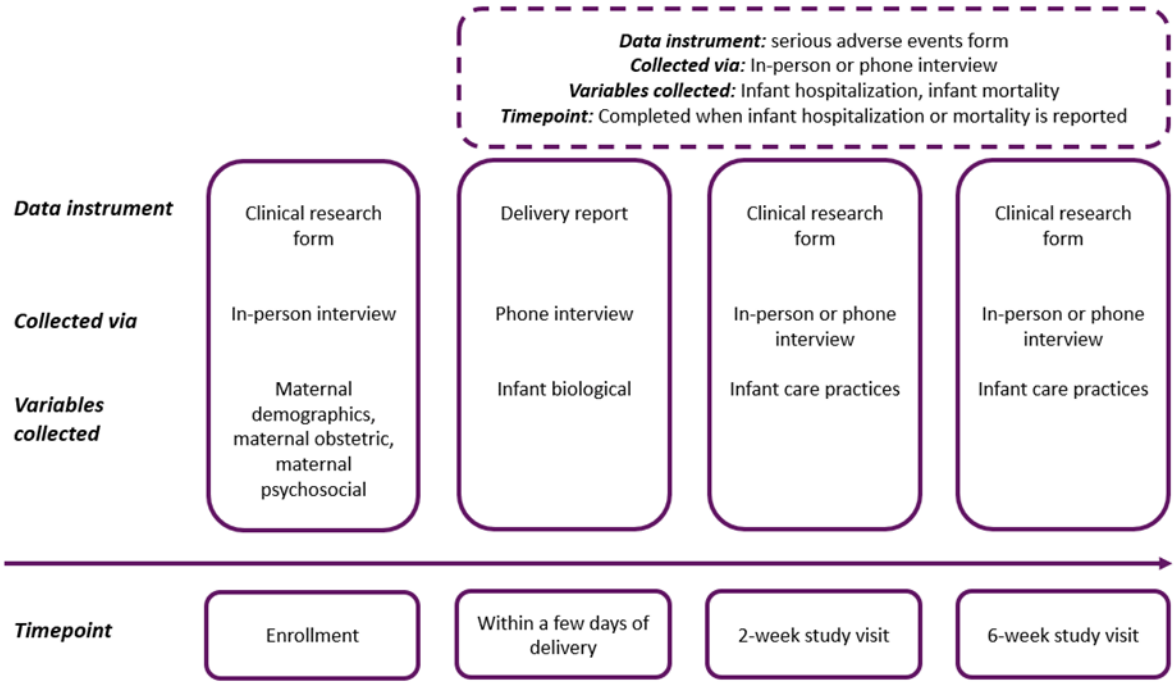


Figure 1: Sequence of data collection for typical participant in Mobile WACh NEO randomized control trial.

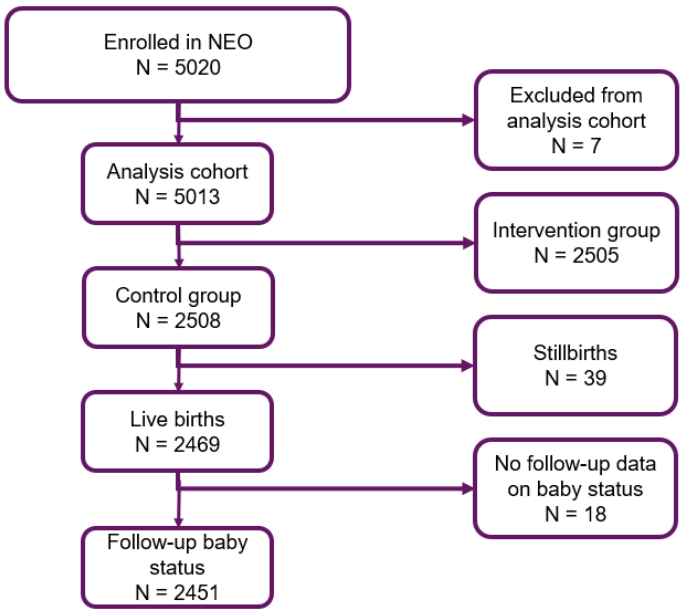


Figure 2. Consort diagram.

Table. 1. Descriptive characteristics of cohort of Kenyan mother-infant pairs.

	N*	Overall (N=2451) n (%); median (IQR)	
Maternal demographic			
Age (years)	2451	25	(22 – 29)
Completed secondary education	2451	1468	(59.9)
Married/cohabitating	2448	2004	(81.9)
Employment	2451	901	(36.8)
Household income (USD)	1416	106 (71 – 177)	
Maternal obstetric			
Primigravida	2451	805	(32.8)
Facility delivery	2417	2365	(97.8)
Maternal psychosocial			
Social support score (MOS)	2448		
Median (IQR) score		82.9	(65.8 – 100)
Self-efficacy score (KPCS)	2115		
Median (IQR) score		45	(41 – 45)
n (%) in mild, moderate or severe clinical range (<40)		399	(18.9)
Depression score (EPDS)	2447		
Median (IQR) score		1	(0 – 4)
n (%) in moderate or severe clinical range (≥13)		78	(3.2)
Infant biological			
Gestational age (weeks)	2451	39.6	(38.1 – 40.7)
Preterm	2451	311	(12.7)
Birthweight (kg)	2409	3.2	(3.0 – 3.5)
Low birthweight	2409	126	(5.2)
Female sex	2429	1192	(49.1)

Infant care practices			
Appropriate cord care (did not apply substances)	2378	1104	(46.4)
Appropriate thermal care (delayed first bath)	2344	2233	(95.3)
Early initiation of breastfeeding (within 1 hour)	2007	1402	(69.9)

*Number of non-missing responses

Figure 3. Kaplan-Meier curve for neonatal mortality and hospitalization among a cohort of Kenyan mother-infant pairs.

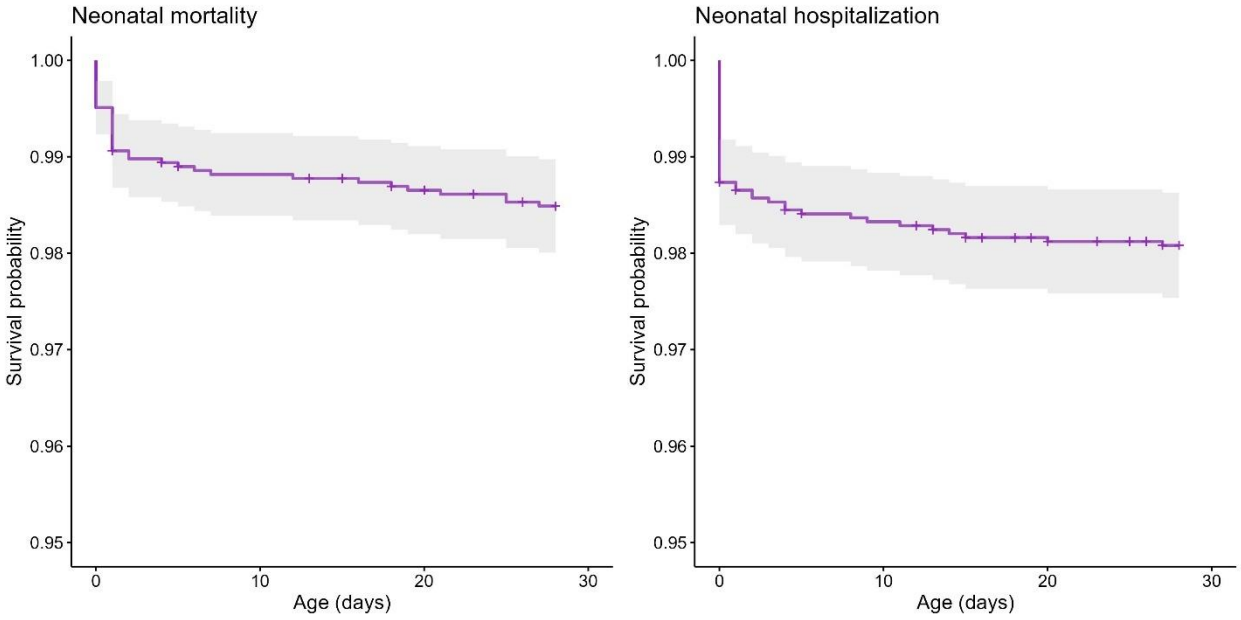


Table 2. Maternal and infant cofactors of neonatal mortality and hospitalization (univariate analyses).

	Mortality			Hospitalization		
	HR	95% CI	P-value	HR	95% CI	P-value
Maternal demographic						
Age	0.938	0.876, 1.003	0.061	0.989	0.937, 1.045	0.704
>12 years education	1.396	0.701, 2.779	0.342	1.963	1.019, 3.781	0.044*
Household income (KES)	1.000	1.000, 1.000	0.328	1.000	1.000, 1.000	0.149
Marital status	0.802	0.366, 1.753	0.580	0.721	0.367, 1.417	0.343
Employment status	1.046	0.538, 2.033	0.895	0.974	0.537, 1.766	0.931
Maternal obstetric						
Primigravida	1.951	1.024, 3.717	0.042*	1.815	1.023, 3.219	0.041*
Facility delivery	0.371	0.089, 1.545	0.173	NA†	NA	NA
Maternal psychosocial						
Social support (MOS)						
Continuous	0.993	0.977, 1.008	0.354	1.000	0.986, 1.015	0.980
Above median score	0.700	0.366, 1.342	0.283	0.921	0.517, 1.641	0.779
Self-efficacy (KPCS)						
Continuous	0.998	0.930, 1.070	0.948	1.019	0.952, 1.09	0.593
Mild, moderate, or severe clinical range (<40)	0.824	0.316, 2.145	0.692	0.594	0.233, 1.513	0.275
Depression (EPDS)						
Continuous	1.040	0.970, 1.115	0.273	1.022	0.955, 1.094	0.523
Moderate or severe clinical range (≥13)	1.737	0.418, 7.222	0.448	1.355	0.329, 5.584	0.675
Infant biological						
Gestational age (weeks)	0.823	0.730, 0.927	0.001*	0.828	0.745, 0.921	0.001*

Preterm	2.942	1.454, 5.954	0.003*	2.975	1.592, 5.558	0.001*
Birthweight (kg)	0.414	0.203, 0.843	0.015*	0.374	0.205, 0.682	0.001*
Low birthweight	4.433	1.818, 10.805	0.001*	4.259	1.976, 9.181	<0.001*
Sex (1=male, 0=female)	2.020	1.015, 4.020	0.045*	1.305	0.732, 2.326	0.367
Infant care practices						
Appropriate cord care^	3.505	0.949, 12.946	0.060	0.728	0.238, 2.226	0.578
Appropriate thermal care^	NA†	NA	NA	NA†	NA	NA
Early initiation of breastfeeding^	0.430	0.087, 2.130	0.301	0.160	0.043, 0.604	0.007*

^Outcomes from delivery hospitalization excluded

†Model did not converge

Table 3: Maternal and infant cofactors of neonatal mortality (multivariate analyses).

	Birthweight^			Gestational age^		
	HR	95% CI	P-value	HR	95% CI	P-value
No care practices, all deaths† (N=2451)						
Birthweight (kg)	0.405	0.198, 0.827	0.013*			
Gestational age (weeks)				0.828	0.736, 0.932	0.002*
Primigravida	1.898	0.792, 4.546	0.151	1.644	0.744, 3.632	0.219
Maternal age	0.987	0.905, 1.075	0.760	0.967	0.893, 1.047	0.405
Sex (1=male, 0=female)	2.235	1.049, 4.761	0.037*	1.911	0.959, 3.811	0.066
Care practices, no delivery hospitalization deaths‡ (N=2428)						
Birthweight (kg)	0.53	0.143, 1.965	0.342			
Gestational age (weeks)				0.951	0.763, 1.186	0.657
Primigravida	0.885	0.217, 3.606	0.865	1.406	0.303, 6.527	0.663
Maternal age	0.966	0.845, 1.104	0.610	1.006	0.871, 1.161	0.936
Sex (1=male, 0=female)	2.000	0.601, 6.652	0.258	2.550	0.652, 9.982	0.179
Appropriate cord care	3.477	0.937, 12.901	0.062	2.846	0.732, 11.062	0.131

^Models included either birthweight or gestational age to avoid collinearity.

†Models include covariates with p<0.1 in the univariate models except for infant care practices. All deaths are included in the outcome measure.

‡Models include all covariates with p<0.1 in the univariate models, including infant care practices. Therefore, only deaths occurring after delivery hospitalization are included in the outcome measure.

Table 4: Maternal and infant cofactors of neonatal hospitalization (multivariate analyses).

	Birthweight^			Gestational age^		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
No care practices, all hospitalizations† (N=2451)						
Birthweight (kg)	0.389	0.212, 0.715	0.002*			
Gestational age (weeks)				0.812	0.729, 0.905	<0.001*
Primigravida	1.513	0.813, 2.816	0.191	1.614	0.894, 2.914	0.112
>12 years education	1.487	0.746, 2.961	0.259	1.951	0.988, 3.854	0.054
Care practices, no delivery hospitalizations‡ (N=2417)						
Birthweight (kg)	0.875	0.244, 3.143	0.838			
Gestational age (weeks)				0.997	0.751, 1.323	0.982
Primigravida	0.369	0.077, 1.777	0.214	0.327	0.07, 1.538	0.157
>12 years education	2.958	0.616, 14.206	0.175	3.471	0.737, 16.354	0.116
Early initiation of breastfeeding	0.105	0.022, 0.494	0.004*	0.156	0.041, 0.590	0.006*

^Models included either birthweight or gestational age to avoid collinearity.

†Models include covariates with p<0.1 in the univariate models except for infant care practices. All hospitalizations are included in the outcome measure.

‡Models include all covariates with p<0.1 in the univariate models, including infant care practices. Therefore, only hospitalizations occurring after delivery discharge are included in the outcome measure.

Appendix

Table A1: Cord care practices among a cohort of Kenyan mother-infant pairs.

	Overall N=2541 n (%)
Substance applied	
No substance applied	1104 (45.0)
Antiseptics	1037 (42.3)
Natural substances	30 (1.2)
Water	34 (1.4)
Other	173 (7.1)
Missing	73 (3.0)
Type of antiseptic applied	N=777
Did not apply antiseptic	470 (60.5)
Applied antiseptic	307 (39.5)
Chlorhexidine	252 (82.1)
Other antiseptic	55 (17.9)

Table A2: Univariate hazard ratios of infant cord care with neonatal mortality among a cohort of Kenyan mother-infant pairs, where the reference group is no substance application.

	HR	95% CI	P-value
5 category model†			
Antiseptics	NA	NA	NA
Water	NA	NA	NA
Natural substances	NA	NA	NA
Other	NA	NA	NA
3 category model†			
Antiseptics	NA	NA	NA
Other	NA	NA	NA
2 category model			
Antiseptics	0.351	0.095, 1.295	0.116

† Model did not converge

Table A3: Univariate hazard ratios of infant cord care with neonatal mortality among a cohort of Kenyan mother-infant pairs, where no application of substances and application of chlorhexidine are coded as appropriate cord care.

	HR	95% CI	P-value
Entire cohort (n=2541)	8.372	1.081, 64.847	0.042
Among those asked chlorhexidine question† (n=777)	NA	NA	NA

† Model did not converge

Figure A1: Kaplan-Meier curves for neonatal mortality by maternal age (younger vs. older than median age), primigravida status, preterm, low birthweight, infant sex, and cord care practices.

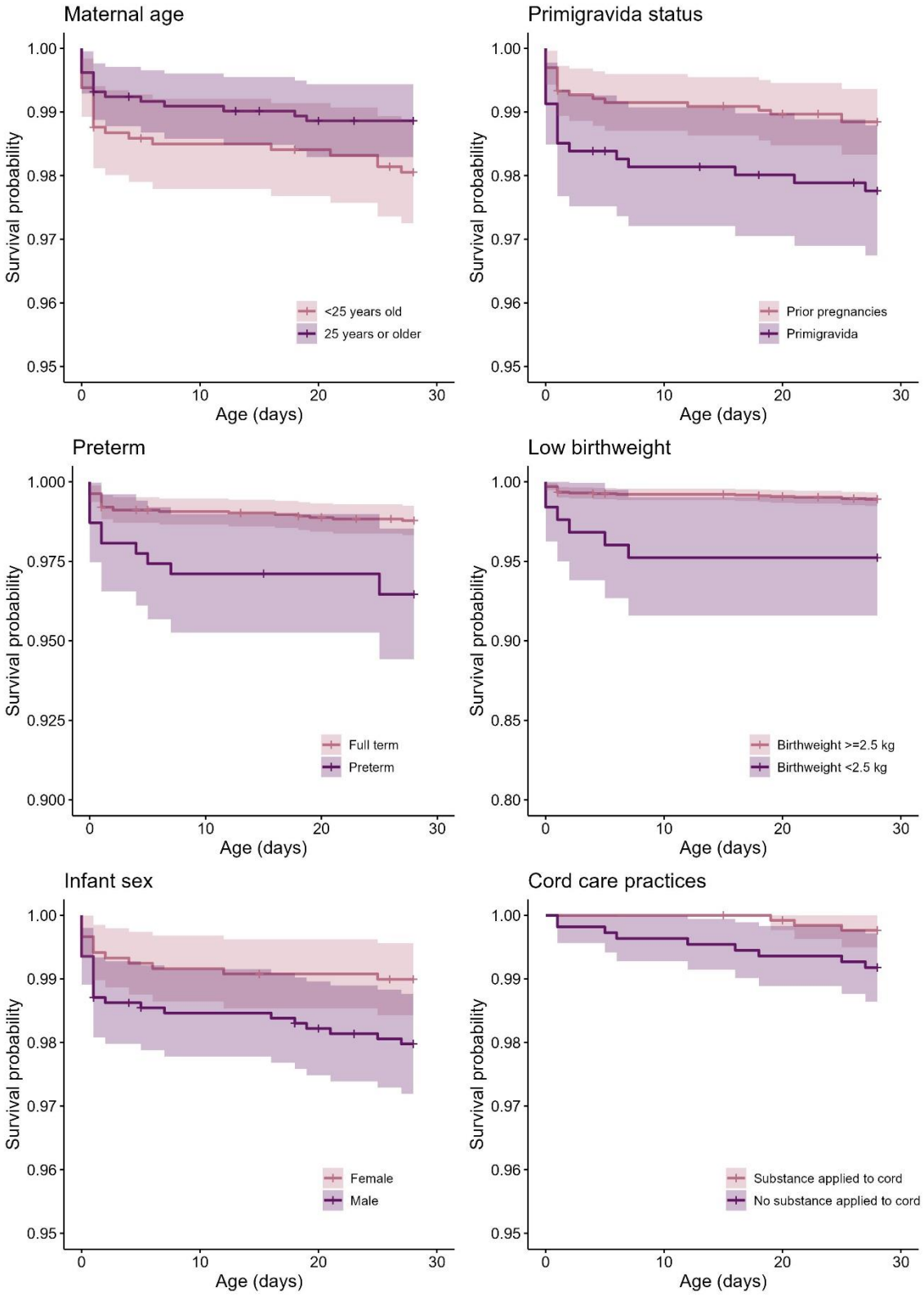
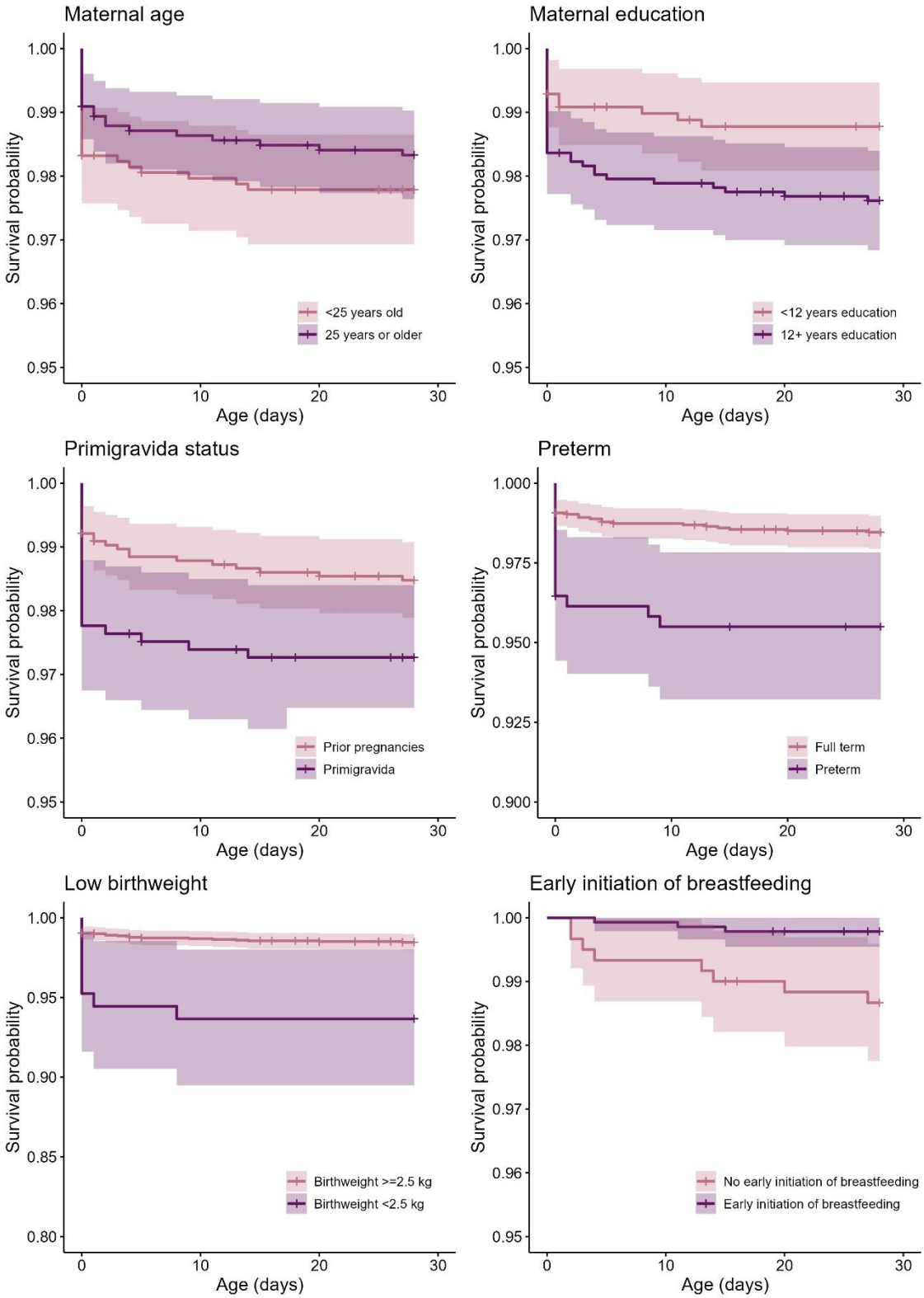


Figure A2: Kaplan-Meier curves for neonatal hospitalization by maternal age, maternal education, primigravida status, preterm, low birthweight, and early initiation of breastfeeding.



References

1. CME Info - Child Mortality Estimates. https://childmortality.org/profile.
2. Rurangwa, J. & Rujeni, N. Decline in Child Hospitalization and Mortality after the Introduction of the 7-Valent Pneumococcal Conjugative Vaccine in Rwanda. *Am. J. Trop. Med. Hyg* **95**, 680–682 (2016).
3. Emukule, G. O. *et al.* Influenza-associated pneumonia hospitalizations in Uganda, 2013-2016. *PLoS One* **14**, e0219012 (2019).
4. Roddy, P. *et al.* Quantifying the incidence of severe-febrile-illness hospital admissions in sub-Saharan Africa. *PLoS One* **14**, e0220371 (2019).
5. Briegleb, C. *et al.* Predictors of Hospitalization During the First Year of Life among 31 999 Tanzanian Infants. *J Trop Pediatr* **61**, 317–328 (2015).
6. Brockway, M., Benzies, K. & Hayden, K. A. Interventions to Improve Breastfeeding Self-Efficacy and Resultant Breastfeeding Rates: A Systematic Review and Meta-Analysis. *J Hum Lact* **33**, 486–499 (2017).
7. Viviana Paredes Mondragón, C., Molano Dorado, H., Yamile Martínez Gómez, S., Alirio Ortiz Martínez, R. & Arias Linthon Andrés Camilo López Benavides, S. Artículo original Relación entre la ausencia de soporte social adecuado durante el embarazo y el bajo peso al nacer. (2017) doi:10.1016/j.rcp.2017.11.002.
8. Dibaba Wado, Y., Afework, F. & Hindin, M. J. Effects of Maternal Pregnancy Intention, Depressive Symptoms and Social Support on Risk of Low Birth Weight: A Prospective Study from Southwestern Ethiopia. doi:10.1371/journal.pone.0096304.
9. Dadi, A. F., Akalu, T. Y., Wolde, H. F. & Gebreegziabher Baraki, A. Effect of perinatal depression on birth and infant health outcomes: a systematic review and meta-analysis of observational studies from Africa. doi:10.1186/s13690-022-00792-8.
10. Jarde, A. *et al.* Neonatal Outcomes in Women With Untreated Antenatal Depression Compared With Women Without Depression: A Systematic Review and Meta-analysis. *JAMA Psychiatry* **73**, 826–837 (2016).

11. Sokefun, E. E. & Atulomah, N. O. Predictors of infant-survival practices among mothers attending paediatric clinics in Ijebu-Ode, Ogun State, Nigeria. doi:10.1186/s12889-020-09310-3.

12. O'Leary, M. *et al.* A cohort study of low birth weight and health outcomes in the first year of life, Ghana. *Bull World Health Organ* **95**, 574–583 (2017).

13. Mallick, L., Yourkavitch, J. & Allen, C. Trends, determinants, and newborn mortality related to thermal care and umbilical cord care practices in South Asia. doi:10.1186/s12887-019-1616-2.

14. Draiko, C. V., Mckague, K., Maturu, J. D. & Joyce, S. The effect of umbilical cord cleansing with chlorhexidine gel on neonatal mortality among the community births in South Sudan: a quasi-experimental study. *Pan African Medical Journal* **38**, (2021).

15. Pretorius, C. E., Asare, H., Genuneit, J., Kruger, H. S. & Ricci, C. Impact of breastfeeding on mortality in sub-Saharan Africa: a systematic review, meta-analysis, and cost-evaluation. *Eur J Pediatr* **179**, 1213–1225 (2020).

16. Lunze, K., Bloom, D. E., Jamison, D. T. & Hamer, D. H. The global burden of neonatal hypothermia: systematic review of a major challenge for newborn survival. (2013) doi:10.1186/1741-7015-11-24.

17. Thomas, J. C., Letourneau, N., Bryce, C. I., Campbell, T. S. & Giesbrecht, G. F. Biological embedding of perinatal social relationships in infant stress reactivity. *Dev Psychobiol* **59**, 425–435 (2017).

18. Hummel, A. D. *et al.* Perinatal depression and its impact on infant outcomes and maternal-nurse SMS communication in a cohort of Kenyan women. *BMC Pregnancy Childbirth* **22**, (2022).

19. Ronen, K. *et al.* Evaluation of a two-way SMS messaging strategy to reduce neonatal mortality: rationale, design and methods of the Mobile WACh NEO randomised controlled trial in Kenya. *BMJ Open* **11**, e056062 (2021).

20. Sherbourne, C. D. & Stewart, A. L. The MOS social support survey. *Soc Sci Med* **32**, 705–714 (1991).

21. Črnčec, R., Barnett, B. & Matthey, S. Development of an instrument to assess perceived self-efficacy in the parents of infants. *Res Nurs Health* **31**, 442–453 (2008).

22. Cox, J. L., Holden, J. M. & Sagovsky, R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* **150**, 782–786 (1987).

23. Dafaalla, M. *et al.* Validity and reliability of Arabic MOS social support survey. *Springerplus* **5**, (2016).

24. Margolis, R., Bellin, M. H., Sacco, P., Harrington, D. & Butz, A. Evaluation of MOS social support in low-income caregivers of African American children with poorly controlled asthma. *J Asthma* **56**, 951–958 (2019).

25. Wan Mahmud, W. M. R., Awang, A. & Mohamed, M. N. Psychometric Evaluation of the Medical Outcome Study (MOS) Social Support Survey Among Malay Postpartum Women in Kedah, North West of Peninsular Malaysia. *Malays J Med Sci* **11**, 26 (2004).

26. Yu, D. S. F., Lee, D. T. F. & Woo, J. Psychometric testing of the Chinese version of the medical outcomes study social support survey (MOS-SSS-C). *Res Nurs Health* **27**, 135–143 (2004).

27. Mannocci, A. *et al.* Happy mama project (Part 1). assessing the reliability of the italian karitane parenting confidence scale (kpcs-it) and parental stress scale (pss-it): A cross-sectional study among mothers who gave birth in the last 12 months. *Int J Environ Res Public Health* **18**, (2021).

28. Yang, J. L. X., Zhang, Y., Zhang, L. F. & Cao, H. [Reliability and validity test of Chinese version of the Karitane parenting confidence scale]. *Zhonghua Yu Fang Yi Xue Za Zhi* **55**, 811–817 (2021).

29. Pinto, T. M., Costa, R., Dias, C. C., Borger, F. & Figueiredo, B. Karitane Parenting Confidence Scale: measuring parenting self-efficacy in Portuguese mothers during the first year postpartum. *J Reprod Infant Psychol* (2023) doi:10.1080/02646838.2023.2169264.

30. Tsai, A. C. *et al.* Reliability and Validity of Instruments for Assessing Perinatal Depression in African Settings: Systematic Review and Meta-Analysis. *PLoS One* **8**, 82521 (2013).

31. Mutiso, V. N. *et al.* Edinburgh Postnatal Depression Scale (EPDS) for screening for depression in the first year post delivery in a low-resourced rural setting in Kenya. *Transcult Psychiatry* (2022) doi:10.1177/13634615211043764/FORMAT/EPUB.

32. McCabe-Beane, J. E., Segre, L. S., Perkhounkova, Y., Stuart, S. & O'Hara, M. W. The identification of severity ranges for the Edinburgh Postnatal Depression Scale. *J Reprod Infant Psychol* **34**, 293–303 (2016).

33. Pettker, C. M., Goldberg, J. D., El-Sayed, Y. Y. & Copel, J. A. *Methods for Estimating the Due Date*. *Replaces Committee Opinion Number* vol. 700 https://www.acog.org/-/media/project/acog/acogorg/clinical/files/committee-opinion/articles/2017/05/methods-for-estimating-the-due-date.pdf (2017).
34. Oluoch, D. A. *et al.* "You cannot know if it's a baby or not a baby": uptake, provision and perceptions of antenatal care and routine antenatal ultrasound scanning in rural Kenya. *BMC Pregnancy Childbirth* **15**, 127 (2015).
35. WHO. *Postnatal care of the mother and newborn*. (2013).
36. World Health Organization & Special Programme of Research and Development. *WHO recommendations on maternal and newborn care for a positive postnatal experience.* (WHO, 2022).
37. Kenyan Ministry of Health. *A guideline for the use of Chlorhexidine for newborn umbilical cord care in Kenya*. (2016).
38. Foreign Exchange Rates. *Central Bank of Kenya* https://www.centralbank.go.ke/rates/forex-exchange-rates/ (2017).
39. *Kenya Demographic and Health Survey 2022 Key Indicators Report*. www.DHSprogram.com. (2023).
40. Republic of Kenya National Bureau of Statistics. *Kenya Demographic and Health Survey 2014*. www.DHSprogram.com. (2015).
41. Imbo, A., Mbuthia, E. & Ngotho, D. Determinants of Neonatal Mortality in Kenya: Evidence from the Kenya Demographic and Health Survey 2014. *International Journal of Maternal and Child Health and AIDS (IJMA)* **10**, 287–295 (2021).
42. Ahmed, I. *et al.* Population-based rates, timing, and causes of maternal deaths, stillbirths, and neonatal deaths in south Asia and sub-Saharan Africa: a multi-country prospective cohort study. *Lancet Glob Health* **6**, e1297–e1308 (2018).
43. Dietz, O., John-Stewart Daniel Enquobahrie, G. A. & John-Stewart, G. Preterm Birth and Cofactors of Survival Time and Time to First Hospitalization in Western Kenya Preterm Birth and

Cofactors of Survival Time and Time to First Hospitalization in Western Kenya Chair of the Supervisory Committee. (2022).

44. Hagel, C., Paton, C., Mbevi, G. & English, M. Data for tracking SDGs: challenges in capturing neonatal data from hospitals in Kenya. *BMJ Glob Health* **5**, e002108 (2020).

45. Kozuki, N. *et al.* The associations of parity and maternal age with small-for-gestational-age, preterm, and neonatal and infant mortality: a meta-analysis. *BMC Public Health* **13**, S2 (2013).

46. Harron, K., Gilbert, R., Fagg, J., Guttmann, A. & van der Meulen, J. Associations between pre-pregnancy psychosocial risk factors and infant outcomes: a population-based cohort study in England. *Lancet Public Health* **6**, e97–e105 (2021).

47. Saleem, S. *et al.* Neonatal deaths in infants born weighing ≥ 2500 g in low and middle-income countries. *Reprod Health* **17**, 158 (2020).

48. Oza, S., Lawn, J. E., Hogan, D. R., Mathers, C. & Cousens, S. N. Neonatal cause-of-death estimates for the early and late neonatal periods for 194 countries: 2000–2013. *Bull World Health Organ* **93**, 19–28 (2015).

49. Lehtonen, L., Gimeno, A., Parra-Llorca, A. & Vento, M. Early neonatal death: A challenge worldwide. *Semin Fetal Neonatal Med* **22**, 153–160 (2017).

50. Walker, D. *et al.* Effect of a quality improvement package for intrapartum and immediate newborn care on fresh stillbirth and neonatal mortality among preterm and low-birthweight babies in Kenya and Uganda: a cluster-randomised facility-based trial. *Lancet Glob Health* **8**, e1061–e1070 (2020).

51. Mbuagbaw, L. *et al.* Health system and community level interventions for improving antenatal care coverage and health outcomes. *Cochrane Database of Systematic Reviews* **2016**, (2015).

52. Khan, J., Vesel, L., Bahl, R. & Martines, J. C. Timing of Breastfeeding Initiation and Exclusivity of Breastfeeding During the First Month of Life: Effects on Neonatal Mortality and Morbidity—A Systematic Review and Meta-analysis. *Matern Child Health J* **19**, 468–479 (2015).

53. Debes, A. K., Kohli, A., Walker, N., Edmond, K. & Mullany, L. C. Time to initiation of breastfeeding and neonatal mortality and morbidity: a systematic review. *BMC Public Health* **13**, S19 (2013).

54. Hadisuyatmana, S. *et al.* Women's Empowerment and Determinants of Early Initiation of Breastfeeding: A Scoping Review. *J Pediatr Nurs* **56**, e77–e92 (2021).

55. Gato, S. *et al.* Promotion of early and exclusive breastfeeding in neonatal care units in rural Rwanda: a pre- and post-intervention study. *Int Breastfeed J* **17**, 12 (2022).

56. Abdulahi, M., Fretheim, A., Argaw, A. & Magnus, J. H. Breastfeeding Education and Support to Improve Early Initiation and Exclusive Breastfeeding Practices and Infant Growth: A Cluster Randomized Controlled Trial from a Rural Ethiopian Setting. *Nutrients* **13**, 1204 (2021).

57. *Protecting, promoting and supporting Breastfeeding in facilities providing maternity and newborn services: the revised BABY-FRIENDLY HOSPITAL INITIATIVE*. http://apps.who.int/bookorders. (2018).

58. Pérez-Escamilla, R., Martinez, J. L. & Segura-Pérez, S. Impact of the Baby-friendly Hospital Initiative on breastfeeding and child health outcomes: a systematic review. *Matern Child Nutr* **12**, 402–417 (2016).

59. Agrawal, P. K. *et al.* Clean cord care practices and neonatal mortality: evidence from rural Uttar Pradesh, India: Table 1. *J Epidemiol Community Health (1978)* **66**, 755–758 (2012).

60. Sazawal, S. *et al.* Efficacy of chlorhexidine application to umbilical cord on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial. *Lancet Glob Health* **4**, e837–e844 (2016).

61. Semrau, K. E. A. *et al.* Effectiveness of 4% chlorhexidine umbilical cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised controlled trial. *Lancet Glob Health* **4**, e827–e836 (2016).

62. Osrin, D. & Colbourn, T. No reason to change WHO guidelines on cleansing the umbilical cord. *Lancet Glob Health* **4**, e766–e768 (2016).

63. Ndugwa, R. P. & Zulu, E. M. Child morbidity and care-seeking in Nairobi slum settlements: the role of environmental and socio-economic factors. *Journal of Child Health Care* **12**, 314–328 (2008).

64. Omore, R. *et al.* Health Care-Seeking Behavior During Childhood Diarrheal Illness: Results of Health Care Utilization and Attitudes Surveys of Caretakers in Western Kenya, 2007–2010. *Am J Trop Med Hyg* **89**, 29–40 (2013).

65. Wambui, W. M., Kimani, S. & Odhiambo, E. Determinants of Health Seeking Behavior among Caregivers of Infants Admitted with Acute Childhood Illnesses at Kenyatta National Hospital, Nairobi, Kenya. *Int J Pediatr* **2018**, 1–11 (2018).

66. Okemo, J., Temmerman, M., Mwaniki, M. & Kamya, D. Preconception Care among Pregnant Women in an Urban and a Rural Health Facility in Kenya: A Quantitative Study. *Int J Environ Res Public Health* **17**, 7430 (2020).

67. Hedstrom, A. B. *et al.* Risk factors for stillbirth and neonatal mortality among participants in Mobile WACh NEO pilot, a two-way SMS communication program in Kenya. *PLOS Global Public Health* **2**, e0000812 (2022).

68. Jones, R. M. *et al.* A Short Message Service (SMS) increases postpartum care-seeking behavior and uptake of family planning of mothers in peri-urban public facilities in Kenya. *PLoS One* **15**, e0239213 (2020).

69. McConnell, M., Ettenger, A., Rothschild, C. W., Muigai, F. & Cohen, J. Can a community health worker administered postnatal checklist increase health-seeking behaviors and knowledge?: evidence from a randomized trial with a private maternity facility in Kiambu County, Kenya. *BMC Pregnancy Childbirth* **16**, 136 (2016).

70. Madeghe, B. A., Kogi-Makau, W., Ngala, S. & Kumar, M. Risk factors and experiences of prepartum depression in urban- low-income settlement Nairobi Kenya: a mixed-method study. *F1000Res* **9**, (2020).

71. Larsen, A. *et al.* Comparing depression screening tools (CESD-10, EPDS, PHQ-9, and PHQ-2) for diagnostic performance and epidemiologic associations among postpartum Kenyan women: Implications for research and practice. *J Affect Disord* **324**, 637–644 (2023).

72. Madeghe, B. A., Kogi-Makau, W., Ngala, S., Kumar, M. & Inwani, I. Risk factors and experiences of prepartum depression in urban-low-income settlement Nairobi Kenya: a mixed-method study. (2021) doi:10.12688/f1000research.27434.1.

73. Kumar, M., Ongeri, L., Mathai, M. & Mbwayo, A. Translation of EPDS Questionnaire into Kiswahili: Understanding the Cross-Cultural and Translation Issues in Mental Health Research. (2015) doi:10.4172/2376-127X.1000134.

74. Green, E. P. *et al.* Developing and validating a perinatal depression screening tool in Kenya blending Western criteria with local idioms: A mixed methods study. *J Affect Disord* **228**, 49–59 (2018).

75. Gitobu, C. M., Gichangi, P. B. & Mwanda, W. O. The effect of Kenya's free maternal health care policy on the utilization of health facility delivery services and maternal and neonatal mortality in public health facilities. *BMC Pregnancy Childbirth* **18**, 77 (2018).

76. de Graft-Johnson, J. *et al.* Cross-sectional observational assessment of quality of newborn care immediately after birth in health facilities across six sub-Saharan African countries. *BMJ Open* **7**, e014680 (2017).

77. Naanyu, V. *et al.* A qualitative exploration of barriers to health-facility-based delivery in Bomachoge-Borabu and Kaloleni, Kenya. *International Journal of Gynecology & Obstetrics* **153**, 273–279 (2021).