

**Exploring the association between postnatal depressed mood
and infant morbidity, growth, and feeding at 12 weeks
postpartum in a peri-urban South African setting**

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DECLARATION MPH (Epi) Mini-Dissertation

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declare that the work that I have submitted is my own and where the work of others has been used (whether quoted verbatim, paraphrased or referred to) it has been attributed and acknowledged.

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Date: May 19, 2014

Depression is a significant and often overlooked form of maternal morbidity, which has implications not only for a woman but also for her children. While studies from many parts of the world have shown that the mental well being of mothers, especially during the postnatal period, can have significant effect on a child's health, there is a paucity of literature examining such associations in the South African context.

It is hypothesized that depression can compromise the level of care mothers give their children, which in turn could have negative effects on their child's health outcomes. Infants of mothers with symptoms of postnatal depression (PND) will have higher rates of morbidity from infectious diseases such as diarrhea and poorer nutritional status than infants of psychologically well mothers. Furthermore, mothers with symptoms of depression will be less likely to be exclusively breastfeeding their infants at 12 weeks than psychologically well mothers.

This cross-sectional analysis uses data collected for a cluster randomized controlled trial (Good Start III) to assess the effect of a package of community health worker home visits on a variety of maternal and child health outcomes in the peri-urban setting of Umlazi near Durban in South Africa between 2008 and 2011. The study area was divided into 30 clusters randomly allocated into two arms (15 clusters in each arm). The study population consisted of all consenting pregnant women over 16 years of age residing in one of the clusters during the time of the trial. Live mother and infant dyads were assessed at 12 weeks postpartum through a questionnaire and a medical record review. Anthropometric measurements and blood samples for laboratory analysis were also taken (n= 3494). Multivariate linear, binomial and multinomial logistic regression analysis were undertaken to assess the hypothesized associations.

Prevalence of postnatal depressed mood in mothers from this community was 16% at 12 weeks postpartum. Results from this large population based study show children of mothers with postnatal depressed mood are at increased risk of both diarrheal disease and being mixed or not breastfed at 12 weeks of age. These factors are important parts of the complex pathway between maternal mood status and child health, having mediating effects on nutritional outcomes. Though the reduction in standardized growth indices in children of mothers with depressed mood vs. non-depressed mood was clinically marginal (but statistically significant) at 12 weeks postpartum, it is possible that if this trend were to continue, bigger impact of this exposure on nutritional status could be seen.

Mothers with postnatal depression should be identified for support, not only to improve their own mental health state, but also to help safeguard the health of infants in order to ensure every child has the best possible start in life.

Part A: Protocol

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Abbreviations

CAB	Community Advisory Board
CHW	Community Health Worker
CMD	Common Mental Disorder
DBS	Dried Blood Spot
DSM	Diagnostic Standard Manual
EPDS	Edinburgh Postnatal Depression Scale
HAZ	Height for age Z score
HIV	Human Immunodeficiency Virus
IMCI	Integrated Management of Childhood Illness
LMIC	Low and Middle Income Countries
NPV	Negative Predictive Value
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother to Child Transmission
PND	Post Natal Depression
PPV	Positive Predictive Value
RCT	Randomized Controlled Trial
SOP	Standard Operating Procedures
WAZ	Weight for age Z score

Introduction

Problem Identification

Depression is a significant and often overlooked form of maternal morbidity, which has implications not only for the woman but also for their children. (1) It is estimated that around 13% of all mothers are affected by postnatal depressed mood in the developed world. Epidemiological studies from low and middle-income countries (LMIC) suggest that prevalence rates of maternal depression are often much higher than those found in developed countries. (2) Poverty has been found to be both a predictive risk factor for maternal depression and a key moderator of the effects of this morbidity on child development. (2) These findings have implications for families, mothers and children living in poor economic environments. The increased risks posed by wide spread socio-economic adversity in many of these contexts have significant repercussions for the health and well-being of mothers and their children living in developing countries.

Review of the Literature

Prevalence of postnatal depressed mood

WHO has ranked depression as the fourth leading cause of global disease burden, and the largest amount of non-fatal burden, accounting for almost 12% of all total years lived with disability worldwide. (3) The postpartum period has been shown to be a time of particular increased risk for depression, perhaps because of stressors related to parenting alongside hormonal changes associated with childbirth. (4) Prevalence rates for postnatal depressed mood have been widely reported at 10% to 15% in the developed world. (5,6) Studies globally, however, have shown far wider variation across countries, with prevalence rates ranging from 4.9% in Nepal to 50% in Guyana. Furthermore, a wide range in prevalence is reported *within* populations. Inconsistent definitions, screening tools and cut off scores, along with different times of measurement postpartum may account for some of the reported variation. (2) While further explorations into cultural and sociological factors for these varied reported rates are warranted, it is clear that postnatal depressed mood is a widespread condition afflicting many women. (7)

Impact of postnatal depressed mood on child health: a theoretical framework

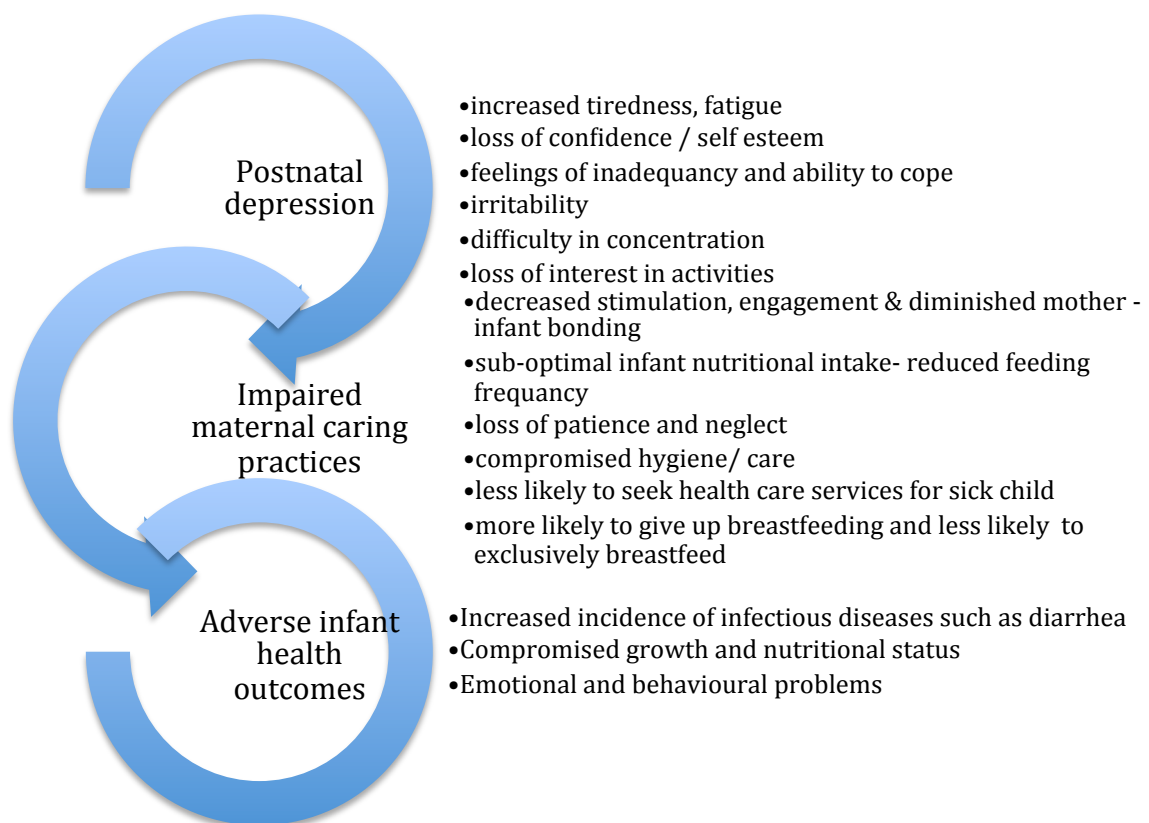
Depression is a debilitating mood disorder, which can result in fatigue, despondency and reduced and impaired interaction with others. (1) This causes significant morbidity for those afflicted and has implications for family members and others around them. This is especially true for the youngest children who are particularly dependent in the first few months of life where development requires significant emotional, nutritional and cognitive input and care.

Mothers suffering from depression are emotionally removed and less likely to respond to their babies and provide them with less quantity and poorer quality of stimulation. Researchers in South Africa found maternal sensitivity of engagement with their infants to be significantly poorer in depressed versus non-depressed women. (8) The emotional quality of parenting may therefore be an important mediator in the effect of postnatal depressed mood on infant growth, compromising the level of care provided by mothers to their infants.

Poverty, overcrowding, poor sanitation and other such factors that so often characterize underdeveloped settings pose considerable threat to a child's physical health and if care-taking practices are compromised, the child can become at increased risk to a variety of illnesses. This, combined with diminished stimulation and engagement, may place infants of depressed mothers at considerable risk for several negative outcomes.

The association between maternal mood and child health are no doubt multi-factorial and complex. Figure 1 below postulates one possible mechanism by which this complex etiological process may occur.

Figure 1 Conceptual framework: Impact of postnatal depressed mood on child health outcomes



Postnatal depressed mood and infant feeding outcomes

It is universally recognized that breastfeeding in poor settings is critical for child survival.(9) Optimal infant feeding requires that all infants are breastfed exclusively for the first 6 months of life with continued breastfeeding up to two years of age. Studies across the world have shown that breastfed infants are at significantly decreased risk of morbidity and mortality and have improved nutrition and growth. (10) In light of such compelling evidence, efforts to encourage and promote universal breastfeeding have become crucial components of public health policy. Identifying risk factors for early cessation of breastfeeding are important to achieving widespread practice.

The association between maternal depression and cessation of breastfeeding has been explored in numerous studies. A prospective cohort study that followed 1745 Australian women for one year postpartum found that women who developed postnatal depressed mood had a 1.25 (1.03–1.52) times increased risk of breastfeeding cessation compared to women who did not develop depression, even after adjusting for confounders. A similar study in Canada found that mothers were significantly more likely to discontinue breastfeeding at 4 and 8 weeks if they were depressed at 1 week postpartum. (11) This association has also been seen in research conducted in low and middle-income countries. A small study of 60 women in Turkey found an association between higher EPDS scores and breastfeeding cessation by 4 months, (12) while a cross sectional study in Pakistan also found statistically significant difference in mean depression scores for lactating and non-lactating mothers while no other significant differences between known risk factors for breastfeeding cessation (age, parity, socio-economic status and educational level) was found between the two groups.(13) Similarly, a secondary outcome of a longitudinal cohort study of mothers in Nigeria found that women who had postnatal depressed mood were less likely to be breastfeeding at 6 weeks, 3, 6, and 9 months than psychologically well mothers.(14) A qualitative systematic review of studies of postnatal depressed mood and infant feeding outcomes found compelling evidence to support the theory that depression in the postpartum period has a negative effect on infant feeding. (15)

Breastfeeding requires commitment and effort on the part of the mother. Depressed women may be less confident in their ability to breastfeed, more vulnerable to feelings of inadequacy and unable to cope with challenges in breastfeeding and therefore more likely to give up breastfeeding than psychologically well mothers.(16) Depressed mothers in Canada were

more likely to report lower levels of breastfeeding self-efficacy, (11) which has been linked, not only to the initiation and duration but to exclusivity of breastfeeding. (15)

Breastfeeding in the context of the HIV pandemic

The double burden of HIV and high infant mortality in resource poor countries has placed breastfeeding at the forefront of an intense debate. This is especially true in the context of South Africa, which has the lowest rates of breastfeeding and exclusive breastfeeding amongst developing countries and the highest antenatal HIV prevalence rate in the world. (17) HIV positive women have high reported prevalence of perinatal depression with rates of 41%- 54% found in South Africa and Zimbabwe. (18) (19) Exclusive breastfeeding practices are critical for HIV exposed children in resource poor settings, reducing risk of morbidity and mortality from diarrhea and pneumonia as well as mitigating the risk of vertical transmission that occurs through mixed feeding. (20,21) Efforts to improve exclusive breastfeeding rates for this population are critical.

A recent prospective study in a community near Durban, South Africa examined the impact of infant feeding mode on the health of HIV positive mothers and their children over a 9-month period. (22) One reported outcome of the study was that significantly fewer HIV positive women who breastfed their infants had depression when compared to HIV positive women who formula fed their infants.

Postnatal depressed mood and infant growth and nutritional status

Nutritional status is a significant predictor of child morbidity and mortality. (23) The associations between maternal mood and infant under-nutrition have been explored in numerous studies. In a recent systematic review and meta-analysis of maternal depression and early childhood growth (2011), Surkan et al. pooled data from 17 studies for a total of 13 923 mother and child pairs from 11 countries and found that children of mothers with depression or depressive symptoms were more likely to be underweight (OR: 1.5; 1.2–1.8) or stunted (OR: 1.4; 1.2–1.7) than those of psychologically well mothers. This association was even stronger for longitudinal studies. (4)

Numerous studies from South Asia have examined the association and potential etiological role of maternal depression on infant under nutrition. In a hospital based cohort study conducted in Goa, India, children 6 months of age who were under the 5th percentile for weight were 2.3 times more likely to have a mother who was depressed at 6 weeks postpartum ($p < 0.01$), even after adjusting for known confounders (gender, education, feeding, infant morbidity and prematurity). (24) Similarly, a community-based case control study in Vellore, Tamil Nadu found maternal depressed mood to be a significant risk factor for

malnutrition in children aged 6-12 months (OR 7.4; 1.6- 38.5). This association also remained significant after adjusting for “maternal intelligence”, breast-feeding, birth weight, immunization and economic status. Similarly, undernourished (below the 3rd centile for weight for age) children aged 9 months in Pakistan had 3.9 (1.9 -7.8) increased odds of having a mother with maternal mental distress than children who were not undernourished, independent of numerous confounders. (25) Similar results were found in Bangladesh. (26)

Evidence from studies in Africa however have been mixed. A longitudinal case-control study of 876 mothers from Nigeria showed that infants of depressed mothers had poorer growth by the 3rd and 6th month of life than infants of non-depressed mothers. (14) However, a large prospective cohort study of 1065 pregnant women in Butajira, Ethiopia did not find any statistically significant differences in the prevalence of underweight or stunted infants in mothers with high levels of common mental disorders (CMD) compared to those with low levels at 6 and 12 months postpartum. (27) Smaller cross-sectional studies examining adverse infant health outcomes and maternal depression in Zambia and Malawi (28,29) examining associations between CMD and infant growth impairment have also had mixed results. In Malawi, infants of mothers with CMD were more likely to be stunted but not underweight at 9 months as compared to infants of mothers without CMD. (29) In Zambia, no statistically significant differences were found between health outcomes of infants of mothers with CMD vs. infants of psychologically well mothers. In South Africa, Tomlinson et al. followed 147 mother-infant dyads recruited over an 8-month period from the socio-economically disadvantaged peri-urban settlement of Khayelitsha near Cape Town. Infant weight and length and maternal mood was assessed at 2 and 18 months, however, no clear effect of postnatal depressed mood on infant growth were found. (30) Thus, these findings differ from studies in South Asia, which have shown a clear association between maternal depression and infant under-nutrition, though the reasons for this continental difference remain unclear.

Postnatal depressed mood and diarrhea

One of numerous possible pathways by which maternal depression may have an effect on infant nutritional status is through the increased risk for diarrheal disease. Diarrhea is one of the top causes of death in infants and young children globally and remains a major public health concern, especially in low and middle-income countries. (31) Furthermore, frequent episodes of diarrheal disease in childhood also result in sub-optimal growth and development. Prevention of diarrhea requires attention to hygienic practice and is particularly challenging in contexts with poor sanitation and increased prevalence of diarrheal disease in the community. Mothers with depressed mood may have reduced energy, motivation and will to ensure precautions to reduce risk of their infants getting diarrhea.

Few studies thus far have examined this association. Research from Rawalpindi Pakistan found children of mothers with depression have 2.3 (1.6- 3.1) times the relative risk of having five or more diarrheal episodes per year than infants of non-depressed mothers. The association remained significant after controlling for the effects of low birth weight, infant nutritional status, duration of breast-feeding and socioeconomic status. (32) Researchers in Nigeria also found that by 9 months, infants of depressed mothers had greater average number of cases of diarrhea than infants of non-depressed mothers (5.23 cases SD 2.37 vs. 3.70 cases SD 4.14; p=0.001). (14) A large cohort study in the UK found that children born to women with perinatal depression had a 40% increased rate of gastrointestinal infections when compared with children born to women without perinatal depression, independent of other risk factors.(33)

Diarrheal morbidity in infants is of serious concern in LMIC. Improved maternal mental health may be an important mechanism to decrease this risk to the child and further explorations around this association are warranted.

Motivation and Rationale for study

While studies from many parts of the world have shown that the mental well being of mothers, especially during the postnatal period, can have significant effect on child health, there is a paucity of literature examining such associations in the South African context. Perinatal depression rates in South Africa are high, with an estimated one third of all mothers affected.(19,30) This rate is even higher amongst HIV positive women.(18) While maternal depression has been found to have significant negative effects on a range of child health outcomes in South Asia (24-26,32,34-36) studies from African contexts, however, have had mixed results. (4,14,27,29,30)

Evidence of the negative effect of maternal mood on infant nutritional outcomes in Africa have been mixed and most studies have been based on relatively small numbers of women. Furthermore, only one study in South Africa has explored the role of postnatal depressed mood and infant feeding outcomes. This was amongst HIV positive women and may not be generalizable to all postpartum mothers for a variety of reasons. This study thus aims to contribute to the relatively limited but growing body of research examining associations between maternal postpartum mood and early infant health and feeding outcomes in South Africa.

Research Aim

The aim of this study is to determine the association between postnatal depressed mood in mothers and adverse infant health outcomes and infant feeding at 12 weeks postpartum.

Research Objectives

1. To determine prevalence of maternal postnatal depressed mood in a high HIV prevalence peri-urban setting in South Africa.
2. To determine the association of postnatal depressed mood and infant feeding methods at 12 weeks postpartum.
3. To determine the association of maternal postnatal depressed mood and the prevalence of maternal-reported infant diarrhea at 12 weeks postpartum.
4. To determine the association of maternal postnatal depressed mood and infant nutritional status in the first 12 weeks of life.

Hypotheses

It is hypothesized that depression can compromise the level of care mothers give their children, which in turn could have negative effects on their child's health outcomes. Specifically, infants of mothers with symptoms of postnatal depressed mood will have higher rates of morbidity from infectious diseases such as diarrhea and poorer nutritional status than infants of psychologically well mothers. Mothers with symptoms of depression will be less likely to be exclusively breastfeeding their infants at 12 weeks than psychologically well mothers and are more likely to have stopped breastfeeding early.

Definition of terms

Postnatal depression is defined as non-psychotic depressive mood disorder occurring in the postnatal period, typically diagnosed 4 - 12 weeks after childbirth. (37)

Postnatal depressed mood refers to women who have scored consistent with *probable postnatal depression* through a validated screening tool but have not received a definitive clinical diagnosis through a structured interview with a trained clinician for postnatal depression.

Infant feeding refers to the method by which the mother feeds her baby, namely, never having started breastfeeding, currently breastfeeding, currently exclusive breastfeeding or not breastfeeding.

Infant morbidity is assessed through the recalled period prevalence of infant diarrhea. Diarrhea is defined as infant having three or more, loose, liquid or watery stools in one day.

Infant nutritional status refers to growth attained at 12 weeks as determined by weight and height standardized for age.

Methods

Study design

This dissertation will be derived from secondary analysis of data collected for an effectiveness study of an integrated, community-based package for maternal, newborn, child and HIV care. The aim of the primary study was to assess the effect of structured community health worker (CHW) home visits to pregnant and postnatal women on a variety of maternal and child health and behavioral outcomes.¹ The primary study is the third in a series of studies termed Good Start that focused on exploring maternal and child health outcomes.

The design of Good Start III was an un-blinded cluster randomized controlled trial conducted in Umlazi, a peri-urban settlement near Durban in the KwaZulu Natal Province of South Africa. The trial commenced in 2008 and ran until 2011, and was conducted by the Medical Research Council of South Africa, Health Systems Research Unit in collaboration with Stellenbosch University, and the University of the Western Cape. Funding for the research component of the trial was provided by the Centers for Disease Control and Prevention (PEPFAR) and through Save the Children (USA) Saving Newborn Lives. The trial is registered: ISRCTN41046462. The Good Start III study protocol was published in 2011. (38)

This mini- dissertation will be based on data collected for the Good Start III study on mother-infant pairs around 12 weeks postpartum. Basic birth information was obtained from hospital records but no other baseline or follow up information is available. The design of this sub-study is predominantly cross sectional though data on birth weight and date of birth is taken from hospital records.

Study context

The setting for the trial was Umlazi, a peri-urban settlement southwest of Durban in the province of KwaZulu Natal. The second largest township in South Africa, Umlazi has a population of approximately 1 million inhabitants, predominantly Black South Africans, residing in a mixture of formal and informal housing. Its HIV prevalence amongst antenatal clients in the district was 41% in 2010, one of the highest in South Africa. Infant mortality is estimated to be 42 per 1000 live births. (17) Over 98% of all births in Umlazi occur in one major hospital, Prince Mshiyeni Memorial Hospital, which also serves as a referral hospital for the surrounding feeder clinics.

¹ See Panel 1 in appendix 1 for detailed list of Good Start III study outcomes

Cluster selection and cluster size

Clusters for the trial were drawn by dividing a map of the area of study into “sub-places”, utilizing population statistics from the 2001 census to generate a total of 30 clusters. Prior to randomization, the clusters were compared in regard to average socio-economic status, gender and age of all household members and selected socio-demographic and mortality data through a baseline assessment to assess cluster homogeneity. As no significant difference was noted, these clusters were then randomly allocated, using a simple computer generated randomization, into an intervention or control arm, with a 1:1 allocation ratio resulting in a total of 15 clusters per arm.

Study Population and Sample Size

The trial study population comprised of all pregnant women and their newborns residing in the clusters identified during the study recruitment period.

Sample size was calculated based on increasing HIV-free survival from 74% to 84%, with 80% power in an individually randomized trial (this would require 279 live births per arm). Assuming an ICC of 0.04 for a cluster-randomized trial the estimated required sample was 750 HIV exposed children per arm (50 per cluster) with a design effect of 3. Loss to follow up of approximately 20% was added to this sample size. Based on an HIV prevalence rate amongst pregnant women of 40% the sample size was calculated to be 120 pregnant women per cluster. The total sample size calculated for the main study was $n=3600$.

Inclusion criteria

Enrolment into the trial included pregnant women 16 years of age or older residing in one of the clusters during the study period who gave written informed consent to participate in the study.

Exclusion criteria

Participants were deemed ineligible if they were:

- less than 16 years of age
- did not give written informed consent to participate in the study
- refused CHW visits or participation in data collection
- had false pregnancies
- were mentally unstable

Mental instability refers specifically to women who were deemed unable to give informed consent due to the presence of an observed mental illness ***or condition compromising cognition***. Each case was assessed individually by a CHW through observation of activities such as failure to carry out simple tasks (such as washing, feeding themselves) and severely compromised hygiene. The inability to respond to any questions asked or giving

responses that were completely irrelevant were also taken into consideration. Family members often assisted in confirming such criteria. Only severe cases observed by the CHW and confirmed to be unable to give informed consent for trial participation were excluded.

Recruitment and Enrolment into the main study

All pregnant women in the intervention and control clusters were identified and registered by trained CHWs at baseline and again at regular intervals throughout the study period. Each CHW was responsible for covering all households and identifying all eligible women in one study cluster.

Eligibility was determined by the CHW based upon recruitment criteria assessed at the first home visit. Every week, data collectors were given a list of women recruited by the CHWs. These data collectors then traveled to the women's homes to provide in-depth information about the study and obtain written, informed consent to participate from women who agreed to participate in data collection. Mothers that did not consent to participate in the study continued to receive ongoing counseling from the CHWs if they opted for it.

Procedures

The Good Start III intervention package

Nature of the intervention

CHWs working in the intervention clusters received ten days of training aimed at enabling them to deliver an integrated package of two antenatal and five postnatal structured home visits.² This training was consistent with existing national guidelines for PMTCT, IMCI, lactation counseling, and newborn care. Mothers with low birth weight babies (<2500 grams) received two extra home visits within the first week of discharge.

Mental health content of visits

The package delivered to the intervention arm also contained a mental health component which included: input regarding infant communication and the mother-infant relationship, warning signs for postnatal depressed mood, support for women who had “the blues”, a newborn interactive assessment, mother –infant interaction modeling and communication input, and assessment for signs of postnatal depressed mood. Support for women who had ‘the blues’ included information regarding what to expect and how to recognize danger signs. Information about the common occurrence of postnatal mood disorders also served to help

² See panel 1 of appendix in Part A for visit schedule and content for intervention in Good Start III

alleviate stigma around the illness and encourage open discussion about feelings and challenges mothers were experiencing.

The main study posited that the delivery of messages about maternal mood within an integrated package of home visits, together with the supportive counselling aspect provided by the CHWs, and would positively impact maternal mood. This was one of the outcomes of the main trial.

CHWs were thus trained and provided with a manual that included health promotion messages, and information/ education about symptoms of postnatal blues and depression. Supportive counseling to mothers was provided overall during the antenatal and postnatal period through visits enquiring about health and well being of the mother and child overall and encouragement of the adoption of health promotion and discussion about challenges and feelings around motherhood.

Mothers in the control clusters received information from CHWs on obtaining social welfare grants during the antenatal period, a postpartum visit around 6 weeks to assist with grant application problems and a visit at 10 weeks postpartum to remind the mother to go with her baby for data collection at the main hospital at 12 weeks.

Secondary data analysis

Dissertation study population and sample size

All eligible mother-infant pairs from the main study that completed the data collection survey at 12 weeks were included in the analysis for this sub-study.

This excluded all multiple births, perinatal and/ or maternal deaths and all those that were lost to follow up. A full description of the trial study profile is located in Figure 3 in Appendix 1. The resulting sample size for this dissertation is 3493 mother-infant pairs.

A sample size calculation is included to demonstrate a theoretical sample size estimate that would be needed for the purposes of this sub- study.

Equation 1 Sample size formula for comparison of two proportions

$$N = 2 \cdot \frac{\left[z_{crit} \sqrt{2 \bar{p}(1-\bar{p})} + z_{pow} \sqrt{p_1(1-p_1) + p_2(1-p_2)} \right]^2}{D^2}$$

To calculate a sample size for the purpose of detecting a 20% difference (D) in infant diarrhea prevalence between mothers with postnatal depressed mood and mothers without postnatal depressed mood, one would use the above equation. The general population has period prevalence of diarrhea in the last two weeks of 20% (P). An increase of 20% is set as clinically significant (P_1 16%; P_2 24%). With an alpha of 1.96 (Z_{crit}) and power of 0.80 (Z_{pwr}), one would need a minimum combined sample size from this population of $N= 2894$.

A post hoc analysis will be conducted to determine the power of the actual sample used though there is some debate on the utility of post-hoc power estimates. Confidence intervals will be included to inform readers of possibility of inadequate sample size. (39)

Data collection

All women who gave written informed consent to participate in the study were asked at the start of the study to come to the assessment site at the Prince Mshiyeni Hospital around 12 weeks postpartum for data collection purposes. Mothers that did not show for the interview were contacted by data collectors and asked to come to the hospital to attend the interview. CHWs were unaware if the mothers were participating in the data collection at the end of the study unless the mother disclosed this to them. Data collectors were unaware of the activities of the CHWs and thus blinded to study arm.

Definitions of variables of interest

It is important to note that standard definitions are used for most variables to promote consistency and facilitate comparison of research results across a wider range of studies.

Infant feeding

Never breastfed

Mothers who had never put their child to their breast for feeding after birth were categorized as never breastfed.

Stopped Breastfeeding

Mothers who had started breastfeeding after birth and reported that they had not breastfed their baby from the time they woke up yesterday morning until they woke up this morning (24 hour recall period) were classified as having stopped breastfeeding before 12 weeks.

Mixed feeding

This included women who reported that they breastfed their infants in the past 24 hours **and** gave their infant food or nutritive fluids. To assess *mixed feeding status*, mothers were asked

if they had breastfed their baby from the time they woke up yesterday morning until they woke up this morning (24 hour recall period). Those who answered yes were classified as currently breastfeeding and those who answered no were classified as currently not breastfeeding. Those who answered yes to currently breastfeeding **and** answered yes to giving their babies any of a list of 19 food and fluid items in the past 24 hours were categorized as mixed feeding.

Currently exclusively breastfeeding

To assess *current exclusive breastfeeding status*, mothers who answered yes to the above question were given a further list of 19 food and fluid items and asked if they had given any of the items mentioned to their baby to consume in the last 24 hours. Mothers who answered 'no' to all 19 items, *except* prescribed and over the counter medicines, were classified as currently exclusively breastfeeding. All mothers who were currently breastfeeding but answered 'yes' to any items except prescribed medicines were classified as not currently exclusively breastfeeding.

Infant morbidity

Diarrhea

Infant morbidity was assessed by asking the mother at 12 weeks if at any time during the last two-week period that ended the preceding morning, their child had diarrhea? Diarrhea is defined as the infant having three or more, loose, liquid or watery stools per day.

Infant nutritional status

Weight-for-age and height-for-age Z scores

Standard normal deviates for weight-for-age, length-for-age and weight-for-length will also be used to assess infant growth. These will be calculated according to WHO gender specific standards, using weight and length measurements and age at the time of the interview to assess general nutritional status. The use of weight-for-length has been omitted from this study as it is rare with only 16 of all 3494 infants having <-2 SD weight for length Z scores.

Maternal mood

Postnatal depressed mood

Maternal mood was assessed at 12 weeks postpartum through the use of the *Edinburgh Postnatal Depression Scale*. Scores will be summed for each participant and a cut off of >12 will be used to identify women with postnatal depressed mood.

Instruments and their validity and reliability

24 hour recall of infant feeding

The 24-hour recall methodology for infant feeding is a standard format in accordance with the WHO standard indicators and definitions of infant feeding practices for household surveys. (40) While it is used to assess ‘exclusive breast feeding’ rates in infants 6 months and below, it can be argued that such a current status indicator (based on a 24 hour time period) may be inadequate and often misleadingly reported as an indicator implying exclusive breastfeeding since birth. In fact, the 24-hour recall does not take into consideration the possibility that many infants who were exclusively breastfed the day before the interview may have received other foods before that. In a descriptive longitudinal prospective study of Swedish mother-infant pairs, Aarts et al compared daily recordings on infant feedings to single 24 hour recording of infant feeding at 2, 4 and 6 months and found a wide discrepancy between the results of the two analyses with a difference between the two measurements of exclusive breastfeeding of over 40 percentage points at both 2 and 4 months of age. The authors thus propose making a distinction between *current exclusive breastfeeding* and *exclusive breastfeeding since birth*. Similarly, in a study seeking to validate maternal recall of exclusive breastfeeding in a South African group of mothers, the authors conclude that current exclusive breastfeeding status does not accurately reflect feeding patterns since birth. (31,41)

It is thus important to clarify these definitions and to note that infant feeding in this study is measured as *never breastfed*, *stopped breastfeeding*, *mixed feeding* and *current exclusive breastfeeding* (implying exclusively breastfed in the 24 hours prior to the interview) Data for *exclusive breastfeeding since birth* was obtained in the interview through maternal recall of food and fluid items given since birth however. However, it has been noted that long-term exclusive breastfeeding recall tends to overestimate the true duration of exclusive breastfeeding.(41)

Two week maternal recall of diarrhea

Diarrhea is defined by WHO as “the passage of 3 or more loose or liquid stools per day.” (42) During the 12-week interview, data collectors asked mothers if during the last two weeks that ended the preceding morning, their child had had diarrhea. The definition of diarrhea was explained to each mother according to the definition above. This two-week maternal recall is the standard format used in household surveys for measuring the period prevalence of diarrhea in a population. Neither longitudinal prevalence nor incidence of diarrhea is captured through this question.

Maternal re-call of diarrhea in infants.

In a recent update exploring epidemiological methods in diarrhea studies, Schmidt et al point out that while recall errors in reporting diarrhea episodes may exist depending on duration of recall period, severity and duration of symptoms, and even across socio-economic groups, this would not pose a big problem to studies that aim to explore disease trends or compare risks across treatment arms “if it can be assumed that re-call error is non-differential among the groups compared”. (42) For the purposes on this study, a period prevalence of diarrhea is used as a comparison between infants of mothers with and without postnatal depressed mood and it is assumed that misclassification due to recall error will be random between the groups.

Anthropometric data

Weight and recumbent length measurement was measured for each child at the time of the 12-week interview by trained data capturers. Both measurements were taken at the study office in Prince Mshiyeni Hospital in Umlazi at the time of the 12-week interview.

Babies were weighed naked being held by their mothers. Mothers were asked to step on calibrated scales, remaining still and centered while data collectors then tare the scale by switching it off and turning it to 0.00 kg. The data collectors then handed the mother her undressed infant to hold while they record the shown weight to the nearest 10 grams (e.g. 4.02g).

Length was measured using a roller meter (TALC) with infants laid on their back with the crown of the head touching the fixed headboard and the shoulders touching the base of the roller meter. The movable footboard was pushed to the soles of the infant’s feet after ensuring that the legs of the infant were fully extended, at which point the length reading was taken.

A standard operation procedure (SOP) detailing procedures for measuring infant weight and length was developed to reduce intra-observer bias and improve validity of the anthropometry data collection. Anthropometric measurements were validated during the study through the further application of data quality SOPs whereby data collectors were given ample opportunities to practice taking length and weights on babies (at least 10 per week) and given refresher trainings once a week in taking anthropometric measurements.

Attained infant size at 12 weeks

Attained infant size at 12 weeks will be converted to weight for age, weight for height and height for age z-scores in accordance with WHO child growth standards. (43)

This is in order to provide a common standard for analysis of growth data, allowing a child's nutritional status to be evaluated in comparison to a normal population and is based on the premise that, if given an optimum start in life, children all have the potential to grow and develop to within the same range of height and weight for age, regardless of ethnic differences. (43)

The Z-score system uses a reference mean or median value to evaluate anthropometric measurements within several standard deviations (SDs or Z value) below or above this value. Summary statistics such as means, SDs and standard errors can be computed from Z-score values and are helpful for grouping growth data by age and sex. Binary variables describing nutritional status can also be created.

- Wasting, measured by weight relative to length or height, is a short term response to inadequate nutritional intake and helps to identify children suffering from current or acute under nutrition. Children with weight for length z-scores <-2 are categorized as wasted, Wasting is appropriate for examining short-term effects of nutritional stress brought about by for example, illness.(44) *Wasting* will not be assessed in this study as is a rare condition and it would not be expected to be visible in this population at 12 weeks of age.
- Stunting, measured by length/ height relative to age, on the other hand, reflects the slowing or interruption of growth and therefore is a long-term response to past or chronic malnutrition but it cannot measure short-term changes in malnutrition.(44) Infants with length for height z-scores <-2 are classified as *stunted*.
- Underweight, defined by a low weight for age, on the other hand is a composite measure of stunting and wasting. It does not discriminate between short and longer-term forms of malnutrition. Weight for age is therefore recommended as the indicator to assess changes in the magnitude of malnutrition over time.(44) Infants with weight for age z-score <-2 are classified as *underweight*

Maternal mood and post natal depression

Maternal mood was assessed at the 12-week interview using the *Edinburg Postnatal Depression Scale* (EPDS). Developed as a screening tool for clinical and research purposes and designed specifically for the postnatal period, (45) the EPDS is one of the most extensively used screening instruments for postnatal depression world wide. (2) The scale

consists of 10 questions, each having 4 possible answers. Women are asked to respond by rating how they have felt in the previous 7 days. Each response is scored 0-3 for severity of symptoms experienced with a resulting range of 0-30.³

Developed in England in 1987 and originally validated on British women by Cox (45) the EPDS has since been used in a variety of cultural settings and translated into numerous languages.(46) Studies have shown the EPDS to be a valid and reliable screening scale for postnatal depression though different thresholds have been proposed for use in different settings. (47) While studies in the UK show that using a cut off point of 12/13 at 6 weeks postpartum result in a sensitivity of 68-95% and a specificity of 78-96% when compared to the gold standard DSM-IV administered through psychiatric interview, it has been cautioned that different cultural groups warrant different cut off scores. (47)

The EPDS was validated in an urban South African community against the DSM-IV criteria for depression. The scale was administered verbally to participants and translated into a local language where necessary. In this study, the recommended threshold of 12/13 resulted in a combined sensitivity and specificity of 76% and 81.8% respectively for both major and minor depression. The PPV was 57.6%. (48). Lowering the threshold to 11/12 identified 100% of women with major depression and 70.6% of women with minor depression resulting in a combined sensitivity of 80%, specificity of 76.6%, PPV of 52.6% and NPV of 92.2%. A study validating the Shona version of the EPDS scale in a peri-urban economically depressed community outside Harare, Zimbabwe showed similar results with a cut-off score of 11/12 reflecting a sensitivity, specificity and positive predictive value of 88%, 87%, and 74% respectively. (49) Therefore, this analysis will use the locally validated threshold of greater or equal to 12 to indicate probable postnatal depression or postnatal depressed mood.

While the EPDS has been shown to identify cases of postnatal depressed mood correctly, it is also important to question whether or not the psychopathological construct of *depression* is an appropriate construct in a non-western context. In an investigation into the construct validity and reliability of an isiXhosa version of the EPDS conducted amongst impoverished women in the township of Khayelitsha, South Africa, researchers concluded that symptoms of postnatal depression in this group “manifest in a way that is consistent with theoretical descriptions and observations obtained from Europe and North America.” (50) This supports

³ See Part D (appendices) for a copy of the EPDS

the notion that what is being measured across these cultures is a similar postpartum affective disorder. (2,17,50)

In this study, the EPDS was administered via trained data collectors at the 12-week interview. These interviews were conducted in a room where privacy was insured and confidentiality of all information assured. Questions were translated into Zulu where needed. Though the scale has not been validated in the study context, the study population represent a similar population to those described in South African validity studies above, namely women from a low income, socially disadvantaged urban Black community. Therefore, it is reasonable to assume similar validity and reliability of the EPDS for detecting postnatal depressed mood in this population.

Confounders

Measurements of possible confounders were made through interview questions administered by data collectors at 12 weeks. These include questions assessing socio-demographic information such as maternal age, education level, durable asset list, and household amenities and pregnancy history.

Maternal HIV status was ascertained through a question asking mothers to disclose HIV status. This was correlated with postnatal ward hospital records. Mothers who reported an HIV positive status were then requested to give a sample for dried blood spots for lab analysis and confirmation of HIV status. Laboratory analysis of this DBS then confirmed the status of the mother. Maternal HIV status in this sub-study is thus based on the outcome of this laboratory analysis.

Infant HIV status was ascertained through PCR test of dried blood spots taken from heel pricks of infants of mothers who were reported HIV positive.

Reliance on self reported HIV status might under estimate true HIV prevalence in this population. The HIV prevalence in this population will be compared with anonymous antenatal HIV prevalence for the area to ensure consistency.

Data Management and Analysis

Data sources

Data was collected from the following sources:

Interviews with Mothers

1). A structured in-person interview assessment conducted by trained interviewers with the mother and anthropometric measurement of the infant at approximately 12 weeks. Interviews were conducted in the language preference of participant and lasted approximately 45-60 minutes. Interviews were conducted in an office in the hospital dedicated to the trial. The space was private and no one else was present at the interview except the mother, child and field researcher.

Medical Record Review

2.) A medical record review of hospital delivery records and patient held record including Road to Health cards for each child participant was done by data collectors. Data extracted included date of birth, birth weight along with delivery method and complications, HIV specific information including maternal HIV status, CD4 counts and medications given for PMTCT.

Laboratory records

3.) Dried blood spot samples for ELISA were taken from mothers who reported being HIV positive. Similar samples were taken on infants of mothers who reported a positive serostatus. HIV DNA PCR testing was then conducted on these dried blood spot samples to determine true HIV status of the infants.

Sources of data obtained for the purpose of this dissertation are described in Table 1 below.

Table 1 Sources of data for sub-study

Verbal interview and assessment	Medical Record Review	Laboratory records
<ul style="list-style-type: none">• Mother's socio-demographic information• Maternal mood assessment (EPDS)• Infant morbidity- two week diarrhea recall• Maternal feeding practice/ history – 24 hour infant feeding recall• Child anthropometric data (weight and length)	<ul style="list-style-type: none">• Child date of birth (hospital delivery record)• Child weight at birth (hospital delivery record)• Maternal HIV status as reported in postnatal hospital records.	<ul style="list-style-type: none">• Maternal HIV status through ELISA on DBS• Infant HIV status through PCR test of DBS of HIV exposed infants

<ul style="list-style-type: none"> Maternal HIV status (self-reported) 		
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Data collectors received one week training in the study tools, operating procedures and general research issues prior to commencing data collection for the study. The researchers also had had prior experience in conducting interviews, blood collection, anthropometry data, and reading medical records from data collection for the previous Good Start study.

Data collection strategy

Mobile phones were used for collecting data at the 12-week endpoint assessment. A survey software package developed by Mobenzi Researcher was run on the Nokia 5000 model phone. Programming and testing of the collection method was conducted for several months to ensure quality and comprehensiveness of the system. Logical, range, missing data and other checks were included in the programming to minimize error in data entry by collectors. The phone was then used to collect and upload numeric and text data. No network coverage was necessary to complete the surveys and the phones were able to store up to 50 completed standard surveys at a time.

Data collectors were trained in practical aspects of phone navigation, checking for software updates, use of the software, how to upload collected data. Baseline survey information was used to practice usage of, and become familiar with, the data collection technique. During this time multiple tests were run to ensure that all data entered on the phone were uploaded and that the response entered on the mobile corresponded to the value stored in the database. More detailed information on the development and use of this collection strategy can be found in an article published by Tomlinson et al in 2009. (51)

Data management

Data collected was automatically uploaded upon completion of each survey to a central server in the Medical Research Council Information Systems Unit in Cape Town. Confidentiality of responses was maintained through encryption of survey data captured. Numerous methods were used to ensure safety and security of the system and data itself, including firewalls to prevent unauthorized access and denial of service attacks and NOD-32 anti-virus technology to protect data from virus threats. Communication between the browser and server was encrypted using 128-bit SSL and access to the web-interface of the system was protected by

passwords for authorized users only. During the course of the main study, access to the data was restricted to the principal investigator, the project manager, data quality officer and web administrator.

The raw data can be exported from the console to Excel format and will be imported directly into STATA SE version 12 for Mac for statistical analysis.

Data exploration

Exploratory, outcome and confounding variables used in this dissertation will be explored through univariate and bivariate analysis and presented in frequency tables such as Table 2 and Table 3 below. Categorical data will be analyzed using frequencies, cross-tabulations with chi-square and 95% confidence intervals for the risk ratio or risk difference. Continuous data will be analyzed using means and variance, and comparison of mean differences and 95% confidence intervals around the mean difference. For detailed breakdown of the framework for the analysis plan see Table 4.

Table 2 Univariate exploratory data analysis

Data exploration						
	Continuous variables	mean	SD	med	range	p ²⁵ p ⁷⁵
Nutritional status	Weight-for-age Z score (WAZ) at 12 weeks					
	Length-for-age Z score (HAZ) at 12 weeks					
	Frequency variables	yes % (n)		no % (n)		
	Underweight (<-2 WAZ score)					
	Stunted (<-2 HAZ score)					
Maternal mood	PND (EPDS score > =12)					
Diarrhea	Diarrhea episode in past 2 weeks					
Infant feeding	Never breastfed					
	Stopped breastfeeding					
	Currently mixed feeding (24 hour recall)					
	Currently EBF (24 hour recall)					

Table 3 Bivariate exploratory data analysis

Distribution of key variables by postnatal depressed mood status			
Exploratory variable	EPDS score >=12	EPDS score <12	Statistical test:

		N(%) mean (sd)	N(%) mean (sd)	chi2 ttest ranksum
Outcome variables	Mean WAZ at 12 weeks			
	Mean HAZ at 12 weeks			
	Diarrhea episode in past 2 weeks			
	Never breastfed			
	Stopped breastfeeding			
	Mixed feeding			
	Currently EBF (24 hour recall)			
Possible confounders	Median maternal age			
	Education			
	Water source			
	Parity			
	Trial arm			
	SES based on asset index (ownership of durable goods ie: TV/ fridge)			
	Maternal employment			
	Breast infection			
	Mean birth weight			
	Mother HIV positive			
	Infant HIV positive			

Data analysis

In this proposed study, all living mother and baby pairs followed up at 12 weeks will be assessed according to their mood status to estimate the prevalence for postnatal depressed mood. For infant feeding methods and diarrhea outcomes, only mothers and babies that were assessed between 9 and 18 weeks will be analyzed in keeping with timeliness as these outcomes may be influenced. Possible interactions and effect modifications between maternal HIV status and EPDS score, maternal HIV status and feeding and maternal HIV status and infant health outcomes will be assessed.

Stratified analysis, logistic or linear regression will be used to adjust for potential confounding in the data. Associations between outcomes and maternal mood scores will be assessed using:

1. Multivariate linear regression for nutritional z-scores outcomes
2. Multivariate binomial logistic regression for diarrhea disease and for underweight and stunting
3. Multivariate multinomial logistic regression for infant feeding outcomes

Trial arm (intervention or control) will be included as a confounder as the main study was designed to have an effect on the same outcomes (and exploratory variables) as are being assessed in this sub-study. Point estimate relative risk (RR) ratios and 95% confidence intervals will be generated for the outcomes of diarrhea and infant feeding and will be assessed for statistical significance at the 0.05 alpha. Beta coefficients with 95% CI will be reported for unadjusted and adjusted effects of maternal mood on z-scores. All multivariate analyses will take into account the cluster design effect of the study.

Proposed models for these outcomes are diagramed in figures 2-4 below. For models 2 and 3 (see figure 3 and 4), unadjusted, fully adjusted and adjusted without the inclusion of the mediating variables identified will be presented.

Proposed models

Figure 2 Conceptual model 1 Maternal Mental Health and Infant Feeding

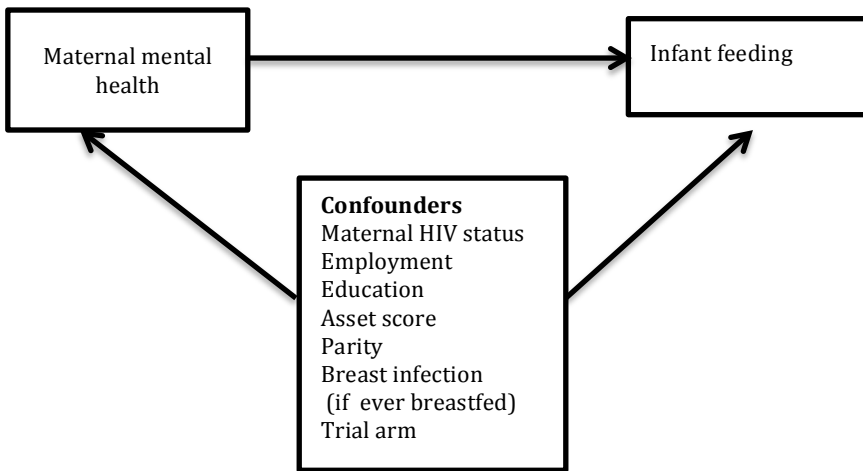


Figure 3 Conceptual model 2 Maternal mental health and Diarrhea

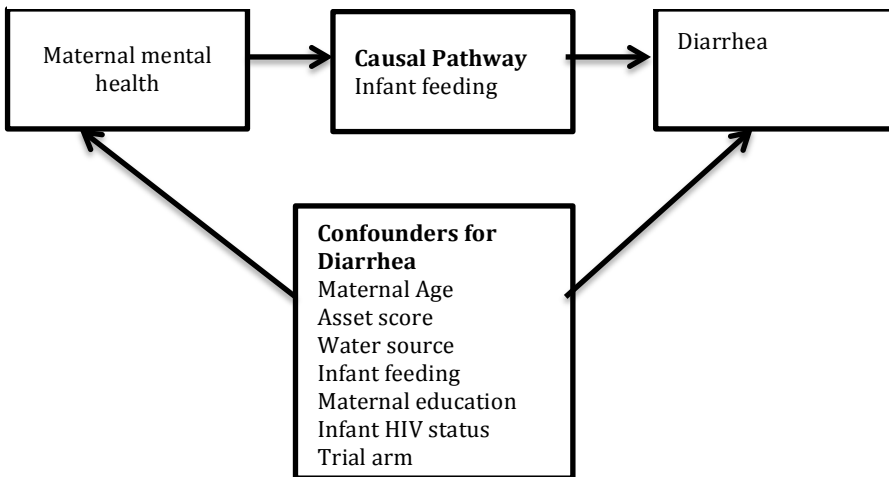


Figure 4 Conceptual model 3 Maternal mental health and infant nutritional status

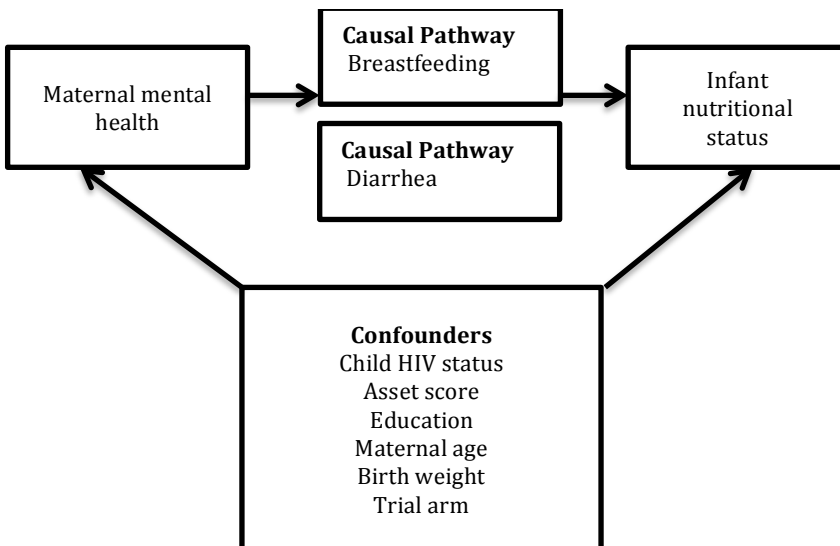


Table 4 Summary framework for data analysis

Frame work for analysis						
Study Objectives:	Variable description Variable number of questionnaire	Data source	variable creation and type		statistical analysis	
1. Determine the prevalence of (or proportion of women with) postnatal depressed mood around weeks postpartum	Maternal depressed mood	Edinburgh Postnatal Depression Scale	0= EPDS score<12	binary	Tabulations Frequencies	
			1= EPDS score>=12			
2. Explore the association between postnatal depressed mood and a) infant diarrhea b) infant feeding c) and infant nutritional status at 12 weeks postpartum	Explanatory variable	Maternal depression score d_281-290	0-30	numerical ordinal discreet		
	variables	a. morbidity				
		diarrhea episode d_222	During the last two weeks that ended yesterday morning, did Child's Name (9.1) have diarrhea?	0= no 1=yes	binary	Tabulations Chi square test Multivariate binary logistic regression (controlled for cluster design)
		b. feeding				
never breastfed d_164		0= never breastfed	Categorical	Tabulations Chi square test Multivariate multinomial logistic regression (controlled for cluster design)		
stopped breastfeeding d_165	Answered yes to Answered no to: From the time you woke up yesterday morning till you woke up this morning did you breastfeed your baby?	1= stopped breastfeeding 2= currently breastfeeding 3- currently exclusively breastfeeding				

	d_166- d_185	<i>From the time you woke up yesterday morning till you woke up this morning did you any of the following items to Child's name? Must answer yes to at least one item except prescribed and over the OTC medicines.</i>			
	<i>currently exclusively breast feeding</i> d_165 + d_166- d_185	<i>From the time you woke up yesterday morning till you woke up this morning did you any of the following items to Child's name? Must answer no to all but prescribed and over the OTC medicines.</i>			
	<i>c. infant attained size at 12 weeks</i>				
	<i>WAZ and HAZ</i> d_274 d_273 BCD_001 gender	<i>baby weight recorded at interview in grams</i> <i>baby height recorded at interview in cms</i> <i>baby age in days at time of interview</i> <i>gender of baby</i> converted to standard deviates using WHO macro software for calculation of z-scores	Weight for age z score height for age z score Underweight 0= >=-2 z score 1=<-2 z score Stunted 0= >=-2 z score 1=<-2 z score	numerical, continuous Binary	Tabulations Two sample Wilcoxon-Mann-Whitney test Multivariate linear regression (controlled for cluster design) Chi2 tests Multivariate logistic regression
	Confounders				
<i>Possible confounders</i>	<i>trial arm</i> rec_003	Randomized by cluster	0= control 1= intervention	binary	Use in multivariate regression with relevant outcome variables
	<i>maternal hiv status</i> LAB_009	Laboratory confirmation of reported maternal HIV status	0= HIV negative 1= HIV positive	binary	
	<i>infant hiv status</i> LAB_007	Laboratory result of PCR test on DBS of Infant HIV status	0= HIV negative 1= HIV positive	binary	
	<i>maternal age</i> d_003	<i>How old are you (in completed years)?</i>	15- 45	numerical ordinal discreet	
	<i>parity</i> d_008	<i>Have you given birth to any children previously?</i>	0= primipara 1= multipara	binary	

	<i>education level</i> d_005 d_006	<i>What is your highest level of education?</i> (have you ever attended school (d_005))	0= none/ primary 1= some secondary 2= completed secondary 3= tertiary	categorical	
	<i>asset index</i>	<i>Do you have a television in your household? =2</i> <i>Do you have a working fridge in your household? =2</i> <i>Do you have a stove in your household=2</i> <i>Do you have a mobile phone=1</i> <i>Do you have a radio in your household=1</i> <i>Do you have a car in your household=3</i> <i>Does your household have electricity? =1</i>	0-12	numerical ordinal discreet	
	<i>water source piped into house</i> d_020	<i>What is the main source of drinking water?</i>	0= piped public, other 1= piped yard 2= piped dwelling 3= other	categorical	
	<i>participant employed</i> d_021	<i>Are you employed?</i> 0= no/ temporary 1=full time/ part time	0= no 1= yes	binary	Use in multivariate multinomial logistic regression with infant feeding outcome variables
	<i>breast infection</i> d_150	<i>Have you had any infection, or problem with your breasts since Child's Name (9.1) was born?</i>	0= no 1= yes	binary	
	<i>Birth weight</i> bcd_004	<i>Baby's birth weight in kilograms from hospital record</i>		numerical continuous	Use in multivariate regression with nutritional outcome variables

Ethical issues

- The ethics review board of the Medical Research Council (EC08-002) approved the main study and monitored the study protocol over time. Permission to conduct the main study was also sought from, and approved by, the Ethekewini District Municipality.
- The main study was registered with the appropriate RCT database and a Data and Safety Monitoring Board was established along with a Community Advisory Board (CAB).
- SOP development and training of data collectors in confidentiality ensured that strict confidentiality of the data was maintained at all times.
- Compensation for time was paid to mothers in the form of an R80 voucher for a local supermarket administered by a data collector at the 12-week endpoint visit.
- CHWs did not know the HIV status of the mothers unless the mothers voluntarily disclosed their status. Data collectors were aware of mother's HIV status as they had access to maternal health records, which was only obtained after the participant granted informed consent.
- Mothers were able to obtain on going counselling from the CHWs even if they chose not to consent to participate in the study. The CHWs did not know, unless told by the mother, whether or not the mother was traveling to the hospital for data collection.
- Women who screened positive for mood problems were referred to existing mental health services in the Umlazi community and KwaZulu Natal Province. Extra mental health services outside of routine services were not provided for women scoring positive for mood disorders on the EPDS screening scale or for those reporting suicidal ideation.
- A safety and insurance plan for field workers was established to mitigate the threat of criminal violence to field staff.

Recruitment of study participants

Informed consent

Informed, written consent was obtained from mothers. Participant “Information sheets” written in both English and Zulu were given to each participant before they were enrolled into the trial.⁴ These sheets were also read out loud to all eligible mothers to account for illiterate/sub-literate mothers and clarified where needed. SOPs were developed for all CHWs and data collectors to guide the process of obtaining informed consent. Data collection supervisors regularly reviewed this process with data collectors over the course of the study. All mothers were informed again at the 12-week interview as to the purpose of the study and their consent for participation was confirmed before the interview commenced. Women were also asked to sign a consent form for disclosing their HIV status and for agreeing to DBS collection for themselves and their infants.

All women were free to withdraw from the study at any point.

Benefits and disadvantages to mothers and infants

Mothers and infants who participated in this study did not receive any direct benefits as a result of this sub-study. Similarly, there are no disadvantages to these participants through the analysis done for the purposes of this dissertation. Therefore, the analysis proposed for this mini-dissertation has no direct impact on the psychological outcome or well being of the women and infants who participated in the main trial study as the study has already been long completed (2011).

Results of the study will add to the evidence guiding policy for addressing maternal psychological morbidity and mitigate negative effects on child health. If the hypotheses posited in this proposal are shown to be true, it is hoped that the outcome of this analysis will help to encourage policy makers of the need not only to identify women with postnatal mood disorders but to provide needed support for these women and families through strengthening and adding needed mental health services in the public health sector. This would be not only to ameliorate mothers’ suffering from postnatal mood disorders but to improve health outcomes their babies and their families. This will benefit other mothers, infants and families in the population in the long term.

⁴ See Part D (appendices) for English copies of participant information sheets and trial consent forms.

Policy context and importance of knowledge

Results from this study will add to the body of evidence around the relationship between maternal mood and its association with adverse infant health outcomes in African and particularly South African contexts.

Data management

Data is stored under participant id numbers and identities of participants are completely unknown to the researcher. The data used for this analysis is stored on a personal computer can be accessed only by the researcher who has the computer password.

Stakeholders

Stakeholders in the outcomes of this study include: participants, women, children, families and communities at risk for, and affected by, postnatal depressed mood. Health care workers including nurses, clinicians, community health service providers and others involved in delivery of maternal and child health care services. National and Provincial Department of Health including program managers for Maternal and Child Health, and Mental Health. Other researchers in the field.

The proposed sub- study was granted ethics approval by UCT on December 20 2012. The UCT Human Research Ethics Committee approval can be found in Part D (appendices).

Dissertation Structure

This dissertation will consist of four parts:

- A) Protocol
- B) Literature review
- C) Article
- D) Appendices

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Appendix

Panel 1 Visit schedule and content for intervention in Good Start III

Antenatal visit 1	<p>Antenatal care action – immunisations/micronutrient supplementation</p> <p>Focus on the importance of VCT (linking this with the PMTCT programme and the benefits of testing to the mother)</p> <p>Emphasise the importance of antenatal care</p> <p>Key messages on appropriate infant feeding</p> <p>Encourage exclusive breastfeeding in HIV negative women or women of unknown HIV status.</p> <p>For HIV positive women, assist with thinking about infant feeding options</p> <p>Input regarding infant communication and the mother-infant relationship</p>
Antenatal visit 2	<p>Birth plans – place of birth, support during labour, care plans if returning to work</p> <p>Danger signs and emergency plans – this will be done, if possible together with other family members in order to elicit their input regarding possible plans in the event of an emergency, including recognition of danger signs, emergency transport plan and emergency funds if needed</p> <p>Homecoming arrangements</p> <p>Follow up and re-emphasis on VCT, PMTCT, the key messages on appropriate infant feeding that were provided in antenatal visit 1; further discussion in terms of assisting with the implementation of chosen feeding option</p> <p>Additional input on infant communication and the warning signs of postnatal depression</p>
Postnatal visit 1 (24- 48hrs)	<p>Assessment of newborn– breathing, thermal care, colour, bleeding, neonatal eye care, checklist of danger signs</p> <p>Assessment of mother - bleeding, signs for infection, mastitis</p> <p>Early recognition of illness (superficial or systemic) and help seeking</p> <p>Exclusive breastfeeding or appropriate infant feeding support</p> <p>Hygienic cord care and what to expect regarding when the cord will drop off</p> <p>Thermal care, skin to skin care and Kangaroo care if needed for preterm babies</p> <p>Ensure that babies of HIV positive women have received Nevirapine</p> <p>Information about warning signs for mother or baby and what to do</p> <p>Support for women who have ‘the blues’</p>
Postnatal visit 2 (3- 4 days)	<p>Assessment of the mother and the newborn, Further input on the early recognition of illness (superficial or systemic) and help seeking</p> <p>Monitoring and follow up of breastfeeding or appropriate feeding and possible feeding problems</p> <p>Further support for hygiene, thermal care and cord care, with Kangaroo care input if needed for preterm babies</p>

	<p>1st week clinic visit reminder</p> <p>Information about warning signs for mother or baby and what to do</p> <p>Newborn Interactive Assessment - demonstration of the abilities of infants and infant communication and social responsiveness. Sleeping, crying, consolability and wider concerns</p>
<p>Postnatal visit 3 (10-14 days)</p>	<p>Early recognition of illness (superficial or systemic) and help seeking</p> <p>Ongoing monitoring of breastfeeding or other appropriate feeding</p> <p>Information about warning signs for mother or baby and what to do</p> <p>Promote attendance at clinic for 6 week visit for mother to have access to family planning and baby to receive immunisations and the babies of HIV+ women been given bactrim and HIV testing</p> <p>Mother infant interaction modelling and communication input</p> <p>Assess for signs of postnatal depression</p>
<p>Postnatal visit 4 (3- 4 weeks)</p>	<p>Early recognition of illness (superficial or systemic) and help seeking</p> <p>Ongoing monitoring of breastfeeding or other appropriate feeding</p> <p>Information about warning signs for mother or baby and what to do</p> <p>Promote attendance at clinic for 6 week visit for mother to have access to family planning and baby to receive immunisations and the babies of HIV+ women been given bactrim and HIV testing</p> <p>Mother infant interaction modelling and communication input</p> <p>Assess for signs of postnatal depression</p>
<p>Postnatal visit 5 (7- 8 weeks)</p>	<p>Further input on feeding including advice regarding weaning</p> <p>Infant weight from clinic card (6 week visit)</p> <p>Mother infant attachment</p> <p>Checklist of signs of postnatal depression</p> <p>Has the child been tested for HIV at six weeks and receiving cotrimoxazole</p> <p>Formula sustainability for HIV positive women using formula milk</p> <p>Family planning and counselling</p> <ul style="list-style-type: none"> • Input on milestones and information and specific skills about the stimulation of infants

PART B: Literature Review

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Introduction and objectives of literature review

The first few months of life are critical for the future well-being of a child with increasing evidence showing that early life experiences and exposures are biologically embedded and have lifelong consequences.(1)

Depression is a significant and often overlooked form of maternal morbidity, which has implications not only for the woman but also for their children.(2) It is estimated that around 13% of all mothers are affected by postnatal depression (PND) or postnatal depressed mood in the developed world.(3) Epidemiological studies from low and middle-income countries (LMIC) suggest that prevalence rates of maternal depression are often much higher than those found in high income countries.(4) Poverty has been found to be both a predictive risk factor for maternal depression and a key moderator of the effects of this morbidity on child development.(5) The increased risks posed by wide spread socio-economic adversity in many of these contexts have significant repercussions for the health and well being of mothers and their children living in developing countries.

This literature review aims to present a picture of postnatal depressed mood, its clinical features and diagnosis, reported global rates and risk factors, particularly for LMIC. It will provide a summary of the literature examining the association between postnatal depressed mood and adverse infant outcomes and present theories of mediating mechanisms for this association. It will review studies that examine the negative physical effects of postnatal depressed mood on infant nutritional status and morbidity as evidenced by the growing body of research emerging from LMIC. It will include research examining the association between infant feeding and specifically exclusive breastfeeding and the presence of postnatal depressed mood. Finally, it presents of picture of postnatal depressed mood in South Africa (the context of the proposed research) and summarizes evidence from, and highlights gaps in research conducted in this context around maternal mental health and its association with infant health and feeding outcomes.

Search strategy

Literature for this review was accessed through pubmed, medline, academic search premier CINHAL for peer-reviewed papers published between 1970 and January 2013. Search terms included: “post-partum” “postnatal” “perinatal” AND “depression”, “depress*” alone and in combination with one of the following: “growth”, “nutrition*”, “malnutrition”, “child development”, “diarrhea”, “infant morbidity”, “feeding”, “breastfeeding”. These were further narrowed down for regional findings with the terms “Africa”, “Asia”, “developing countries”, “low middle income country”, and “South Africa”. The reference lists of review articles

accessed were also searched for relevant articles, book chapters and reports. Original research and systematic reviews in peer-reviewed journals were included if relevant to the aims and objectives noted above.

Definition and clinical presentation and diagnosis of postnatal depression

Major depression is one of the most widespread and common mental illnesses across the world, occurring at any time in the lifespan.(6) New mothers are at particularly increased risk of new onset of mood disturbances with postpartum non-psychotic depression recognized as the most common complication of childbearing affecting, on average, 13% of women worldwide.(3)

Antenatal depression refers to the first onset of depression during pregnancy. Perinatal depression refers to onset of depression during the third trimester or early postpartum where postpartum depression refers to the onset of depression in the post partum period and may continue into the first year of life. Though there are clearly overlaps in definitions depending on the time of onset of depression, this literature review will focus mainly on the postpartum period. Some studies have been cited that allude to perinatal period, which encompasses both the late pregnancy and early postpartum onset of depression if they have implications on relevant child health outcomes.(7)

The diagnosis of depression is most often based on clinical signs and symptoms as reported by the patient. (6)The essential features of a major depressive episode have been defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.(8) The standard approach to diagnosis is for a mental health professional to perform a structured clinical interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* axis I disorders.

The clinical presentation of postnatal depression is generally the same as that of major depression with the defining difference being that the episode occurs after childbirth, usually beginning within the first 6 weeks postpartum. This time interval differs among research studies however, the time of onset commonly used based on results from epidemiological studies ranges from 2 weeks to 12 months after childbirth. (9) Signs and symptoms include depressed mood, anhedonia, low energy and frequently, suicidal ideation and are similar to patterns and symptoms of those who have depression unrelated to childbirth. A mother with post partum depression may present with tearfulness, hopelessness, labile emotions, feelings of guilt and low self-esteem, loss of appetite, and sleep disturbance. She may also have feelings of inadequacy and feel unable to cope, poor concentration and memory, fatigue and

irritability. (10) In fact, post partum depression does not have its own diagnosis but is based on the standardized diagnostic criteria for depression as a psychiatric classification for affective or mood disorders using either the American Psychiatric Association Diagnostic Standards Manual (DSM) IV or the World Health Organization (WHO) International Classification of Diseases (ICD)-10.

Diagnosing Postnatal Depression

Semi-structured standardized clinical interviews increase the reliability of diagnosis between researchers and allow for probing questions to distinguish between ‘normal’ symptoms associated with childbirth and those characterized by depression. This method of diagnosis however, has cost and time limitations when considering the assessment of large numbers of women. Structured scales are usually used to screen for probable depression, most commonly the Edinburgh Postnatal Depression Scale.

Edinburg Postnatal Depression Scale

Designed as a screening tool for clinical and research purposes specifically for the postpartum period, (11) the EPDS is one of the most extensively used screening instruments for PND world wide. (4) The scale consists of 10 questions, each having 4 possible answers. Women are asked to respond by rating how they have felt in the previous 7 days. Each response is scored 0-3 for severity of symptoms experienced with a resulting range of 0-30. The EPDS excludes many of the above-mentioned somatic symptoms of depression that may be caused by the normal physiological changes associated with childbirth. (12)

Developed in England in 1987 and originally validated on British women by Cox (11) the EPDS has since been used in a variety of cultural settings and translated into numerous languages. (13) Studies have shown the EPDS to be a valid and reliable screening scale for PND though different thresholds have been proposed for use in different settings. (14) Having said that, the EPDS remains a screening tool and therefore cannot give a definitive clinical diagnosis for PND. Therefore, women who score about the threshold on the EPDS are said to have “probable depression” or “postnatal depressed mood.”

A major challenge in comparing EPDS use has been the wide variation across different settings in sensitivity, specificity, positive and negative likelihood ratios in validation studies of the scale. (13) In a systematic review of 37 studies validating the EPDS, the authors found heterogeneity of results across studies due to “significant differences in study design,

population sampled, the timing of testing, language version of the EPDS used and diagnostic criteria". (13)

Prevalence of postnatal depressed mood, globally and in LMIC

While the EPDS is the most extensively used measure for probable postnatal depression, other studies have used a range of other self-reporting scales. This wide range of measurement tools, methods of assessment, time period under evaluation and varying screening tool cut offs for diagnosing probable depression has resulted in significant heterogeneity in prevalence rates of post-natal depression across and within study populations.

Pooled results in a meta-analysis from 59 studies conducted by O'Hara et al (of largely high income countries) have estimated an average global postnatal depressed mood prevalence of 13% (95% confidence interval 12.3% to 13.4%) (15), while another systematic review of mothers in high income countries put the rate as high as 19% (period prevalence) in the first three months postpartum for minor depression (7.1% major depression). (7) In a systematic review of postnatal depressed mood in LMIC by Parsons et al, the authors found mean prevalence rates for individual countries ranging from 4.9% to 50%. (4) This was echoed in a study that examined cross cultural and social diversity of postnatal depressed mood prevalence, which concluded that the wide variability could be due to cross cultural variables, reporting styles, and perceptions of mental health. (16) There is also great variation of mean estimates reported across regions with, for example, 30.9% in Pakistan, 22% in Bangladesh and 4.9% in Nepal. The authors conclude that it is hard to obtain reliable estimates of the prevalence of postnatal depressed mood without an established consensus on cut-off scores, timing of assessment and scales. (4) In a systematic review of the prevalence and determinants of non-psychotic common perinatal mental disorders (CPMDs) in World Bank categorized low-and lower-middle-income countries, the authors found the pooled prevalence for postpartum common mental disorders was estimated at 19.8% (95% CI: 19.2–20.6). (17) In another systematic review of perinatal mental health across Africa, probable depression was identified as the most commonly identified psychological complication of the prenatal and postnatal period in African women with a reported weighted mean prevalence from 35 studies across 8 African countries calculated at 18.3% (95% CI 17.6%–19.1%). (18)

Risk Factors for Postnatal Depressed Mood

Numerous studies have sought to identify common risk factors for postnatal depressed mood across cultures and settings. While there is some evidence that genetic and biological factors may contribute, some of the strongest predictors are psychosocial determinants, such as lack of social support, poor partner/ marital relations, recent negative life events, a history of any psychopathology, poverty and economic adversity. (4,15,18,19) One of the strongest risk

factors for postnatal depressed mood is the onset of depression during pregnancy. In a review of antenatal risk factors for postnatal depression, results of the studies examined consistently found that experiencing depressed mood or anxiety during pregnancy were significant predictors of postpartum depression (20,21) Increased socio-economic hardship coupled with prevalence of other risk factors, such as low education, may elevate the risk of maternal depression and therefore partially explain the relatively high prevalence rates of postnatal depressed mood in LMIC as compared to high-income countries. (4,4,4,6,20) Another factor may be related to the HIV pandemic, which affects up to a third of all pregnant women sub-Saharan African countries and may contribute to elevated rates of postnatal depressed mood in these settings. (4) HIV screening is frequently done during the antenatal period and many women find out their sero-status at this time. The implications of an HIV diagnosis for a woman and her unborn child are extremely disturbing for a mother and may negatively impact her mental state and risk for depression. (22)

Effects of postnatal depressed mood on child developmental outcomes

The effects of postnatal depressed mood on child development have been well researched in high-income contexts. (23,24) Much of the focus has been on parent-child interactions and the effects of depressed mood on what has been termed responsive parenting. Responsive parenting is a reciprocal process of recognizing and interpreting verbal and non-verbal communication signals between mothers and infants and forms a basis for emotional bonding that is essential to healthy social-emotional functioning. (25) Depressed mood may cause the mother to become more withdrawn, less attuned to infant cues, be inconsistent and less likely to respond to their babies and provide them with less quantity and poorer quality of stimulation.

Researchers in South Africa found maternal sensitivity of engagement with their infants to be significantly poorer in depressed versus non-depressed women. (26) The emotional quality of parenting may therefore be an important mediator in the effect of postnatal depressed mood on child development, compromising the level of care provided by mothers to their children. This, combined with diminished stimulation and engagement, may place infants of depressed mothers at considerable risk for several negative outcomes.

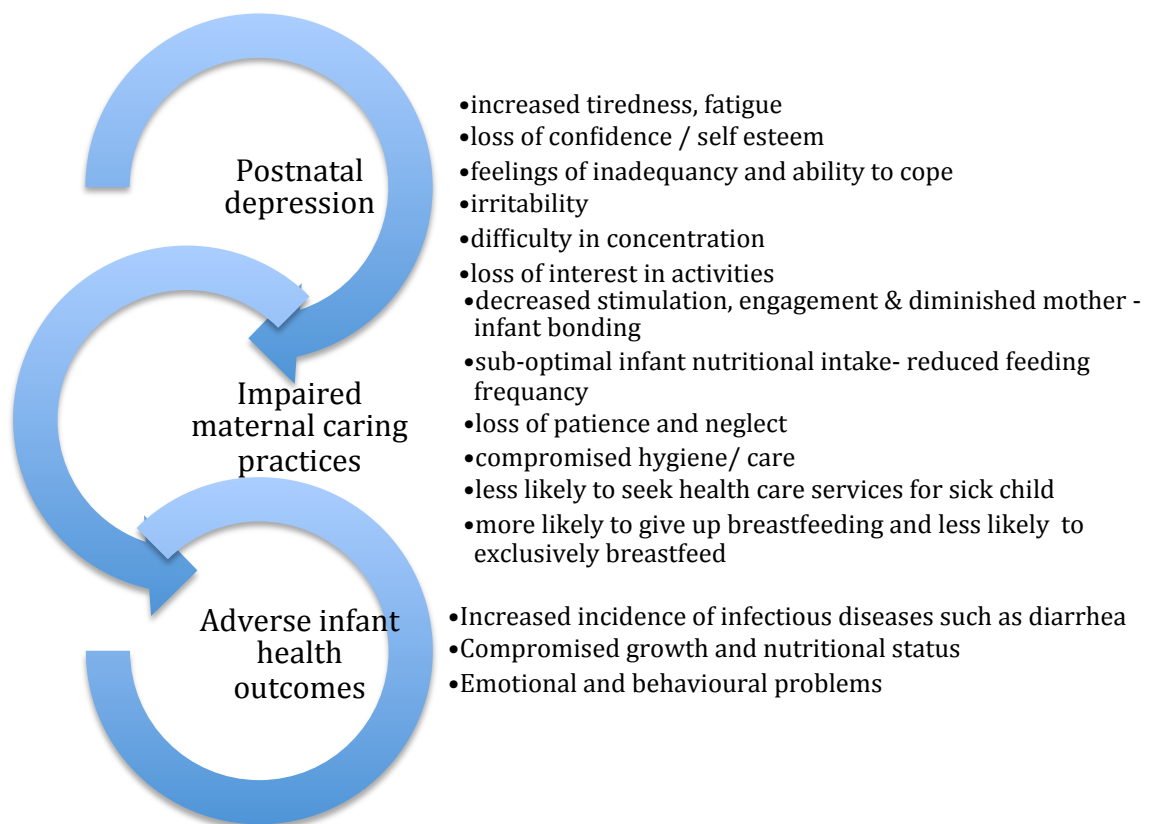
Poverty and other mediating pathways

Children growing up in economic hardship are already at significantly increased risk of illness and impaired growth and development. Poverty in most LMIC is characterized by a living environment lacking basic amenities such as water, fuel for cooking, decent sanitation, poor access to macro and micro-nutrient rich diets, increased exposure to pathogens through

unhygienic living environments, overcrowding and a greater prevalence of infectious disease. Furthermore, social adversity may coincide with economic hardship. As the main caregiver, a mother plays a vital role in her child’s survival, development and well-being. ‘Quality of care’ is a recognized determinant for healthy children.(27) However, this is difficult to quantify, may be dictated by cultural practice and can too often become an exercise in blame for the caregiver who may also be a victim of socio-economic adversity. Furthermore, care-giving behaviors such as ensuring adequate hygiene, optimal nutrition through breastfeeding, immunization, recognizing illness and seeking care, along with the rest of responsive parenting and mother-infant bonding that is needed for physical and mental development of a child may all be affected and severely compromised by a debilitating mood disorder like depression.

The association between maternal mood and child health are no doubt multi-factorial and complex. Figure 1 below postulates one possible mechanism by which this complex etiological process may occur.

Figure 1 Conceptual framework: Impact of postnatal depression on child health outcomes



Postnatal depression and infant growth and nutritional status

Nutritional status is a significant predictor of child morbidity and mortality (28) and one of the best global indicators of child well-being. Not only is nutritional status a measure of a child's current physical health but poor nutrition has longer-term implications for a child's cognitive development. Evidence points to an association between childhood malnutrition and poor school performance and significant functional impairment in adult life. (29) In fact, examination of nutritional status assesses and predicts performance, health and survival of individuals and reflects the economic and social well being of populations. (30) A scientific consensus is emerging that sees the early months and years as critical for establishing human development that will greatly impact health outcomes later in life. (1) Furthermore, it is the young child that is at the highest risk of malnutrition, with the great majority of malnourished children becoming malnourished before their second birthday. (27)

The physical result of poor nutrition can be measured through non-invasive and cost effective methods of anthropometry. Weight, height, age and gender are used to create a set of standard growth indices that describe a child's body response to poor nutrition. Each of these indices reflects different nutrition related conditions.

- Wasting, measured by weight relative to length or height, is a short term response to inadequate nutritional intake and helps to identify children suffering from current or acute under nutrition. Wasting is appropriate for examining short-term effects of nutritional stress brought about by for example, illness. (30)
- Stunting, measured by length/ height relative to age, on the other hand, reflects the slowing or interruption of growth and therefore is a long-term response to past or chronic malnutrition but it cannot measure short-term changes in malnutrition. (30)
- Underweight, defined by a low weight for age, on the other hand is a composite measure of stunting and wasting. It does not discriminate between short and longer-term forms of malnutrition. Weight for age is therefore recommended as the indicator to assess changes in the magnitude of malnutrition over time. (30)

Malnutrition is caused by a complexity of factors including birth weight, infant feeding practices, frequency, duration and severity of illness. Socio-economic status and maternal characteristics such as age and education have also been linked to child nutritional status, and

in some regions, the child's gender. (27) These contextual factors may all play important confounding and mediating roles between the effects of postnatal depressed mood on infant nutritional status.

The associations between maternal depressed mood and infant under-nutrition have been explored in numerous studies. In a recent systematic review and meta-analysis of maternal depression and early childhood growth (2011), Surkan et al. pooled data from 17 studies for a total of 13 923 mother and child pairs from 11 countries and found that children of mothers with depression or depressive symptoms were more likely to be underweight (OR: 1.5; 1.2–1.8) or stunted (OR: 1.4; 1.2–1.7) than those of psychologically well mothers. This association was even stronger for longitudinal studies (underweight OR: 2.2; 95% CI: 1.5–3.2; stunted OR: 2.0; 95% CI: 1.0–3.9). (31)

The strongest evidence base for the association and potential etiological role between postnatal depressed mood and infant under-nutrition has emerged from South Asia. (32-37) Evidence from studies in Africa however have been mixed. (37-42) A longitudinal case-control study of 876 mothers from Nigeria showed that infants of depressed mothers had poorer growth by the 3rd and 6th month of life than infants of non-depressed mothers, (Unadjusted OR 3.41; 1.3-8.52 for weight and OR 3.28; 1.03-10.47 for length at 3 months and OR 4.21; 1.36–13.20 for weight and OR 3.34; 1.18–9.52 for length at 6 months). (38) Two large studies from Ethiopia (one prospective cohort and one cross sectional), however, did not find any statistically significant differences in the prevalence of underweight or stunted infants in mothers with high levels of common mental disorders (CMD) compared to those with low levels. (36,39) Smaller cross-sectional studies examining adverse infant health outcomes and maternal depression in Zambia and Malawi (40,41) examining associations between CMD and infant growth impairment have also had mixed results. In Malawi, infants of mothers with CMD were more likely to be stunted but not underweight at 9 months as compared to infants of mothers without CMD. (41) In Zambia, no statistically significant differences were found between health outcomes of infants of mothers with CMD vs. infants of psychologically well mothers.(40) In South Africa, Tomlinson et al. followed 147 mother-infant dyads recruited over an 8-month period from the socio-economically disadvantaged peri-urban settlement of Khayelitsha near Cape Town. Infant weight and length and maternal mood was assessed at 2 and 18 months, however, no clear effect of postnatal depressed mood on infant growth were found. (42) Data examined from a longitudinal birth cohort in Soweto; Johannesburg that measured the effect of postnatal depressed mood on the growth of children at age 2 concluded children of depressed mothers were at increased risk for having stunted growth, compared to non-depressed mothers (OR 1.61 (95% CI 1.02 to 2.56). (43) Thus,

findings across Africa and within countries have been mixed and differ from studies in South Asia, which have shown a clear association between maternal depression and infant under-nutrition.

The reasons for the heterogeneity between studies remain unclear but could partly be due to methodological difference. In a review of the evidence of maternal depression on infant growth, Stewart notes that the impact of maternal depressed mood on growth is expected to be most evident in the early postnatal period when the infant is more exclusively the responsibility of the mother and points to results of cohort studies that suggest the effect is most evident between 4 and 6 months of age, declining after this. Contextual factors may vary across settings and are not always included in multivariate analyses. For example, the effect of infant birth weight and gestational age may be large, and are often not included in settings where obtaining this information is difficult. (44) The effects of maternal depressed mood on child nutrition no doubt result from a complex set of interactions between psychosocial, socio-economic and socio-cultural factors at play across countries and cultures. (4)

Postnatal depression and diarrhea

One of numerous possible pathways by which maternal depressed mood may have an effect on infant nutritional status is through the increased risk for diarrheal disease. Diarrhea is one of the top causes of death in infants and young children globally and remains a major public health concern, especially in low and middle-income countries. (45) Furthermore, frequent episodes of diarrheal disease in childhood also result in sub-optimal growth and development. (46,47) Prevention of diarrhea requires attention to hygienic practice and is particularly challenging in contexts with poor sanitation, unsafe water sources and increased prevalence of diarrheal disease in the community. For those in overcrowded impoverished living conditions, maintaining a high standard of hygiene is extremely difficult. Mothers with depressed mood may have reduced energy, motivation and will to ensure precautions such as hand-washing, safe refuse disposal, latrine use, personal hygiene and maintaining a healthy environment to reduce risk of their infants getting diarrhea.

Few studies thus far have examined the association between maternal mood and diarrhea in infants. Research from a cohort study in Rawalpindi Pakistan found children of mothers with depressed mood have 2.3 (95% CI: 1.6- 3.1) times the relative risk of having five or more diarrheal episodes per year than infants of mothers without depressed mood. The association remained significant after controlling for the effects of low birth weight, infant nutritional status, duration of breast-feeding and socioeconomic status. (48) A study in Nigeria also

found that by 9 months, infants of mothers with depressed mood had greater average number of cases of diarrhea than infants of mothers with no depressed mood (5.23 cases SD 2.37 vs. 3.70 cases SD 4.14; $p=0.001$). (38) A large cohort study in the UK found that children born to women with perinatal depressed mood had a 40% increased rate of gastrointestinal infections when compared with children born to women without perinatal depressed mood, independent of other risk factors. (49)

Diarrheal morbidity and mortality in infants is of serious concern in LMIC. It is estimated to be the 3rd leading cause of death in infants under one in South Africa after HIV/ AIDS and low birth weight. (50) Improved maternal mental health may be an important mechanism to decrease this risk to the child and further explorations around this association are warranted.

Postnatal depressed mood and infant feeding outcomes

Poor nutrition results from a myriad of factors and does not just have to do with lack of food. Good nutrition, especially in the early months of life, is usually determined by feeding practices, particularly exclusive breastfeeding, the frequency of feeds, as well as how often, how severe and how long a child is ill. (51)

It is universally recognized that breastfeeding in poor settings is critical for child survival. (52) Optimal infant feeding requires that all infants are breastfed exclusively for the first 6 months of life with continued breastfeeding up to two years of age. Studies across the world have shown that breastfed infants are at significantly decreased risk of morbidity and mortality and have improved nutrition and growth.(52-54) Furthermore, the importance of breastfeeding on maternal and infant bonding and healthy social and emotional development for children has been discussed in numerous studies both in high and LMI countries. (25,55,56). In light of such compelling evidence, efforts to encourage and promote universal breastfeeding have become crucial components of public health policy. Reducing risk factors for early cessation of breastfeeding are important to achieving widespread practice.

The association between maternal depression and early cessation of breastfeeding has been explored in numerous studies. A prospective cohort study that followed 1745 Australian women for one year postpartum found that women who developed postnatal depressed mood had a 1.25 (95% CI: 1.03–1.52) times increased risk of early breastfeeding cessation compared to women who did not develop depression, even after adjusting for confounders.(57) A similar study in Canada looking at breastfeeding practices at 4 weeks and 8 weeks found that mothers were significantly more likely to discontinue breastfeeding by both these time points if they were depressed at 1 week postpartum. (58) A recent Italian

study of infant feeding at 12-14 weeks postpartum found that the risk of bottle-feeding at 3 months increased dose-dependently with an increase in maternal EPDS score (OR 1.06, 95% CI 1.01-1.11). (59)

This association has also been seen in research conducted in low and middle-income countries. A small study of 60 women in Turkey found an association between higher EPDS scores and breastfeeding cessation by 4 months, (60) while a cross sectional study in Pakistan also found statistically significant difference in mean depression scores for lactating and non-lactating mothers while no other significant differences between known risk factors for breastfeeding cessation (age, parity, socio-economic status and educational level) was found between the two groups. (61) Similarly, a secondary outcome of a longitudinal cohort study of mothers in Nigeria found that women who had postnatal depressed mood were less likely to be breastfeeding at 6 weeks, 3, 6, and 9 months than psychologically well mothers. (38) Maternal mood at 7 weeks postpartum predicted feeding behavior at 6 months in a study of mothers in Barbados. (62) A qualitative systematic review of studies of postnatal depressed mood and infant feeding outcomes found compelling evidence to support the theory that probable depression in the postpartum period has a negative effect on infant feeding. (63)

Breastfeeding requires commitment and effort on the part of the mother. Women with depressed moods may be less confident in their ability to breastfeed, more vulnerable to feelings of inadequacy and unable to cope with challenges in breastfeeding and may therefore be more likely to give up breastfeeding than psychologically well mothers. (57) Numerous studies have shown a mother's confidence in her ability to breastfeed her infant to be predictive of breastfeeding outcomes. (58,64,65) Mothers who had depressed moods in Canada were more likely to report lower levels of breastfeeding self-efficacy, (58) which has been linked, not only to the initiation and duration but to exclusivity of breastfeeding. (63)

Postnatal depressed mood and exclusive breastfeeding

Exclusive breastfeeding in the first 6 months of life is critical to a child's growth and health. Exclusively breastfed means *nothing* other than breast milk and prescribed medication are consumed by the child. This provides significant protection from the risk of infection and growth faltering. (66) It has been suggested that postnatal depressed mood is an influential factor in a mother's commitment to exclusively breastfeed her child. (63) One pathway whereby the effect of depression may adversely influence the exclusivity of breastfeeding lies in a mother's negative self-perception in her capability to produce sufficient milk, and thereby increased likelihood of supplementing her baby's diet with bottle milk. Supplemental milk

can reduce breastfeeding frequency and the volume of milk the infant extracts, which in turn can result in, engorged breasts, reduced breast health and increased risk for clinical mastitis.(65) This causes the mother significant pain when feeding and makes it more difficult for the infant to extract milk which may negatively effect infant weight gain which in turn may lead to the mother believing her milk is insufficient and therefore deciding to wean her infant entirely.

Breastfeeding and maternal depression in the context of the HIV pandemic

The double burden of HIV and high infant mortality in resource poor countries has placed breastfeeding at the forefront of an intense debate. This is especially true in the context of South Africa, which has the lowest rates of breastfeeding and exclusive breastfeeding amongst low and middle income countries and one of the highest antenatal HIV prevalence rates in the world. (67) HIV positive women have high reported prevalence of probable perinatal depression with rates of 41%- 54% found in South Africa and Zimbabwe. (22) (68) Furthermore, women who are HIV positive are often discouraged in these settings from breastfeeding due to their serostatus and the perceived beliefs around transmission risks to the child, which result in this group of women being even less likely to choose this feeding method.(69) Exclusive breastfeeding practices are critical for HIV exposed children in resource poor settings, reducing risk of morbidity and mortality from diarrhea and pneumonia as well as mitigating the risk of vertical transmission that occurs through mixed feeding. (70,71) Efforts to improve exclusive breastfeeding rates for this population are critical.

A recent prospective study in a community near Durban, South Africa examined the impact of infant feeding mode on the health of HIV positive mothers and their children over a 9-month period. (72) One reported outcome of the study was that significantly fewer HIV positive women who breastfed their infants had depressed moods when compared to HIV positive women who formula fed their infants.

The South African context

The picture of perinatal and postnatal depression in South Africa

Depression is a common perinatal disorder in South Africa. Reported prevalence rates of perinatal depression vary according to context, time of assessment, methodology and scale used and are reported in table 1 below. Studies on probable antenatal depression found prevalence rates ranging between 16% (in peri-urban Cape Town) and 41% (in rural clinic based Kwazulu Natal) using the EPDS. (22,73) Pooled results from a meta-analysis of studies by Parsons et al show a mean postnatal depressed mood prevalence rate of 20%. (4) Most

studies around perinatal depression in South Africa have focused on prevalence and associated risk factors across different study settings. Two studies thus far have examined the association of postnatal depressed mood with infant growth outcomes (as detailed previously) (42,43) and two have examined its association with infant behavioral outcomes. (26,74) No studies have yet reported the association between postnatal depressed mood and infant morbidity, such as diarrhea. Furthermore, only one study in South Africa has reported on the association between postnatal depressed mood and infant feeding though this was a secondary outcome. Furthermore, this was amongst HIV positive women and may not be generalizable to all postpartum mothers for a variety of reasons. (72) Intervention models for the improvement of maternal mental health and subsequent child health outcomes have been developed and reported on in 3 studies in South Africa. (73,75,76)

Table Summary of studies of perinatal and postnatal depression undertaken in South Africa

	Study design	Place	N	Time of assessment	Measurement	Prevalence	Focus
Manikkam & Burns, 2012	Cross sectional survey	Urban public hospital, KZN	387	3 rd trimester	EPDS	38.5%	Prevalence Risk factors
M. Hartely et al., 2011	Cross sectional survey	Peri-urban township, Cape Town	1062	2 nd /3 rd trimester	EPDS	39%	Prevalence Risk factors
Rochat et al, 2006	Cross sectional survey	Clinic- based, Rural KZN	242	2 nd /3 rd trimester	EPDS	41%	Prevalence Risk factors
Rochat et al., 2011	Cross sectional survey	Clinic- based, Rural KZN	109	2 nd /3 rd trimester	DSM IV clinical interview	47%	Prevalence, Clinical presentation
Cooper et al., 2009	RCT	Population based Peri-urban township, Cape Town	449 354 346	2 nd /3 rd trimester 6 months post partum 12 months post-partum	EPDS	16% 12.4% -15.8% 10.9% -15.5%	Mother-infant relationship
Tomlinson et al., 2006	Longitudinal cohort	Population based Peri-urban township, Cape Town	147 98	8 weeks postpartum 18 months	DSM IV clinical interview	34.7% 12%	Child growth outcomes
Lawrie et al., 1998	Cross sectional survey	High risk post natal clinic, Johannesburg	103	6 weeks postpartum	EPDS/ DSM IV clinical interview	24.5%	Validation of EPDS
Ramchandani et al. 2009	Longitudinal cohort	Population based, Soweto-Johannesburg	1035	6 months post partum 2 years or age	Pitt Depression scale	16.4%	Risk factors Child growth and behavior
Avan et al, 2010							
C. Hartley et al., 2010	Cross sectional survey	HIV+ mothers at hospital in Western Cape	83	10-12 months	EPDS	42.2%	Infant social withdrawal

Motivation and Rationale for study

While studies from many parts of the world have shown that the mental well being of mothers, especially during the postnatal period, can have a significant effect on child health, there is a paucity of literature examining such associations in the South African context. Rates of postnatal depressed mood in South Africa are high, with an estimated one third of all mothers affected. (42,68) This rate is even higher amongst HIV positive women. (22) While maternal depression has been found to have significant negative effects on a range of child health outcomes in South Asia (33,34,37,48,77-79) studies from African contexts, however, have had mixed results. (31,38,39,41,42) Evidence of the negative effect of maternal mood on infant nutritional outcomes in Africa have been mixed and most studies have been based on relatively small numbers of women.

Exclusive breastfeeding rates for South Africa are extremely low, with the Demographic and Health Survey 2003 reporting only 8% of children less than 6 months of age being exclusively breastfed. (80) Reported exclusive breastfeeding rates in the peri-urban community of Umlaazi, Kwazulu Natal South Africa were as low as 6% at 12 weeks postpartum (24 hour recall).(53) Furthermore, diarrhea is the third largest cause of death for infants under one and 30% of child deaths are attributed to malnutrition. (50) Clearly these outcomes are interlinked. This study proposes to examine the role of maternal mental health in major preventable causes of infant morbidity and mortality in South Africa and add to the knowledge of its effects on infant health and development.

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Title

Exploring the association between postnatal depressed mood and infant morbidity, growth, and feeding at 12 weeks postpartum in a peri-urban South African setting

Running head: Post-natal depression and infant health in South Africa

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Abstract

Background Depression is a common yet often overlooked form of maternal morbidity, which has implications not only for the woman affected but also for their children. This study aims to determine the association between postnatal depressed mood in mothers and adverse infant feeding, health and nutritional outcomes at 12 weeks postpartum.

Methods and findings This sub-study is a cross sectional analysis of data collected for a cluster randomized controlled trial (Good Start III) assessing the impact of community health worker home visits on maternal and child health outcomes in a peri-urban setting in South Africa between 2008- 2011. Infant weight and length measurements, maternal recall of infant diarrheal disease and 24-hour infant feeding history were recorded at 12 weeks postpartum along with maternal mood, using the Edinburg Postnatal Depression Scale (EPDS). 3494 mother-infant dyads were assessed of whom 568 (16.3%) had postnatal depressed mood consistent with an EPDS score of ≥ 12 . Multivariate regression analysis showed that infants of mothers with probable postnatal depression had increased risk of diarrheal disease (Adjusted RR 1.47, 95% CI: 1.28- 1.68) and clinically marginal but significantly lower nutritional z-scores for weight for age (WAZ) and length for age (HAZ) relative to infants of mothers who were not depressed (Adjusted WAZ -0.132, 95% CI: -0.243; -0.021; HAZ -0.104, 95% CI: -0.205; -0.004). Infant feeding method and a history of diarrheal disease mediated the relationship between maternal mood and infant nutritional outcomes. Maternal depressed mood was negatively associated with breastfeeding exclusivity at 12 weeks postpartum.

Conclusion Screening South African woman in the early postpartum period for signs of depression will help identify mothers and babies in need of support to ensure an integrated strategy for promotion of exclusive breastfeeding and prevention of infant morbidity and poor growth.

Introduction¹

Depression is a significant and often overlooked form of maternal morbidity, which has implications not only for women affected but also for their children. It is estimated that around 13% of all mothers are affected by postnatal depression in the developed world. Epidemiological studies from low and middle-income countries (LMIC) suggest that prevalence rates of postnatal depressed mood are often much higher than those found in high income countries. (1) In South Africa an estimated 25% to 35% of mothers are affected.(1) This rate has been found to be even higher amongst HIV positive women.(2)

Poverty has been found to be both a predictive risk factor for maternal depressed mood and a key moderator of the effects of this morbidity on child development.(3) This is especially true for the youngest children who are particularly dependent in the first few months of life when development requires significant emotional, nutritional and cognitive input and care. Care-giving behaviors such as ensuring adequate hygiene, optimal nutrition through breastfeeding, immunization, recognizing illness and seeking care, along with the rest of responsive parenting and mother-infant bonding that is needed for physical and mental development of a child may all be affected and severely compromised by a debilitating mood disorder like depression.

The association between maternal mood and child health and nutrition are no doubt multi-factorial and complex. Figure 1 offers a conceptual framework for how this complex etiological process may occur.

Nutritional status is a significant predictor of child morbidity and mortality and one of the best global indicators of child well-being. (4) Under nutrition results from a myriad of factors and is not solely due to lack of food. Good nutrition, especially in the early months of life, is usually determined by feeding practices, particularly exclusive breastfeeding, the frequency of feeds, as well as how often, how severe and how long a child is ill. The association between maternal depressed mood and infant under nutrition has been well established in numerous studies in South Asia(5-9) yet results from studies in other socio-economically deprived settings have been inconsistent.(9-15) Thus far, only two studies in South Africa

¹ The journal PLOS One does not have a specified word limit for manuscripts. In accordance with journal specifications, tables and figures are not included in the main body of the manuscript but are included at the end of the paper.

have examined the relationship between postnatal depressed mood in mothers and infant growth with discordant results. (11,12) Furthermore, few studies have examined the association between maternal mood and diarrhea in infants (13,16) and the vast majority of studies on infant feeding and maternal depression have come from the developed world.(17) We have found no published research focusing on the association between postnatal depressed mood and infant morbidity or infant feeding methods in South Africa to date.

South Africa has extremely low exclusive breastfeeding rates with the Demographic and Health Survey reporting rates of only 8% of children less than 6 months being exclusively breastfed in 2003. (18) In some areas the rates are even lower with only 6% of mothers reporting exclusive breastfeeding at 12 weeks postpartum in the study area in Kwazulu Natal.(19) Diarrhea is the third largest cause of death for infants under one and 30% of all child deaths are attributed to malnutrition. (20) Clearly these outcomes are all interlinked. The role of maternal mental health as a risk factor for these outcomes warrants further exploration in the South African context.

The aim of this analysis is to examine the association between maternal mental health and major preventable causes of infant mortality and morbidity. It is hoped these results will inform public health policy makers in South Africa on the need for an integrated strategy for promotion of exclusive breastfeeding and prevention of infant morbidity and poor growth through addressing maternal mental health needs while adding to the growing body of literature describing the effect of PND on infant feeding methods and child health outcomes.

Methods

Study design

This study used data collected for a cluster randomized controlled trial to assess the effect of a package of community health worker (CHW) home visits on a variety of maternal and child health outcomes in a peri-urban setting in South Africa between 2008 and 2011 (Good Start III; Trial registration: ISRCTN41046462).

Study site

A total of 30 clusters were defined in Umlazi, a township with approximately one million residents located 20 km outside of Durban in Kwazulu Natal where infant mortality rate and

antenatal HIV prevalence was estimated at 42/1000 live births and 41% in 2010.(21) (See Figure 2 for map of Umlaazi.) The clusters were assessed at baseline for differences in socio-economic and age profiles and randomly divided into trial arms. A detailed methodology for the Good Start III study is described elsewhere. (21)

Study sample

All pregnant women 16 years or older residing in the clusters during the study period who gave informed consent were asked to participate in the study trial. Women with observed severe mental illness (such as may render them unable to give informed consent) were excluded. All eligible participating women with live singleton births were asked to come to the Prince Mshiyeni hospital at 12 weeks after birth for a detailed structured interview by trained data collectors. Data collected consisted of a series of interview questions, blood tests and anthropometric measures on infants along with medical record review of hospital and patient held records.

Intervention

Eligible pregnant women residing in intervention cluster areas received two antenatal and five postnatal visits from CHWs trained in maternal, child and newborn care guidelines. Women in the intervention arm also received education on postpartum mental health which included: input regarding infant communication and the mother-infant relationship, warning signs for postnatal depression, support for women who had “the blues”, a newborn interactive assessment, mother –infant interaction modeling and communication input, and an assessment for signs of postnatal depression. Women in the control arm of the study received one antenatal and one postnatal visit from a CHW with key information and support on how to receive social welfare grants. A further home visit was conducted in the control arm at 10-12 weeks to remind women to go to the assessment site for data collection at 12 weeks. This paper is a cross-sectional analysis of maternal mood score at 12 weeks on selected infant feeding, health and nutrition outcomes.

Measures

Mental Health Measure

Maternal mood was assessed at the 12-week interview using the *Edinburg Postnatal Depression Scale* (EPDS). Developed by Cox et al. as a screening tool for clinical and

research purposes and designed specifically for the postnatal period, (22) the EPDS is one of the most extensively used screening instruments for postnatal depression world wide.(1) The scale consists of 10 questions, each having 4 possible answers. Women were verbally administered the questionnaire and asked to respond by rating how they have felt in the previous 7 days. Each response is scored 0-3 for severity of symptoms experienced with a resulting range of 0-30. Though international cut offs are set at of ≥ 13 indicating the presence of probable postnatal depression, the resulting scores were dichotomized to reflect a locally validated threshold of ≥ 12 (sensitivity 80%, specificity 76.6%, positive predictive value (PPV) 52.6, negative predictive value (NPV) of 92.2%). (23) Field researchers were trained in administering the questionnaire verbally.

Diarrheal morbidity

Maternal recall of infant diarrhea was assessed at 12 weeks using the WHO definition of diarrhea (the passage of 3 or more loose or liquid stools per day in the last 14 days), in the standard format used in household surveys for measuring the period prevalence of diarrhea in a population. (24)

Infant Feeding Measures

Infant feeding was ascertained through maternal 24 hour feeding recall of 19 food and fluid items. Results are divided into four categories; (1) mothers who *never breastfed* their infants, (2) mothers who reported having breastfed their infants after birth but had *stopped breastfeeding* their infants by the time of the interview (reporting no breastfeeding in the past 24 hours), (3) mothers who reported *mixed feeding*, which included breastfeeding their infants in the past 24 hours **and** giving their infant food or nutritive fluids and, (4) mothers who reported *exclusive breastfeeding*, giving their infants nothing but breast milk and prescribed medications over the previous 24 hours.

Anthropometric Measurements and nutritional indices

Weight and recumbent length measurement was measured for each infant at the time of the 12-week interview by trained data capturers at the study office. Weight was recorded to the nearest 10 grams (e.g. 4.02 kg) on calibrated scales. Length was measured using a roller meter (TALC).

Standardized z-scores (length-for-age and weight-for-age) were generated using new WHO child growth standards and calculated from WHO Anthro-2005 software. Infants were then categorized as underweight if they had a WAZ score of < -2 and stunted if they had a HAZ score of < -2 . (25)

Demographic measures

Data on maternal socio- demographic information were collected during structured interviews with participating mothers. A composite index of socio-economic status was constructed based on ownership of household assets such as radio, television, car, stove, electricity, cellphone or refrigerator. A weighted value was given to each item and a total “asset score” was created through simple summation. This score was included in analysis as a continuous variable. Date of birth, infant birth weight and birth history was obtained from medical record review of hospital birth records and patient held records such as the Road to Health Card.

Maternal and child HIV status

Maternal HIV status was ascertained through maternal self-disclosure. This was correlated with postnatal ward hospital and patient held records and further confirmed through laboratory testing of maternal dried blood spots (DBS) for those reporting a positive HIV status. Infant HIV status at 12 weeks was determined through HIV PCR testing of DBS samples from heel pricks of HIV exposed infants.

Data management

Mobile phones with built in range check and skip logic were used for collecting data at the 12-week endpoint by trained data collectors blinded to study arm. The development and use of this collection strategy has been described elsewhere (26). Data was automatically uploaded upon completion of each survey to a central server. The raw data was then exported from the console to Excel format and imported directly into STATA 12 SE for statistical analysis.

Analysis

Analysis of infant feeding and diarrheal disease outcomes were restricted to all mothers of live singleton infants with interviews completed between 9-18 weeks after birth. This timeliness cutoff is consistent with other studies on infant feeding in the same population (27). Interview timeliness was not taken into consideration when analyzing infant nutritional outcomes, as age is part of calculation for nutritional indices and therefore would not likely impact z-scores, however, implausible weight or length scores (>5 SD or <-5 SD) were excluded from these analysis.

Univariate and multivariate logistic regression analysis were used to estimate the relationship of maternal PND with all three outcomes. Linear regression was used for examining the association between PND and continuous nutritional z-scores. Binomial logistic regression was used for both the binary outcome of diarrheal morbidity and for underweight and stunting. Categorical infant feeding outcomes were analyzed through multinomial regression analyses with *exclusive breastfeeding* set as the reference level. Confounders were included for all three outcomes in the final adjusted models and were based on epidemiological and/or statistical relevance. As infant feeding and child morbidity are covariates in the causal pathway and therefore potential mediators between postnatal depression and child nutritional status and diarrhea, a 3rd model omitting these covariates was included for these outcomes. All models were adjusted for cluster and trial arm to account for the cluster randomized trial design and were checked for goodness of fit using the Hosmer-Lemeshow test.

Ethical considerations

The ethics review board of the Medical Research Council approved the main study (EC08-002). Signed informed consent written in participants language was obtained from each mother prior to study participation and further confirmed prior to the in-person interview assessment and before any blood tests were drawn. A Community Advisory Board (CAB) was also established. Women who scored high on the EPDS or answered yes to the question of self-harm ideation were immediately referred to existing mental health services for care. The study is registered: ISRCTN41046462.

Results

Of 4127 pregnant women recruited over the 4-year study period, 3917 eligible women were followed to delivery. 118 women had stillbirths or miscarriages and there were 58 multiple births leaving a total of 3741 live singleton births. A further 162 (4.3%) were lost to follow up after birth and there were a further 85 deaths (neonatal, post neonatal and maternal) leaving a total number of 3494 mother-infant dyads who had in-person assessments (figure 3). Of these, 296 were excluded due to timeliness of interview (assessed <9 or >18 weeks), leaving a total of 3198 dyads for the infant feeding and diarrhea analyses in this study. Nine infants were excluded due to implausible anthropometric measurements (recording errors) leaving 3485 dyads for the analysis of nutritional outcomes.

Maternal mood scores

The median EPDS score for this population was 5 (IQR 2-10,). There was no statistical difference between the underlying distributions of the depression scores of mothers who were assessed within or after 18 weeks postpartum ($z = -0.700$; $p = 0.4839$). Of all 3494 mothers with live infants assessed, 568 (16.3%) were categorized as having probable postnatal depression, with a score of 12 and above on the EPDS.

Baseline characteristics of mothers

Selected characteristics of participating mothers taken from the 12- week interview stratified by maternal mood status are presented in Table 1. The majority of participants were single women (87.5%) with a median age of 23. Very few mothers lived alone (1.5%) implying that the great majority lived with extended family. About half of the women were first time mothers (48%) with about 48% having some secondary education, 40% reported completing high school but only 6% having completed any tertiary studies. The vast majority of mothers had electricity (94.7%) with piped water to their house (55%) or yard (25.5%). Only 14.4% were currently employed at the time of the interview. 1271 (36.4%) mothers in the study were confirmed HIV positive. Mother to child transmission of HIV was relatively low with 1.73% of infants confirmed HIV positive by PCR test around 12 weeks post-partum. Chi squared and t tests showed that maternal education, asset score, parity, reported breast infection and maternal and child HIV status were all significantly associated with maternal depression scores of 12 and above.

Diarrheal morbidity

Maternal reported infant diarrheal prevalence in the last 14 days was nearly 20% (631) and was significantly higher for infants of mothers with reported depressed mood than mothers who did not report depressed mood (27% vs 18% $p < 0.000$). (Table 1) Results of bivariate and multivariable logistic regression with PND as the main exposure for infant diarrheal disease are shown in Table 2.² Infants of mothers with depressed mood had a 1.50 fold increased relative risk of having had diarrhea in the past two weeks than infants of mothers without depressed moods (95% CI: 1.30- 1.73). This association remained statistically significant after adjusting for water source, maternal and child HIV status, asset score, maternal education and trial arm (RR 1.44, 95% CI: 1.25-1.64). Controlling for infant feeding slightly decreased the relative risk indicating this was not a strong mediator through which PND has an effect on infant diarrhea (RR 1.47, 95% CI: 1.28- 1.68).

² Tables 1-6 in Part D (appendices) of this dissertation contain detailed models with all covariates included for the 3 main types of outcomes, corresponding to tables 2-4 included in the article.

Infant feeding

Infant feeding distributions for the study population are described in Table 1. Approximately one quarter (778) of mothers reported never breastfeeding their child. A further 18% (581) had stopped breastfeeding their child by the interview time and only 15.5% (494) mothers reported exclusively breastfeeding their infant in the past 24 hours. The majority of women reported mixed feeding their infant (42%, n=1345). A fifth of all women who started breastfeeding reported having breast health problems (20.5%, n= 2142).

Results of multinomial logistic regression with PND as the main exposure for four categories representing infant feeding outcomes are presented in Table 3. The table shows crude and adjusted relative risks of mothers with reported depressed mood (vs non-depressed mood) with different feeding methods (never started breastfeeding, having started but stopped breastfeeding, mixed feeding their infants) relative to mothers who were exclusively breastfeeding their infants. Results from multivariate analysis show that women who had reported depressed mood (vs non-depressed mood) had an increased risk of never starting breastfeeding (RR 1.59, 95% CI: 1.09- 2.31), having stopped breastfeeding (RR 1.94, 95% CI: 1.32- 2.85), or mixed feeding (RR 1.63, 95% CI: 1.15- 2.29), relative to exclusively breastfeeding at 12 weeks, even after controlling for maternal HIV status, age, asset score, education, employment, parity, trial arm and breast infection (for those who had ever breastfed).

Nutritional outcomes

Mean weight for age (WAZ) and length for age (HAZ) z scores for the study population are presented in Table 1. Results show that 178 (5%) infants were underweight and 455 (13%) were stunted at 12 weeks. Modeling the association between PND and infant nutritional status using linear regression showed a relatively small but statistically significant effect of PND on infant nutritional status (see Table 4). Prior to adjustment for possible confounders, infants whose mothers had probable depression had lower WAZ and HAZ scores than infants of mothers who were did not (WAZ -0.192, 95% CI: -0.306, -0.078; HAZ -0.142, 95% CI: -0.242, -0.042). Adjustment for confounders reduced the size of the effect though the association remained significant (WAZ -0.132, 95% CI: -0.243, -0.021; HAZ -0.104, 95% CI: -0.205, -0.004). Controlling for mediators of reduced nutritional status (infant feeding method and diarrhea) further reduced the association and rendered it insignificant.

Logistic regression of postnatal depressed mood on the dichotomous outcomes of underweight and stunting are presented in Table 4. Infants whose mothers reported depressed

mood had 1.26 times the relative risk of being underweight at 12 weeks when compared to infants of mothers who did not report depressed mood (95% CI: 1.07- 1.49). This effect diminished very slightly but remained statistically significant after controlling for confounders (RR 1.24, 95% CI: 1.03- 1.49). When further adjusting for infant feeding and diarrheal morbidity however, the association was rendered insignificant, suggesting these mediating factors are important components in the complex pathway between maternal mood and child health (RR 1.18, 95% CI: 0.98- 1.41).

Infants had a small increased relative risk of being stunted if their mothers reported depressed mood vs. those who did not report depressed mood (RR 1.15, 95%CI: 1.03-1.29), however this association became insignificant when confounding covariates were accounted for (RR 1.11, 95% CI: 0.97- 1.26).

Discussion

Sub-optimal infant feeding practices and chronic illness are well-established mechanisms for under nutrition.(28) Results from this large population based study have shown children of mothers with postnatal depressed mood are at increased risk of both diarrheal disease and being mixed or not breastfed at 12 weeks of age. These factors are important parts of the complex pathway between maternal mood status and child health, having mediating effects on nutritional outcomes.

Our results suggest the difference in nutritional scores between groups, though clinically marginal at 3 months, could result in a more clinically significant difference between groups by 6 months of age, if this trend were to continue. While, infants of mothers with reported depressed mood had significantly lower length for age z-scores relative to infants with psychologically healthy mothers, there was no statistical evidence to show an increased risk in stunting at this time point once adjusting for confounders. Stunting is a longer-term response to inadequate nutritional intake and chronic disease and we would not expect to see a pronounced effect of maternal mood on this outcome by 3 months of age. Weight for age index on the other hand, does not discriminate between short- and longer-term forms of poor nutrition and therefore is more suited to this study's early measurement time point.(25)

Studies examining the association of postnatal depressed mood on nutritional outcomes across countries and regions have reported a wide variation of results. This may be due to methodological, measurement and contextual factors. Though the relative risks are lower, our findings are consistent with a case control study conducted in Nigeria that found children of

mothers with reported postnatal depressed mood had increased odds of scoring below the 5th centile for weight and length for age than children of mothers that reported non-depressed mood at 3 months (OR 3.41; 1.3-8.52 for weight and OR 3.28; 1.03-10.47 for length). This difference peaked at 6 months and decreased by 9 months.(13) Results from cohort studies conducted in South Asia suggest an effect is most evident between 4-6 months of age, but lessens after this. (2) Cross sectional studies have found significant associations only in infants <12 months of age. (14,15) This could be one reason why no effect was found in a longitudinal study of growth between children of mothers with depressed mood vs non-depressed mood in a peri-urban township near Cape Town at 18 months of age.(29)

Maternal depressed mood was negatively associated with breastfeeding exclusivity at 12 weeks postpartum. Mothers who reported depressed mood at 12 weeks postpartum were less likely to have had initiated and sustained breastfeeding and to do so exclusively than women who did not report depressed-mood. This association, however, was only significant when comparing feeding history (never breastfed) and current practice (stopped breastfeeding) relative to mothers who were exclusive breastfeeding their infants but did not hold true for those that were mixed feeding compared to exclusive breastfeeding.

It is widely recognized that breastfeeding in poor settings is critical for child survival. Optimal infant feeding requires that all infants are breastfed exclusively for the first 6 months of life with continued breastfeeding up to two years of age. (4) Studies across the world have shown that exclusively breastfed infants are at significantly decreased risk of morbidity and mortality and have improved nutrition and growth. (28,30) Efforts to encourage and promote universal breastfeeding have become crucial components of public health policy. Identifying risk factors for early cessation and sub-optimal breastfeeding are important to achieving widespread practice. Screening woman who have recently delivered for signs of depressed mood will help identify an important population at increased risk of negative infant feeding outcomes in South Africa.

PND point prevalence

In a systematic review of postnatal depression in LMIC, the authors report a mean postnatal depressed mood prevalence rate of 20.0% for South Africa. Our finding of 16% prevalence at 12 weeks postpartum is lower than has previously been found by other studies in comparable socio-economic settings in South Africa at a similar time after birth. Wide variation in prevalence rates across countries however is not unusual and may have to do with methodological differences. One clinic based study in Soweto, Johannesburg reported 24.5% of 88 high-risk mothers had postnatal depressed mood at 6 weeks postpartum and another

population based study in Khayelitsha, Cape Town reported 35.7% of 147 mothers had clinical diagnosed postnatal depression at 8 weeks postpartum.(31) This study reports results from data collected as part of a cluster randomized control trial and while no effect on postnatal depressed mood was seen across study arms, both groups of women received home visits from CHWs, which may have had an overall ameliorating affect on the prevalence of postnatal depressed mood in this community.

Strengths and limitations

This study has the advantage of being the largest population based study of pregnant women assessed for postnatal depressed mood in Africa. The study recruited pregnant women over a 4-year study period and had low levels of loss to follow-up (less than 1% of eligible women prior to delivery and 4.3% of eligible women after delivery). However, only one early time point for measurement of growth around 12 weeks of age was recorded, preventing the ability to see growth trends over time. Furthermore, it did not have data on infant gestational age at birth. Growth is determined not by size attained but by velocity, or change in size between two time points.(32) While nutritional z-scores provide a standardized measurement for comparison across populations, they do not take into account a child's birth weight and gestational age at birth, which could yet have a significant effect on infant size, attained at 12 weeks, independent of maternal mood status. This study was able to control for birth weight but not for gestational age at birth.

The lack of a depression screening measure in the antenatal or immediate postpartum period limits the ability to make inferences of causality. Most longitudinal studies have found that depressive symptomology precedes breastfeeding cessation with maternal mood influencing feeding outcomes and not vice versa.(25) It is however, plausible that the outcomes of interest preceded the onset of depressed mood, namely; mothers with children with poorer health outcomes were at increased risk of postnatal depressed mood.

Conclusions

These results have demonstrated the importance of identifying women with postnatal mood disorders and providing support for these women and families through strengthening and adding needed mental health services in the public health sector. This would not only ameliorate mothers' suffering from postnatal depressed mood but improve health outcomes for their babies and their families. The results of this study add to the evidence guiding policy

for addressing maternal psychological morbidity with the aim of mitigating negative effects on child health.

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Figures and Tables

Figure 1 Conceptual framework for postnatal depression and adverse infant health outcomes

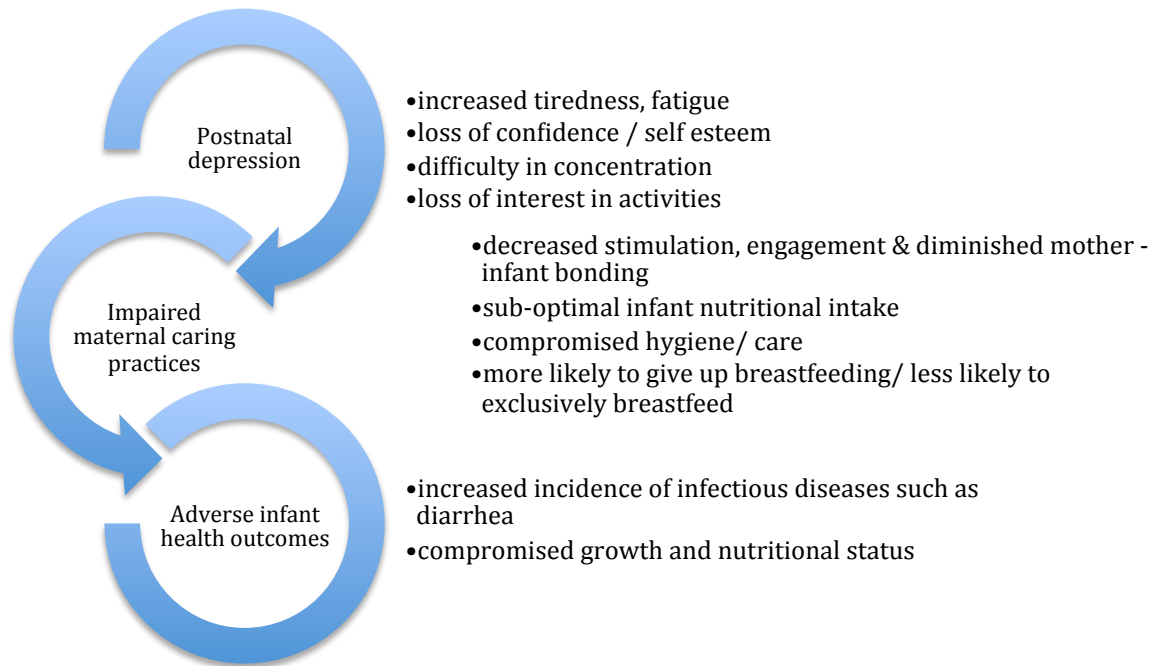


Figure 2 Map of study site, Umlazi Kwazulu Natal

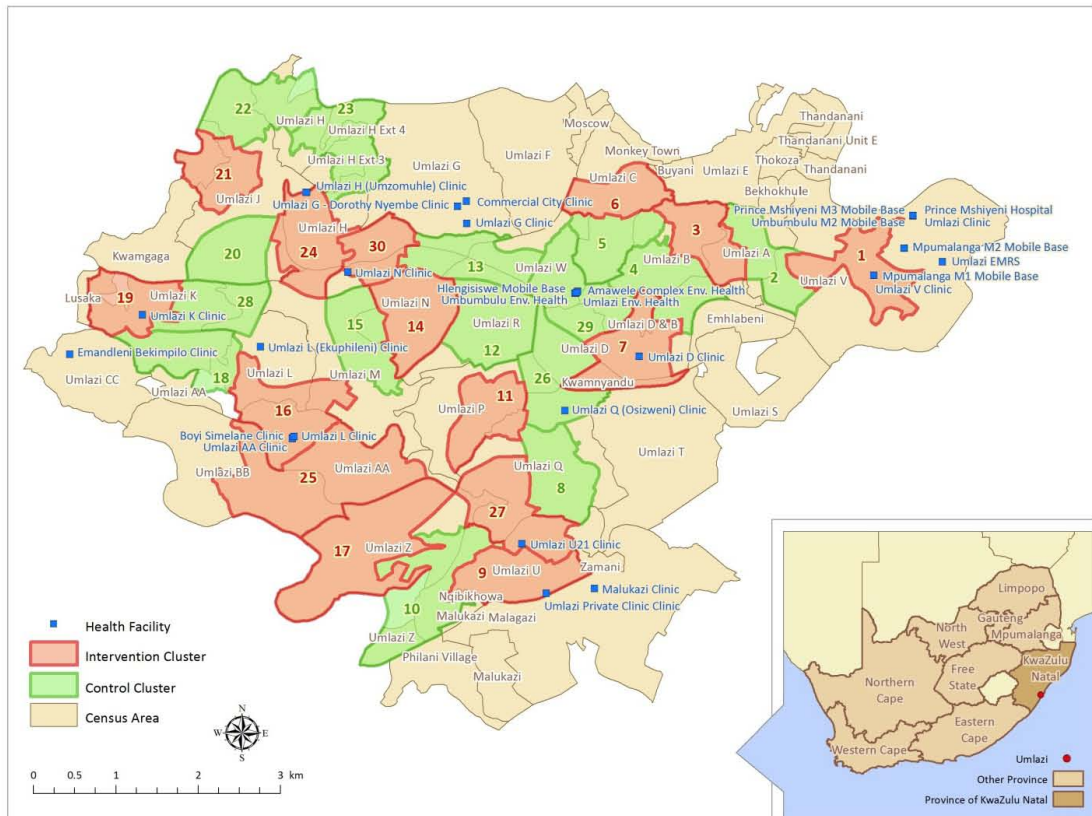


Figure 3 Study Profile

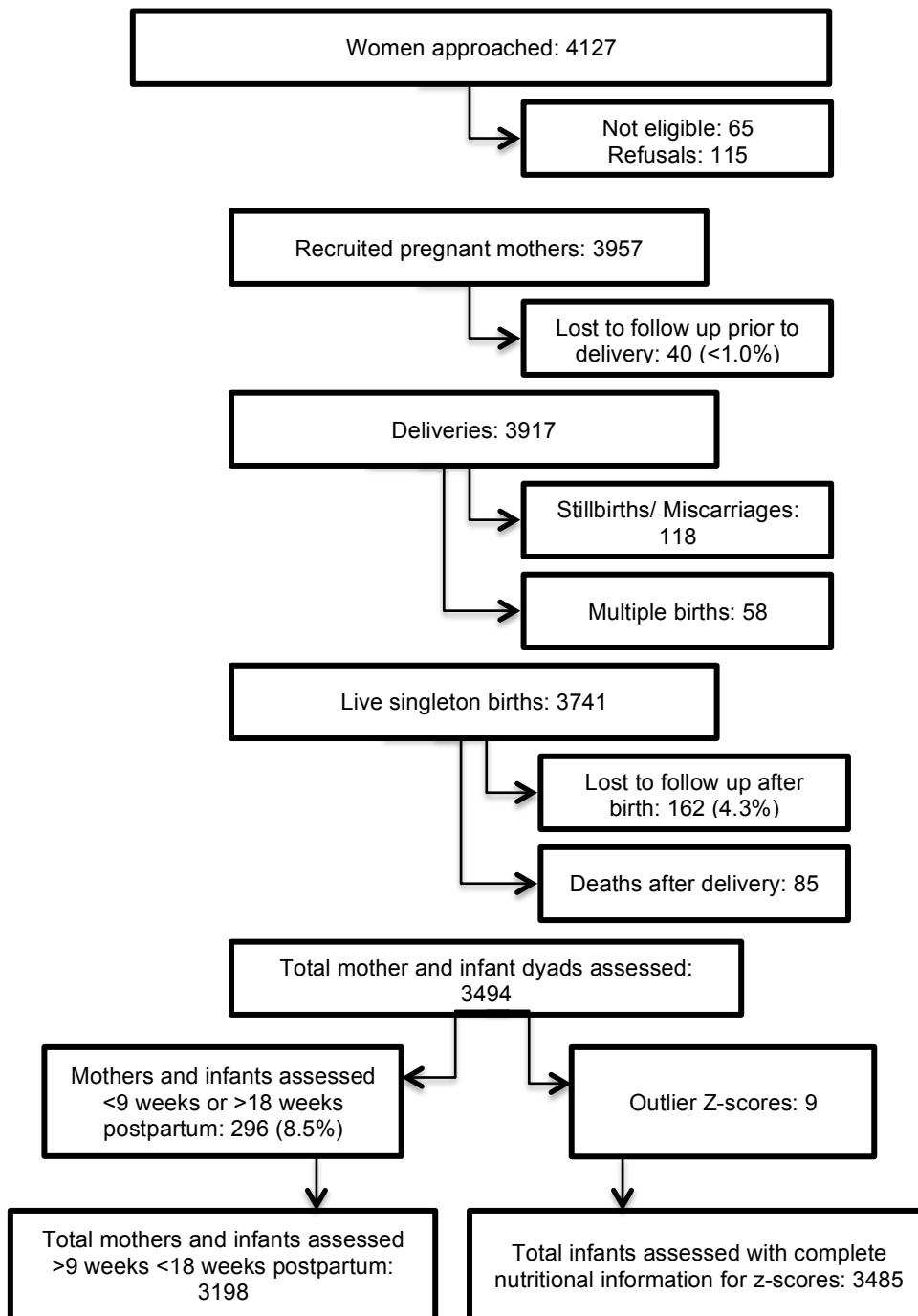


Table 1 Baseline characteristics of mothers and infants in study population and primary outcomes of interest, stratified by maternal mood status *

	Total n= 3493	No depressed mood n=2926	Depressed mood n= 568	p value
Characteristics				
HIV status				
Mother HIV positive	1271 (36.4)	1,003 (34.3)	268 (47.2)	p<0.000
Baby HIV positive	61 (1.75)	40 (1.37)	21 (3.7)	p<0.000
Trial arm				
Control	1864 (53.4)	1542 (52.7)	322 (56.8)	p= 0.074
Intervention	1629 (46.6)	1384 (47.3)	245 (43.2)	
Water source				
pipied house	1927 (55.2)	1629 (55.7)	298 (52.5)	p=0.491
pipied yard	890 (25.5)	742 (25.4)	148 (26.1)	
pipied public	628 (18.0)	514 (17.6)	114 (20.1)	
other	49 (1.4)	41 (1.4)	8 (1.4)	
Has electricity	3307 (94.7)	2775 (94.8)	532 (93.8)	p=0.326
Asset score,[†] median /mean (IQR)	9/ 8.1 (8,9)	9/ 8.2 (8,9)	9 /7.6 (6,9)	p<0.000
Currently employed	503 (14.4)	430 (14.7)	73 (12.9)	p=0.258
Education				
none/ primary	245 (7.0)	193 (6.6)	52 (9.2)	p<0.000
some secondary	1662 (47.6)	1359 (46.5)	303 (53.4)	
completed secondary	1382 (39.6)	1191 (40.7)	191 (33.6)	
tertiary	205 (5.9)	183 (6.3)	22 (3.9)	
Parity				
primipara	1666 (47.7)	1439 (49.2)	227 (40.0)	p<0.000
multipara	1828 (52.3)	1487 (50.8)	341 (60.0)	
Mode of delivery				
Vaginal	2140 (66.9)	1799 (67.2)	341 (65.3)	p= 0.337
C-section	991 (31.0)	825 (30.8)	166 (31.8)	
missing	67 (2.1)	52 (1.9)	15 (2.9)	
Reported breast infection [‡]	495 (20.5)	399 (19.5)	495 (26.0)	p=0.005
Marital status				
single	3058 (87.5)	2558 (87.4)	500 (88.0)	p=0.092
married	132 (3.8)	121 (4.1)	11 (1.9)	
cohabiting	295 (8.4)	240 (8.2)	55 (9.7)	
widowed	8 (0.2)	6 (0.2)	2 (0.4)	
divorced	1 (0.03)	1 (0.03)	0 (0.00)	
Mother lives alone	51 (1.5)	41 (1.4)	10 (2.0)	p=0.510
Mother age median (IQR)	23 (20,27)	23 (20,27)	23 (20,27)	p=0.514
Low birth weight				
No (>=2500 grams)	3258 (93.3)	2728 (93.2)	530 (93.5)	p= 0.834
Yes (<2500 grams)	235 (6.7)	198 (6.8)	37 (6.5)	
Outcomes [§]				
Weight for age Z-score				
mean (sd)	-0.014 (1.19)	0.018 (1.18)	-0.178 (1.25)	p<0.000
Height for age Z-score				
mean (sd)	-0.736 (1.20)	-0.712 (1.19)	-0.859 (1.26)	p=0.008
Underweight (<-2 WAZ score)	178 (5.1)	136 (4.7)	42 (7.4)	p=0.006
Stunted (<-2 HAZ score)	455 (13.0)	366 (12.5)	89 (15.7)	p=0.039
Infant had diarrhea	631 (19.7)	488 (18.2)	143 (27.4)	p<0.000
Infant feeding from 24 hour recall at 12 weeks				
Never breastfed	778 (24.3)	625 (23.4)	153 (29.3)	p=0.001
Stopped breastfeeding	581 (18.7)	474 (17.7)	107 (20.5)	
Mixed breastfeeding	1345 (42.1)	1142 (42.7)	203 (38.9)	
Exclusive breastfeeding	494 (15.5)	435 (16.3)	59 (11.3)	

* Data are number (%) unless specified; p values recorded from chi2 test of association unless median or means reported in which ranksum or ttest used respectively.

[†] Asset score has range of 0-12 with 0 being lowest value of recorded assets and 12 being the most

[‡] Of women who reported ever breastfeeding, n= 2412

[§] n for all nutritional outcomes=3485, n for infant diarrhea and feeding outcomes =3198

Table 2 Logistic regression models of postnatal depression and infant diarrhea at 12 weeks of age with unadjusted and adjusted relative risks (RR) and 95% confidence intervals

	Model 1 [*]	Model 2 [†]	Model 3 [‡]
Diarrheal disease			
Not depressed	1	1	1
Depressed	1.50 (1.30- 1.73)	1.44 (1.25- 1.64)	1.47 (1.28- 1.68)

^{*} Adjusted only for trial arm

[†] Adjusted for confounders and mediator: trial arm, maternal education, maternal age, water source, wealth score, child HIV status, and infant feeding method

[‡] Adjusted for confounders only: trial arm, maternal education, maternal age, water source, wealth score, child HIV status

Table 3 Multinomial logistic regression models of postnatal depression and infant feeding method compared to exclusive breastfeeding at 12 weeks of age with unadjusted and adjusted relative risks (RR) and 95% confidence intervals

	Never breastfed	Stopped breastfeeding	Mixed feeding
Unadjusted[*]			
Not Depressed	1	1	1
Depressed	1.77 (1.25- 2.51)	1.64 (1.11- 2.41)	1.29 (0.95-1.74)
Adjusted[†]			
Not Depressed	1	1	1
Depressed	1.58 (1.09- 2.31)	1.94 (1.32- 2.85) [‡]	1.63 (1.15- 2.29) [§]

^{*} Only adjusted for trial arm

[†] Adjusted for trial arm, maternal HIV status, age, education, employment, parity, asset score

[‡] Also adjusted for self reported breast infection

[§] Also adjusted for self reported breast infection

Table 4 Linear and logistic regression models of postnatal depression and infant nutritional status at 12 weeks of age

	Model 1[*]	Model 2[†]	Model 3[‡]
Nutritional status as a continuous outcome, β Coef (95%CI)			
Weight for age z-score (WAZ)			
Not depressed	0	0	0
Depressed	-0.192 (-0.306; -0.078)	-0.114 (-0.229; 0.001)	-0.132 (-0.243, -0.021)
Length for age z-score (HAZ)			
Not depressed	0	0	0
Depressed	-0.142 (-0.242, -0.042)	-0.088 (-0.189, 0.012)	-0.104 (-0.205, -0.004)
Nutritional status as a binary outcome, RR (95% CI)			
Underweight			
Not depressed	1	1	1
Depressed	1.26 (1.07- 1.49)	1.18 (0.98- 1.41)	1.24 (1.03- 1.49)
Stunted			
Not depressed	1	1	1
Depressed	1.15 (1.03- 1.29)	1.11 (0.97- 1.26)	1.14 (1.00- 1.30)

^{*} Model 1: Adjusted only for trial arm

[†] Model 2: Adjusted for confounders and mediators: trial arm, infant HIV status, maternal age, education, infant birth weight, asset score, diarrheal disease in past 2 weeks, and infant feeding method

[‡] Model 3: Adjusted for confounders only; trial arm, infant HIV status, maternal age, education, infant birth weight and asset score

Part D: Appendices

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Table 1 Logistic regression models of postnatal depression and infant diarrhea at 12 weeks of age*

		Model 1 Unadjusted estimates	Model 2 Excluding infant feeding as mediator	Model 3 Fully Adjusted estimates
Maternal mood	1	Not depressed	1	1
		Depressed	1.50 (1.30- 1.73)	1.44 (1.25- 1.64)
Trial arm	1	Control	1	1
		Intervention	1.00 (0.89- 1.13)	1.04 (0.93- 1.17)
Maternal age		0.98 (0.96-1.00)	0.98 (0.97-1.00)	0.98 (0.96-1.00)
Infant feeding	*	Never breastfed	1	1
	*	Stopped	1.03 (0.87-1.22)	0.99 (0.85- 1.16)
	*	Mixed feeding	0.89 (0.76- 1.05)	0.84 (0.72- 0.99)
	*	EBF	0.73 (0.58- 0.92)	0.70 (0.5- 0.89)
Asset score		(1 unit increase)	0.96 (0.94-0.98)	0.97 (0.94-0.99)
Water source	1	pipid house	1	1
		pipid yard	1.33 (1.15- 1.55)	1.23 (1.06- 1.44)
		pipid public	1.17 (1.00 -1.37)	1.06 (0.88- 1.27)
		other	0.72 (0.37- 1.41)	0.63 (0.33- 1.23)
Education	1	none/ primary	1	1
		some second	1.10 (0.84-1.45)	1.06 (0.80-1.40)
		secondary	0.87 (0.65- 1.16)	0.90 (0.66-1.23)
		tertiary	0.51 (0.32- 0.81)	0.55 (0.35-0.87)
Parity	*	primipara	1	*
	*	multipara	0.96 (0.85- 1.08)	*
HIV status	1	Baby HIV-	1	1
		Baby HIV+	1.23 (0.79- 1.92)	1.06 (0.67- 1.67)
	*	Mother HIV-	1	*
	*	Mother HIV+	1.06 (0.92- 1.21)	*

* Relative risks (RR) and 95% confidence intervals (CI)

Table 2 Multinomial logistic regression models of postnatal depression and infant feeding method compared to exclusive breastfeeding at 12 weeks of age*

		Never breastfed	Stopped breastfeeding	Mixed feeding
Unadjusted model				
Maternal mood	Not Depressed	1	1	1
	Depressed	1.77 (1.25- 2.51)	1.64 (1.11- 2.41)	1.29 (0.95-1.74)
Trial arm	Control	1	1	1
	Intervention	0.45 (0.35- 0.60)	0.52 (0.39-0.69)	0.42 (0.32- 0.56)
Fully Adjusted model				
Maternal mood	Not Depressed	1	1	1
	Depressed	1.59 (1.09- 2.31)	1.94 (1.32- 2.85)	1.63 (1.15- 2.29)
Maternal HIV status	HIV negative	1	1	1
	HIV positive	10.00 (7.32- 13.64)	0.65 (0.47- 0.91)	0.21 (0.16- 0.28)
Parity	Primipara	1	1	1
	Multipara	0.54 (0.39- 0.74)	0.48 (0.35- 0.65)	0.61 (0.48- 0.76)
Maternal education	None/primary	1	1	1
	Some secondary	1.16 (0.71- 1.89)	1.78 (1.01- 3.14)	0.90 (0.49- 1.64)
	Secondary	1.51 (0.90- 2.52)	1.67 (0.97- 2.90)	0.70 (0.40- 1.24)
	Tertiary	4.51 (1.84- 11.05)	4.06 (1.53- 10.78)	1.85 (0.73- 4.69)
Maternal age	1 year increase	1.04 (1.02- 1.07)	1.00 (0.98- 1.02)	0.99 (0.97- 1.01)
Breast infection	No	*	1	1
	Yes	*	2.98 (2.13- 4.18)	1.43 (1.10- 1.86)
Asset score	1 point increase	1.11 (1.05- 1.17)	1.09 (1.04- 1.15)	1.05 (1.00- 1.09)
Employment	No	1	1	1
	Yes	2.48 (1.73- 3.56)	2.81 (2.01- 3.95)	1.64 (1.14- 2.36)
Trial arm	Control	1	1	1
	Intervention	0.48 (0.37- 0.62)	0.49 (0.37- 0.64)	0.40 (0.30- 0.54)

* All data presented as relative risks and 95% Confidence Intervals. RR (95% CI).

Table 3 Linear regression of postnatal depression on weight for age z-score (WAZ) at 12 weeks of age with confounding and mediating covariates*

Characteristics		Model 1 Unadjusted	Model 2 Adjusted without mediators	Model 3 Fully adjusted
Maternal mood	Not depressed	0	0	0
	Depressed	-0.132 (-0.243, -0.021)	-0.192 (-0.306; -0.078)	-0.114 (-0.229; 0.001)
Trial arm	Control	0	0	0
	Intervention	0.045 (-0.041, 0.131)	0.0945 (-0.0027; 0.192)	0.040 (-0.056; 0.135)
Birth weight in kilograms			1.298 (1.211, 1.385)	1.300 (1.213; 1.388)
Maternal age in years			0.003 (-0.002, 0.007)	0.036 (-0.052; 0.125)
Infant feeding	Never breastfed	*		0
	Stopped	*		-0.007 (-0.140; 0.126)
	Mixed feeding	*		0.179 (0.083; 0.275)
	EBF	*		0.226 (0.116; 0.335)
Asset score	1 point increase	0.023 (0.008, 0.038)		0.026 (0.012; 0.040)
Education	none/ primary	0		0
	some second	0.154 (0.016, 0.292)		0.183 (0.042; -0.324)
	secondary	0.237 (0.100, 0.374)		0.276 (0.132; -0.420)
	tertiary	0.397 (0.246, 0.549)		0.453 (0.291; 0.615)
HIV status	Baby HIV-	0		0
	Baby HIV+	-0.877 (-1.201, -0.552)		-0.854 (-1.16; -0.549)
Had diarrhea	No	*		0
	Yes	*		-0.126 (-0.235; -0.022)

* All data presented as β Coefficients with 95% confidence intervals.

Table 4 Linear regression of postnatal depression on length for age z-score (HAZ) at 12 weeks of age with confounding and mediating covariates *

Characteristics		Model 1 Unadjusted	Model 2 Adjusted without mediators	Model 3 Fully adjusted
Maternal mood	Not depressed	0	0	0
	Depressed	-0.104 (-0.205, -0.004)	-0.142 (-0.242, -0.042)	-0.088 (-0.189, 0.012)
Trial arm	Control	0	0	0
	Intervention	0.073 (-0.002, 0.148)	0.119 (0.036, 0.203)	0.066 (-0.009, 0.141)
Birth weight in kilograms			1.286 (1.203, 1.369)	1.283 (1.198, 1.368)
Maternal age in years			0.000 (-0.005, 0.006)	0.001 (-0.005, 0.006)
Infant feeding	Never breastfed	0		0
	Stopped	*		0.005 (-0.124, 0.134)
	Mixed feeding	*		0.075 (-0.014, 0.164)
	EBF	*		0.126 (0.009, 0.243)
Asset score	1 point increase	0.011 (-0.010, 0.032)		0.012 (-0.010, 0.033)
Education	none/ primary	0		0
	some second	0.010 (-0.149, 0.170)		0.017 (-0.147, 0.182)
	secondary	0.061 (-0.092, 0.215)		0.068 (-0.091, 0.227)
	tertiary	0.296 (0.092, 0.500)		0.309 (0.103, 0.514)
HIV status	Baby HIV-	0		0
	Baby HIV+	-0.349 (-0.695, -0.002)		-0.341 (-0.681, -0.001)
Had diarrhea	No	*		0
	Yes	*		-0.082 (-0.199, 0.035)

* All data presented as β Coefficients with 95% confidence intervals.

Table 5 Logistic regression of postnatal depression and underweight status of infants at 12 weeks of age with confounding and mediating covariates*

Characteristics		Model 1 Unadjusted	Model 2 Adjusted without mediators	Model 3 Fully adjusted
Maternal mood	Not depressed	1	1	1
	Depressed	1.24 (1.03- 1.49)	1.26 (1.07- 1.49)	1.18 (0.98- 1.41)
Trial arm	Control	1	1	1
	Intervention	1.06 (0.89- 1.26)	0.99 (0.84- 1.17)	1.08(0.91- 1.30)
Birth weight in kilograms			0.31 (0.26- 0.37)	0.30(0.26- 0.36)
Maternal age in years			0.99 (0.98- 1.00)	0.99(0.97- 1.00)
Infant feeding	Never breastfed	*		1
	Stopped	*		1.01 (0.78- 1.31)
	Mixed feeding	*		0.8 (0.65 - 1.04)
	EBF	*		0.68 (0.50- 0.91)
Asset score	1 point increase	0.97 (0.94- 1.00)		0.97 (0.94- 1.00)
Education	none/ primary	1		1
	some second	0.97 (0.68- 1.39)		0.96 (0.67- 1.36)
	secondary	0.93 (0.65- 1.32)		0.92 (0.65- 1.30)
	tertiary	0.46 (0.25- 0.84)		0.45 (0.24- 0.83)
HIV status	Baby HIV-	1		1
	Baby HIV+	2.70 (1.78- 4.09)		2.70 (1.80- 4.05)
Had diarrhea	No	*		1
	Yes	*		1.20 (1.01- 1.43)

* Adjusted and unadjusted relative risks (RR) and 95% confidence intervals

Table 6 Logistic regression of postnatal depression and stunting of infants at 12 weeks of age with confounding and mediating covariates, adjusted and unadjusted relative risks (RR) and 95% confidence intervals.

Characteristics		Model 1 Unadjusted	Model 2 Adjusted without mediators	Model 3 Fully adjusted
Maternal mood	Not depressed	1	1	1
	Depressed	1.14 (1.00- 1.30)	1.15 (1.03- 1.29)[*]	1.11 (0.97- 1.26)
Trial arm	Control	1	1	1
	Intervention	0.97 (0.85- 1.10)	0.92 (0.83- 1.03)	0.97 (0.86- 1.11)
Birth weight in kilograms		0.22 (0.19- 0.25)	0.22 (0.19- 0.25)	0.22 (0.19- 0.25)
Maternal age in years		1.00 (0.99- 1.01)	1.00 (0.99- 1.01)	1.00 (0.99- 1.01)
Infant feeding	Never breastfed	*	1	1
	Stopped	*	0.95 (0.81- 1.11)	0.94 (0.80- 1.10)
	Mixed feeding	*	0.85 (0.75- 0.97)	0.87 (0.74- 1.03)
	EBF	*	0.90 (0.78- 1.04)	0.86 (0.71- 1.05)
Asset score	1 point increase	0.97 (0.95- 1.00)	0.97 (0.95- 1.00)	0.97 (0.95- 1.00)
Education	none/ primary	1	1	1
	some second	0.92 (0.72- 1.18)	0.96 (0.76- 1.21)	0.91 (0.71- 1.16)
	secondary	0.94 (0.73- 1.20)	0.89 (0.720- 1.11)	0.93 (0.72- 1.19)
	tertiary	0.56 (0.36- 0.85)	0.51 (0.35- 0.74)	0.55 (0.36- 0.82)
HIV status	Baby HIV-	1	1	1
	Baby HIV+	1.56 (0.95- 2.57)	1.56 (1.08- 2.26)	1.53 (0.94- 2.51)
Had diarrhea	No	*	1	1
	Yes	*	1.16 (1.04- 1.29)	1.15 (1.03- 1.29)

^{*} Adjusted for trial arm



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20 December 2012

HREC REF: 583/2012

Ms S Rohde
c/o Dr T Doherty
School of Public Health & Family Medicine
Falmouth Building
FHS

Dear Ms Rohde

PROJECT TITLE: POSTNATAL "DEPRESSION" AND ADVERSE INFANT HEALTH OUTCOMES IN A PERI-URBAN SOUTH AFRICAN CONTEXT: EXPLORING THE ASSOCIATION BETWEEN MATERNAL MOOD AND INFANT MORBIDITY, GROWTH, AND FEEDING AT 12 WEEKS POSTPARTUM"

Thank you for addressing the issues raised by the Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year till the 28 December 2013.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form, if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR M. BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.

sAriefdien

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.



GOOD START 111 INFORMED CONSENT FORM - CARE GIVER

PURPOSE OF THE STUDY

In your area there are women called Community Health Workers who are visiting pregnant women and mothers with newborn babies. These Community Health Workers are counselling pregnant women and mothers of newborn babies on how to access the best and most appropriate care for themselves and their babies. The purpose of this study is to assess if community-based health workers can provide support and advice to pregnant women so that the babies growing in their wombs and newborn babies are protected from HIV infection. The study is being conducted by four organisations: the, Medical Research Council, University of the Western Cape, Maromi and Health Systems Trust.

CONFIDENTIALITY

All information obtained from you and the baby will be kept confidential. No one outside of the study team will be given any of your information. We will not use your name or the child's name in any report of this project.

Information will be collected from you on a cell phone and any reporting of data will be anonymous.

RISKS & BENEFITS

There are no known risks or dangers to you of being involved in this study. Benefits of the study will include:

- Visits by a Community Health Worker until the baby reaches two and a half months
- Information on child health issues or social grant from the Community Health Worker
- Referral to the a clinic or a hospital if the researcher believes that this is needed
- At 12 weeks you will be requested to go to Prince Mshiyeni Memorial Hospital for the baby to be weighed and his length measured.
- You will receive a photograph of your baby during your visit at Prince Mshiyeni Memorial Hospital and a food voucher worth R 100.00.

There will be no other direct benefits to you from this study; however the findings may help us to improve the health, newborn babies in this community.

EXPECTATIONS

- A private interview about health, family and home that will last for approximately 45 minutes.
- Home visits by a Community Health Worker
- If you experience any problems with the study Community Health Worker or supervisor please contact Mark Tomlinson **02193804** or **083 3014868** or Petrida Ijumba **031203**

4736 or 0825058598. This same person will contact you and notify the **Medical Research Council Ethics Committee** if any problems arise with this study.

AGREEMENT

I have been told about this study and my questions have been satisfactorily answered by _____ (name of data collector).

I understand what has been explained to me and I agree to participate in this study, and to be visited at home as indicated above.

I admit that I have been informed about the possible advantages and possible disadvantages which may result from being part of this study.

I admit that I understand and accept that this study involves research and the "Information for Participants" page has been handed to me in connection with this study.

I admit that I understand what is written on this form and agree to take part in this study

I am aware that I may withdraw my consent at any time without this affecting my care at the hospital or clinic.

Printed name of mother (PARTICIPANT): _____

Signed: _____ Date: _____
Participant & Parent/Guardian

Signed: _____ Date: _____
Witness

For illiterate pregnant woman: _____ Date: _____
Mark with a 'X'



Informed Consent to Perform HIV Test



HIV testing is voluntary. You have a right to withdrawn consent at any time by informing the data collector. Please read the content of this form and ask the data collector to explain anything that is not clear to you.

Confidentiality

HIV status was included in the review of your medical records and the data collector is aware of your status; however your status has been held strictly confidential and has not been disclose to anyone else. If you so wish to disclose your HIV status to your health care provider, you are encouraged to do so. Disclosing your HIV status may improve the care and support you receive from the health care provider.

Risks & Benefits of HIV testing

There are no known risks or dangers to you of being tested for HIV. Benefits of testing:

1. Post counselling by a trained counsellor before the results are given to you in 4 -6 weeks
2. If your test result(s) is/ are negative, you will be counseled on how to protect yourself OR your baby from being infected in the future.
3. If your test result(s) is / are positive:
 - You will be counseled on:
 - I. What steps to take to prevent passing the virus to others including your baby
 - II. What treatment for HIV is available and how to access it. As part of treatment, additional tests maybe recommended by your health care provider to determine the best treatment for you and your baby. These tests may include a viral load test
 - III. Other ways to stay healthy.

The HIV Test Process

The process will involve taking drops of blood from you middle finger OR taking blood drops from your baby's heel using a sterile needlelike instrument called lancet.

AGREEMENT

HIV testing has been explained to me and my questions have been satisfactorily answered by _____ (name of data collector).

I understand what has been explained to me and I agree to have the HIV test:

- I. performed on me _____(tick)
- II. performed on my baby _____(tick)

I am aware that I may withdraw my consent at any time without this affecting my care at the hospital or clinic.

Printed name of mother (PARTICIPANT): _____

Signed: _____ Date: _____
Participant & Parent/Guardian

Signed: _____ Date: _____
Witness

For illiterate pregnant woman:
Mark with a 'X' _____ Date: _____



ETHICS COMMITTEE

PO Box 19070, Tygerberg 7505, South Africa.
Francie van Zijl Drive, Parow Valley 7500, Cape Town.
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<http://www.sahelthinfo.org/ethics/ethics.htm>

5 May 2008

Dr M Tomlinson
Health Systems Research Unit
MRC Cape Town

Dear Dr Tomlinson

Protocol ID: EC08-002

Protocol title: An effectiveness study of an integrated, community-based package for maternal, newborn, child and HIV care in a disadvantaged community in South Africa

Meeting date: 25 February 2008

Thank you for your responses to the Ethics Committee, dated 31 March, 23 April and 2 May 2008. Your response was found to be acceptable and I am pleased to inform you that ethics approval is now granted for the study.

Wishing you well with your research.

Yours sincerely

PROF. D DU TOIT
CHAIRPERSON: MRC ETHICS COMMITTEE





ETHEKWINI MUNICIPALITY
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5 November 2008

Dr Mickey Chopra Health Systems Research Unit
MRC

491 Ridge Road -Overpport

Tel: 031 203 4736

Fax: 031 203 4701

Contact Person Petrida Ijumba
Email Petrida.Ijumba@mrc.ac.za
Cell: 0825058598

Dear Dr Chopra

**PROTOCOL AN EFFECTIVENESS STUDY OF AN INTEGRATED,
COMMUNITY-BASED PACKAGE FOR MATERNAL, NEWBORN, CHILD
AND HIV CARE IN A DISADVANTAGED COMMUNITY IN SOUTH
AFRICA**

Approval is granted for the above study to be conducted in Umlazi Community

We wish you all the best in your research. Please send us a report on completion. Please find attached contact details of subdistrict head to whom you can present your research and who will facilitate you. In the;South -Mr Themba Mdluli -0834586591
Please contact Dr. Cheryl WEAICH on 031 - 311 3679 for any queries

Yours faithfully

Mr Sipho CELE
/ **DEPUTY HEAD : HEALTH**

DC 12 Week Visit (English)

Last Modified by: Clyral Support on 10 May 2010 17:11:51 Revision number: 1395 Field Count: 149

Section 1. Interview Identification

1.1 Participant ID

Please enter the participant's unique identifier:

Expects a valid GS1 identifier (required)

1.2 PID check

Please re-enter the participant's unique identifier:

Expects a numeric response (required)

Constraints

Response must be Equals '{q774}'

1.3 Interviewer Code

Please enter your Interviewer Code:

Expects a numeric response (required)

1.4 Interview Date

Please confirm the date of the interview:

Expects a date response (optional)

1.5 Interview Time

Please confirm the time of the interview:

Expects a time response (required)

Section 2. Consent

2.1 Consent Recalled

Do you remember signing an informed consent form for this study?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response Equals 'Yes [1]' then skip to *Mother Age (4.1)*

2.2 Consent Summary

Do you want me to summarise?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response Equals 'No [2]' then skip to *Mother Age (4.1)*

2.3 Informed Consent Acceptance

Was the informed consent form explained and accepted?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response Equals 'Yes [1]' then skip to *Mother Age (4.1)*

Section 3. Refusal

3.1 Refusal Reason

If mother refuses to participate note the reason for non-participation:

Expects a single option response (**required**)

- Don't want finger pricks / blood tests [1]
- Fear of people knowing her HIV status [3]
- Did not know reason for visit to Prince M [4]
- No reason given [5]
- Family member / partner disagree with mother's participation [2]
- Family member / partner does not allow mother to receive explanation [6]

Branches

If response Equals 'Don't want finger pricks / blood tests [1]' then skip to **End (32.2)**

If response Equals 'Fear of people knowing her HIV status [3]' then skip to **End (32.2)**

If response Equals 'Did not know reason for visit to Prince M [4]' then skip to **End (32.2)**

If response Equals 'No reason given [5]' then skip to **End (32.2)**

If response Equals 'Family member / partner disagree with mother's participation [2]' then skip to **End (32.2)**

If response Equals 'Family member / partner does not allow mother to receive explanation [6]' then skip to **End (32.2)**

Section 4. Mother Characteristics

4.1 Mother Age

How old are you (in completed years)?

Expects a numeric response (required)

4.2 Mother DOB

What is your date of birth?

Expects a date response (required)

4.3 Mother Attended School

Have you ever attended school?

Expects a single option response (required)

- Yes [1]
 No [2]

Prerequisites

Skip when *Mother Attended School (4.3)* Equals 'No [2]'

4.4 Mother Education Level

What is your highest level of education?

Expects a single option response (required)

- Grade 1 / Sub A [1]
 Grade 2 / Sub B [2]
 Grade 3 / Std 1 [3]
 Grade 4 / Std 2 [4]
 Grade 5 / Std 3 [5]
 Grade 6 / Std 4 [6]
 Grade 7 / Std 5 [7]
 Grade 8 / Std 6 [8]
 Grade 9 / Std 7 [9]
 Grade 10 / Std 8 [10]
 Grade 11 / Std 9 [11]
 Grade 12 / Std 10 [12]
 Diploma / Cert [13]
 Degree [14]

4.5 Mother Marital Status

What is your marital status?

Expects a single option response (required)

- Single [1]
 Married [3]
 Co-habiting [4]
 Widowed [5]
 Divorced [6]
 Separated [7]

Section 5. Pregnancy History

5.1 Previous Children

Have you given birth to any children previously?

Expects a single option response (**required**)

Yes [1]

No [2]

Prerequisites

Skip when *Previous Children (5.1)* Equals 'No [2]'

5.2 Previous Child Count

How many live children have you given birth to previously?

Expects a numeric response (**required**)

Constraints

Response must be **Greater Than or Equal '1'**

Response must be **Less Than or Equal '10'**

Section 6. Household Member Overview

6.1 Participant Lives with Others

Do you live with others in your household (people who live in the household more than 6 months of the year)?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response Equals 'No [2]' then skip to *HH Electricity (7.1)*

6.2 HH Member Count

How many people normally live in your household including yourself?

Expects a numeric response (**required**)

Constraints

Response must be **Greater Than or Equal '1'**

Response must be **Less Than or Equal '99'**

Section 7. Socio Economic Status

7.1 HH Electricity

Do you have electricity in your household?

Expects a single option response (**required**)

- Yes [1]
 - No [2]
-

7.2 Household Items

Do you have any of the following working items in your household:

Expects multiple selected options (optional)

- Refrigerator [1]
 - Radio [2]
 - Television [3]
 - Stove [4]
 - Telephone / Cellphone [5]
 - Car [6]
-

7.3 HH Main Cooking Fuel

What is the main fuel used for cooking in your household?

Expects a single option response (**required**)

- Wood [1]
 - Charcoal [2]
 - Paraffin / Kerosene [3]
 - Gas [4]
 - Electricity [5]
-

7.4 HH Drinking Water Source

What is the main source of drinking water?

Expects a single option response (**required**)

- Piped dwelling [1]
 - Piped yard [2]
 - Piped public [3]
 - Other [99]
-

Section 8. Activities and Employment

8.1 Participant Employed

Are you employed?

Expects a single option response (**required**)

- Part time [1]
 - Full time [2]
 - Temporary [3]
 - No [4]
-

8.2 HH Income Sources

What are the sources of income for the household?

Expects multiple selected options (**required**)

- Regular income [1]
 - Irregular income [2]
 - Self employment [3]
 - Contribution from others [4]
 - State pension [5]
 - Retirement pension [6]
 - State grant [7]
 - Don't know [9]
 - Other [99]
-

8.3 HH Average Monthly Income

What is the average monthly household income?

Expects a single option response (**required**)

- 0 - 499 [1]
 - 500 - 1000 [2]
 - 1001 - 2000 [3]
 - 2001 - 5000 [4]
 - 5001 - 8000 [5]
 - 8001 and above [6]
 - Dont' know [7]
-

Section 9. Child Info

9.1 Child's Name

What is the child's name?

Expects a single line text response (required)

9.2 Child Gender

Is **Child's Name (9.1)** a boy or girl?

Expects a single option response (required)

Boy [1]

Girl [2]

9.3 Child Has Birth Certificate

Does **Child's Name (9.1)** have a birth certificate?

Expects a single option response (required)

Yes [1]

No [2]

Section 10. Grants

10.1 Participant Has ID

Do you have an ID book?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

10.2 CSG Awareness Instruction

DO NOT read out the following list, mark off only what the mother answers on her own.

10.3 CSG Awareness Sources

How did you hear about how to apply for a child support grant?

Expects multiple selected options (required)

- Radio [1]
 - Family [2]
 - Friend [3]
 - Good Start 3 Community Health Worker [4]
 - Government leaflet [5]
 - Welfare office [6]
 - Health Worker [7]
 - Social Worker [8]
 - Never heard about it [9]
 - Other [99]
-

10.4 Applied for CSG

Have you applied for a child support grant for **Child's Name (9.1)** ?

Expects a single option response (required)

- Yes [1]
- No [2]

Branches

If response Equals 'Yes [1]' then skip to *CSG Being Received (10.7)*

10.5 Plan to Apply for CSG

Are you planning to apply for a child support grant for **Child's Name (9.1)** ?

Expects a single option response (required)

- Yes [1]
- No [2]

Branches

If response Equals 'Yes [1]' then skip to *HIV Status Hospital Records (11.1)*

10.6 CSG Not Applied Reason

Why will you not apply for a child support grant for **Child's Name (9.1)** ?

Expects multiple selected options (required)

- Mother does not have an ID Book [1]
 - Mother does not know how to apply [2]
 - Do not qualify because of financial situation [3]
 - Other [99]
-

Prerequisites

Skip when *Applied for CSG (10.4)* Equals 'No [2]'

10.7 CSG Being Received

Have you started receiving this grant?

Expects a single option response (**required**)

Yes [1]

No [2]

Prerequisites

Skip when *Applied for CSG (10.4)* Equals 'No [2]'

Skip when *CSG Being Received (10.7)* Equals 'Yes [1]'

10.8 CSG Not Being Received Reason

What is the reason that you have not started to receive this grant?

Expects multiple selected options (**required**)

Still on the waiting list [1]

No ID Book [2]

No birth certificate for the child [3]

No road to health card for the child [4]

No proof of income [5]

Other [99]

Section 11. Status

11.1 HIV Status Hospital Records

From the hospital records, is the woman HIV positive?

Expects a single option response (**required**)

- Yes [1]
- No [2]
- Unknown [3]

Branches

If response **Not Equal 'Yes [1]'** then skip to *HIV Positive (11.3)*

11.2 HIV Positive Instruction

Now we want to ask you some questions relating to HIV.

11.3 HIV Positive

In this pregnancy were you tested for HIV during antenatal care?

Expects a single option response (**required**)

- Yes [1]
 - No [2]
 - Don't Know [3]
-

11.4 HIV Status

What is your status?

Expects a single option response (**required**)

- Positive [1]
- Negative [2]
- Don't know [3]
- No response [4]

Branches

If response **Not Equal 'Positive [1]'** then skip to *HIV Mother to Baby Transmission (11.13)*

11.5 Receiving Treatment

Are you receiving any treatment for HIV?

Expects a single option response (**required**)

- Yes - I know what I' receiving [1]
- Yes - but I'm not sure what I'm receiving [2]
- No [3]
- No response [4]

Branches

If response **Not Equal 'Yes - I know what I' receiving [1]'** then skip to *CD4 Test Since Birth (11.7)*

11.6 Treatment Being Received

What treatment are you receiving?

Expects multiple selected options (required)

- Antiretrovirals [1]
 - Cotrimoxazole [2]
 - Other antibiotics [3]
 - Vitamins / Immune boosters [4]
 - Traditional medicine [5]
 - Other [6]
 - No response [7]
-

11.7 CD4 Test Since Birth

Have you had a CD4 test since **Child's Name (9.1)**'s birth?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't know [3]
-

11.8 Baby Tested

Has **Child's Name (9.1)** been tested for HIV?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Unsure [3]
 - No response [4]
-

Prerequisites

Skip when **Baby Tested (11.8)** Not Equal 'Yes [1]'

11.9 Baby Test Result

What was the result of **Child's Name (9.1)**'s HIV test?

Expects a single option response (required)

- HIV infected [1]
 - Not HIV infected [2]
 - Has not received result [3]
 - Don't know [4]
 - No response [5]
-

11.10 Baby Receiving Treatment

Is **Child's Name (9.1)** receiving any treatment for HIV?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't know [3]
 - No response [4]
-

Prerequisites

Skip when *Baby Receiving Treatment (11.10)* Not Equal 'Yes [1]'

11.11 Baby Treatment Being Received

What treatment is **Child's Name (9.1)** receiving?

Expects multiple selected options (required)

- Antiretrovirals [1]
 - Cotrimoxazole [2]
 - Antibiotics [3]
 - Vitamins [4]
 - Immune boosters [5]
 - Traditional medicine [6]
 - Don't know [7]
 - Other [8]
 - No response [9]
-

Prerequisites

Skip when *Baby Receiving Treatment (11.10)* Not Equal 'Yes [1]'

Skip when *Baby Treatment Being Received (11.11)* Excludes 'Cotrimoxazole [2]'

11.12 Co-trimoxazole for Infant

Do you have co-trimoxazole for **Child's Name (9.1)** in the house today?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

11.13 HIV Mother to Baby Transmission

Can HIV be transmitted from a mother to her baby?

Expects a single option response (required)

- Yes [1]
- No [2]
- Unsure [3]
- No Response [4]

Branches

If response **Not Equal 'Yes [1]'** then skip to *Disclosed HIV Status (11.17)*

11.14 HIV Baby Transmission - Instruction

DO NOT read out the next list, mark off only what the mother answers on her own.

11.15 HIV Baby Transmission

In what ways can HIV be transmitted from a mother to her baby?

Expects multiple selected options (required)

- During pregnancy [1]
 - During childbirth [2]
 - By breast feeding [3]
 - Don't Know [4]
 - Other [5]
 - No Response [6]
-

11.16 HIV Knowledge - Baby Feeding

Has your knowledge of HIV transmission affected your plans on how to feed your baby?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't know [3]
 - No Response [4]
-

11.17 Disclosed HIV Status

Have you disclosed your HIV status to anyone?

Expects a single option response (required)

- Yes [1]
- No [2]
- Status unknown [3]
- No Response [4]

Branches

If response **Not Equal 'Yes [1]'** then skip to **Father HIV Status (11.19)**

11.18 HIV Status Disclosed To

To whom have you disclosed your HIV status?

Expects multiple selected options (required)

- Own mother [1]
 - Father of my child [2]
 - Mother-in-law [3]
 - Other family member [4]
 - Friend [5]
 - Health worker [6]
 - Neighbour [7]
 - CHW [8]
 - Other [99]
-

11.19 Father HIV Status

Has **Child's Name (9.1)**'s father been tested for HIV?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't Know [3]
 - No Response [4]
-

Section 12. Antenatal Care

12.1 AN Care - Instruction

Now I would like to ask you some questions about services you may have received during your pregnancy.

12.2 AN Care Received During Pregnancy

Did you receive any antenatal care during the pregnancy of **Child's Name (9.1)**?

Expects a single option response (**required**)

- Yes [1]
- No [2]

Branches

If response **Not Equal 'Yes [1]'** then skip to *Transport During Labour (12.6)*

12.3 AN Care Provider

Whom did you see?

Expects multiple selected options (**required**)

- Doctor [1]
 - Nurse / Midwife [2]
 - Community Health Worker [3]
 - Other [4]
-

12.4 AN Care Location

Where did you receive antenatal care for this pregnancy?

Expects multiple selected options (**required**)

- Clinic [1]
 - Hospital [2]
 - Private Doctor [3]
 - Other [99]
-

12.5 AN Care First Received

How many months pregnant were you when you first received antenatal care for this pregnancy?

Expects a single option response (**required**)

- 1 Month [1]
 - 2 Months [2]
 - 3 Months [3]
 - 4 Months [4]
 - 5 Months [5]
 - 6 Months [6]
 - 7 Months [7]
 - 8 Months [8]
 - 9 Months [9]
 - Don't Know [10]
-

12.6 Transport During Labour

When you went in labour how did you get to the hospital or clinic?

Expects a single option response (required)

- Ambulance [1]
 - Walked [2]
 - Taxi [3]
 - Car [4]
 - Other [99]
-

12.7 Referred to Facility

During your pregnancy were you referred to the hospital or clinic for any reason?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

12.8 Pregnancy Preparations

During your pregnancy did you make any preparations for your delivery?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

Prerequisites

Skip when *Pregnancy Preparations (12.8)* Equals 'No [2]'

12.9 Pregnancy Delivery Preparation - Instruction

DO NOT read out the next list, mark off only what the mother answers on her own.

Prerequisites

Skip when *Pregnancy Preparations (12.8)* Equals 'No [2]'

12.10 Pregnancy Delivery Preparation

What preparations did you make for the delivery?

Expects multiple selected options (required)

- Financial [1]
 - Transport [2]
 - Food [3]
 - Identification of facility [4]
 - What to do in case of emergency [5]
 - Other [99]
-

Section 13. Birth

13.1 Birth Instruction

If the mother has a RTHC for **Child's Name (9.1)**, capture the following information from the card. If the RTHC is not available, ask the mother.

13.2 Child Birth Place

Where was **Child's Name (9.1)** born?

Expects a single option response (required)

- At PMMH [1]
 - At a clinic / health centre [2]
 - At a private hospital [3]
 - While travelling [4]
 - At a public hospital [5]
 - Other [99]
-

13.3 Child Birth Type

What kind of birth was it?

Expects a single option response (required)

- Normal vaginal [1]
 - Caesarean - section [2]
 - Breech [3]
 - Forceps / Vacuum [4]
 - Other [99]
-

13.4 Child DOB

What is **Child's Name (9.1)**'s birth date?

Expects a date response (required)

13.5 Child Weighed at Birth

Was **Child's Name (9.1)** weighed at birth?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't Remember [3]
-

Prerequisites

Skip when *Child Weighed at Birth (13.5)* Not Equal 'Yes [1]'

13.6 Child Birth Weight

What was the birth weight (in kg)?

Expects a decimal response (required)

Section 14. Baby Care

14.1 Breathe Assistance Action

What was done to help **Child's Name (9.1)** cry or breathe at the time of birth?

Expects multiple selected options (required)

- Rubbed / Massaged [1]
- Dried [2]
- Mouth Cleared [3]
- Don't know [4]
- Nothing [5]
- Other [99]

14.2 Feed - Responsible Person

Who was responsible for making a decision on how to feed **Child's Name (9.1)**?

Expects multiple selected options (required)

- Yourself [1]
- Partner / Husband [2]
- Mother in law [3]
- Mother [4]
- Nurse [5]
- Other [99]

14.3 Clinic In First Week

Did you try to take **Child's Name (9.1)** to the clinic in the first week after delivery?

Expects a single option response (required)

- Yes [1]
- No [2]
- Was still in hospital [3]

Branches

If response **Not Equal 'Yes [1]'** then skip to *Clinic First Week - Responsible Person (14.6)*

14.4 Service Received

Did you receive any service?

Expects a single option response (required)

- Yes [1]
- No [2]

Prerequisites

Skip when *Service Received (14.4)* Equals 'Yes [1]'

14.5 Service Not Received Reason

Why did you not receive service?

Expects a single option response (required)

- Nurse sent me home [1]
 - Told to come back in 6 weeks [2]
 - Other [3]
-

Prerequisites

Skip when *Clinic In First Week (14.3)* Not Equal 'Yes [1]'

14.6 Clinic First Week - Responsible Person

Who was responsible for making the decision to take **Child's Name (9.1)** to the clinic?

Expects multiple selected options (**required**)

- Yourself [1]
 - Partner / husband [2]
 - Mother in law [3]
 - Mother [4]
 - Nurse [5]
 - Good Start III CHW [6]
 - Other [99]
-

14.7 Clinic After Six Weeks

Did you take **Child's Name (9.1)** to the clinic six weeks after delivery?

Expects a single option response (**required**)

- Yes [1]
 - No [2]
-

Section 15. Breastfeeding

15.1 Given Breast Milk

Have you ever given breast milk to **Child's Name (9.1)**?

Expects a single option response (required)

- Yes [1]
- No [2]

Branches

If response Equals 'No [2]' then skip to *Not Given Breast Milk Reason (15.6)*

15.2 When Breast After Birth

When did you put **Child's Name (9.1)** to the breast after birth?

Expects a single option response (required)

- Within the first hour [1]
 - After the first hour and up to 12 hours [2]
 - After 12 hours and up to 24 hours [3]
 - After 24 hours and up to 48 hours (2nd day) [4]
 - After 48 hours and up to 72 hours (3rd day) [5]
 - After 72 hours (after the 3rd day) [6]
-

15.3 Breastfed Duration

How long did you give **Child's Name (9.1)** breast milk?

Expects a single option response (required)

- Less than a week [1]
 - 1 week [2]
 - 2 weeks [3]
 - 3 weeks [4]
 - 4 weeks [5]
 - 5 weeks [6]
 - 6 weeks [7]
 - 7 weeks [8]
 - 8 weeks [9]
 - 9 weeks [10]
 - 10 weeks [11]
 - 11 weeks [12]
 - 12 weeks [13]
 - More than 12 weeks [14]
 - Currently breastfeeding [15]
-

15.4 Breast Infection

Have you had any infection, or problem with your breasts since **Child's Name (9.1)** was born?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

Prerequisites

Skip when *Breast Infection (15.4)* Equals 'No [2]'

15.5 Breast Infection - Problems

What problems did you have?

Expects multiple selected options (required)

- Engorgement [1]
 - Cracked nipples [2]
 - Painful nipples [3]
 - Bleeding nipples [4]
 - Full, lumpy, painful breasts [5]
 - Red, painful nipples with fever [6]
 - Other [99]
-

Prerequisites

Skip when *Given Breast Milk (15.1)* Equals 'Yes [1]'

15.6 Not Given Breast Milk Reason

What was the reason(s) for not ever giving breast milk to **Child's Name (9.1)** ?

Expects multiple selected options (required)

- HIV Status [1]
 - Advised by Good Start III CHW not to breastfeed [2]
 - Advised by the nurse or counsellor not to breastfeed [3]
 - Advised by partner not to breastfeed [4]
 - Advised by mother-in-law not to breastfeed [5]
 - Other [99]
 - No response [91]
-

Section 16. Family Planning

16.1 Family Planning Methods Used

What method(s) are you currently using?

Expects multiple selected options (required)

- Condoms / Female condoms [1]
 - Injectable (Depo or Nur- Isterate) [2]
 - Oral contraceptive pill [3]
 - Abstinence [4]
 - Coitus Interruptus (withdraw) [5]
 - None [6]
 - Other [99]
-

Section 17. Dietary 24-hour Recall

17.1 Dietary 24-hour Recall Instruction

I am now going to ask you questions about what you fed your baby from the time you woke up yesterday morning till you woke up this morning.

17.2 24-hour Recall Breastfed

From the time you woke up yesterday morning till you woke up this morning did you breastfeed your baby?

Expects a single option response (required)

- Yes [1]
 No [2]
-

17.3 Given Items

From the time you woke up yesterday morning till you woke up this morning, did you give any of the following items to **Child's Name (9.1)**?

Expects multiple selected options (optional)

- Water [1]
 Water with sugar or glucose [18]
 Fruit juice [2]
 Tea without milk [3]
 Tea with milk [4]
 Diluted cows milk [5]
 Non Diluted cows milk [6]
 Other powdered milk [7]
 Goats milk [8]
 Infant formula [9]
 Fruits / Vegetables [10]
 Meat [11]
 Fish [12]
 Eggs [13]
 Dairy product (e.g. yoghurt, cheese or ice-cream) [14]
 Cereals, porridge or bread [15]
 Prescribed medicines [19]
 Herbs / traditional medicine [16]
 Over-the-counter medicines (e.g. gripe water) [17]
 Other [99]
-

Section 18. Dietary 1-week Recall

18.1 1-Week Recall - Breastfed

Thinking one week back, have you breastfed **Child's Name (9.1)** ?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

18.2 1-week Recall Given Items

Thinking one week back have you given any of these items to **Child's Name (9.1)** ?

Expects multiple selected options (optional)

- Water [1]
 - Water with sugar or glucose [18]
 - Fruit juice [2]
 - Tea without milk [3]
 - Tea with milk [4]
 - Diluted cow's milk [5]
 - Non-diluted cow's milk [6]
 - Other powdered milk [7]
 - Goats milk [8]
 - Infant formula [9]
 - Fruits / vegetables [10]
 - Meat [11]
 - Fish [12]
 - Eggs [13]
 - Dairy product (e.g. yoghurt, cheese, ice-cream) [14]
 - Cereals, porridge or bread [15]
 - Prescribed medicines [19]
 - Herbs / traditional medicine [16]
 - Over-the-counter medicines (e.g. gripe water) [17]
 - Other [99]
-

Section 19. Dietary Recall Since Birth

19.1 Intro - Instruction

I am now going to ask you if you have ever given the following to **Child's Name (9.1)**.

19.2 Ever Given Items

Have you ever given **Child's Name (9.1)** any of the following items?

Expects multiple selected options (optional)

- Water [1]
 - Water with sugar or glucose [18]
 - Fruit juice [2]
 - Tea without milk [3]
 - Tea with milk [4]
 - Diluted cows milk [5]
 - Non Diluted cows milk [6]
 - Other powdered milk [7]
 - Goats milk [8]
 - Infant formula [9]
 - Fruits / Vegetables [10]
 - Meat [11]
 - Fish [12]
 - Eggs [13]
 - Dairy product (e.g. yoghurt, cheese or ice-cream) [14]
 - Cereals, porridge or bread [15]
 - Prescribed medicines [19]
 - Herbs / traditional medicine [16]
 - Over-the-counter medicine (e.g. gripe water) [17]
 - Other [99]
-

Section 20. Vaccinations

20.1 Vaccination Instruction

Now I am going to ask you questions which are related to your baby's health.

20.2 Child Had Vaccinations

Has **Child's Name (9.1)** had any vaccinations?

Expects a single option response (required)

- Yes [1]
 - No [2]
 - Don't know [3]
-

20.3 RTHC Check

Record vaccinations from RTHC if available. If the RTHC is not available, ask the mother.

Expects multiple selected options (optional)

- BCG (right arm) [1]
 - Polio (oral) [2]
 - Polio 1 (oral) [3]
 - DTP 1 (left thigh) [4]
 - Hib 1 (left thigh) [5]
 - DTP 1 / Hip 1 Combined (left thigh) [6]
 - Hep B 1 (right thigh) [7]
 - Polio 2 (oral) [8]
 - DTP 2 (left thigh) [9]
 - Hib 2 (left thigh) [10]
 - DTP 2 / Hip 2 Combined (left thigh) [11]
 - Hep B 2 (right thigh) [12]
 - PCV7(1) (right thigh) [13]
 - Pentaxim 1(upper thigh) [14]
 - Pentaxim 2(upper thigh) [15]
-

Section 21. Diarrhoea 2-week Recall

21.1 2-week Recall Instruction

The definition of diarrhoea is passage of 3 or more loose, liquid or watery stools in a 24 hr period. For breast fed infants ask also about recent change in stool consistency and frequency.

21.2 Had Diarrhoea

During the last two weeks that ended yesterday morning, did **Child's Name (9.1)** have diarrhoea?

Expects a single option response (**required**)

- Yes [1]
 No [2]

Branches

If response Equals 'No [2]' then skip to *Had Cough (22.1)*

21.3 Admitted to Hospital - Diarrhoea

Was the child admitted to a hospital because of this diarrhoea?

Expects a single option response (**required**)

- Yes [1]
 No [2]
-

21.4 Diarrhoea Duration

How many days did the diarrhoea last?

Expects a single option response (**required**)

- 1 - 3 days [1]
 4 - 7 days [2]
 8 - 14 days [3]
 More than 14 days [4]
-

Section 22. Pneumonia Two Week Recall

22.1 Had Cough

During the last two weeks that ended yesterday morning, did **Child's Name (9.1)** have a cough?

Expects a single option response (**required**)

Yes [1]

No [2]

22.2 Had Difficulty Breathing

During the last two weeks that ended yesterday morning, did **Child's Name (9.1)** have fast or difficulty breathing?

Expects a single option response (**required**)

Yes [1]

No [2]

22.3 Admitted to Hospital - Pneumonia

Was the child admitted to a hospital because of this pneumonia (cough, fast and difficult breathing)?

Expects a single option response (**required**)

Yes [1]

No [2]

Not applicable [3]

Section 23. Hospitalisation Overview

23.1 Has Been Admitted

Since birth has **Child's Name (9.1)** ever been admitted to hospital?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response **Not Equal** 'Yes [1]' then skip to *Dangerous Symptoms - Intro (25.1)*

23.2 Admittance Count

How many times?

Expects a numeric response (**required**)

Repeat this section for value of *Admittance Count (23.2)*

Section 24. Hospitalisations

24.1 Hospitalisation Age

Referring to admittance #REPEAT IDX, how old was **Child's Name (9.1)** in weeks?

Expects a numeric response (required)

24.2 Hospitalisation Cause

Referring to admittance #REPEAT IDX, what was the main cause?

Expects a single option response (required)

- Diarrhoea [1]
 - Pneumonia (cough or difficulty breathing) [2]
 - Accident [3]
 - High fever [4]
 - Other [99]
-

Section 25. Health Following Delivery

25.1 Dangerous Symptoms - Intro

DO NOT Read out the next list, mark off only what the Mother answers on her own

25.2 Symptoms Urgent Attention

Sometimes newborns, within the first month of life, have severe illnesses and should be taken immediately to a health facility. What types of symptoms would cause you to take your newborn to a health facility right away?

Expects multiple selected options (optional)

- Convulsions [1]
 - Fever / Hot body [2]
 - Difficulty Breathing [4]
 - Difficulty sucking [3]
 - Redness / discharge around cord [5]
 - Jaundice: Yellow palms, soles, or eyes [6]
 - Baby is weak and soft [7]
 - Weak abnormal cry [8]
 - Other [9]
 - Don't know [10]
-

25.3 Symptoms Experienced

Did **Child's Name (9.1)** experience any of the following symptoms during the first month?

Expects multiple selected options (required)

- Convulsions [1]
- Fever / hot body [2]
- Difficulty sucking [3]
- Difficulty breathing [4]
- Redness / discharge around cord [5]
- Jaundice: Yellow palms, soles, or eyes [6]
- Baby is weak and soft [7]
- Weak abnormal cry [8]
- None of the Above [9]

Branches

If response **Includes 'None of the Above [9]'** then skip to *Previous Child Mortality (26.1)*

25.4 Care Sought

For the last illness in the first month of life when **Child's Name (9.1)** was sick, did you seek care?

Expects a single option response (required)

- Yes [1]
- No [2]

Branches

If response **Equals 'No [2]'** then skip to *Care Not Sought Reasons (25.6)*

25.5 Care Sought Location

Where did you seek care for **Child's Name (9.1)**?

Expects multiple selected options (required)

- Clinic [1]
 - Hospital (PMMH) [2]
 - Private Clinic [3]
 - Private Hospital [4]
 - Private Pharmacy [5]
 - Traditional Practitioner [6]
 - Relative or Friend [7]
 - Private doctor [8]
 - Other [99]
-

Prerequisites

Skip when *Care Sought (25.4)* Equals 'Yes [1]'

25.6 Care Not Sought Reasons

What was / were the reason(s) that you did not seek care?

Expects multiple selected options (required)

- Expecting self resolution of sickness [1]
 - Health facility too far [2]
 - Cost of treatment service high [3]
 - Don't trust facility / poor quality of care [4]
 - Respected family member did not allow [5]
 - The traditional birth attendant didnt allow [6]
 - Not customary to seek care outside of home after childbirth [7]
 - Other [99]
-

Section 26. Previous Child Mortality

26.1 Previous Child Mortality

Did any of your children under 5 years who were born alive, die?

Expects a single option response (**required**)

Yes [1]

No [2]

Branches

If response Equals 'No [2]' then skip to *MHQ - Instruction (28.1)*

26.2 Child Mortality Count

How many?

Expects a numeric response (**required**)

Constraints

Response must be **Greater Than or Equal '1'**

Repeat this section for value of *Child Mortality Count (26.2)*

Section 27. Previous Child Mortalities

27.1 Previous Mortality Age

How soon after birth did child #REPEAT IDX die?

Expects a single option response (**required**)

- Within 24 hours [1]
 - Within 48 hours [2]
 - Within 1 week [3]
 - Within 4 weeks [4]
 - Within 12 months [5]
 - Within 5 years [6]
-

27.2 Previous Mortality Cause

What was the cause of death of child #REPEAT IDX?

Expects a single option response (**required**)

- Diarrhoea [1]
 - Pneumonia [2]
 - Accident [3]
 - High Fever [4]
 - Don't Know [5]
 - Other [99]
-

Section 28. Mental Health Questions

28.1 MHQ - Instruction

Please answer ALL the questions simply by stating which answer most closely applies to you OVER THE PAST 2 WEEKS.

28.2 MHQ - Funny Side

Have you been able to laugh and see the funny side of things?

Expects a single option response (required)

- As much as you always could [1]
 - Not quite so much now [2]
 - Definitely not so much now [3]
 - Not at all [4]
-

28.3 MHQ - Enjoy Things

Have you looked forward with enjoyment to things?

Expects a single option response (required)

- As much as you ever did [1]
 - Rather less than you used to [2]
 - Definitely less than you used to [3]
 - Hardly at all [4]
-

28.4 MHQ - Unnecessary Blame

Have you blamed yourself unnecessarily when things went wrong?

Expects a single option response (required)

- Yes, most of the time [1]
 - Yes, some of the time [2]
 - Not very often [3]
 - No, never [4]
-

28.5 MHQ - Anxious

Have you been anxious or worried for no good reason?

Expects a single option response (required)

- No, not at all [1]
 - Hardly ever [2]
 - Yes, sometimes [3]
 - Yes, very often [4]
-

28.6 MHQ - Scared

Have you felt scared or panicky for not very good reason?

Expects a single option response (required)

- Yes, quite a lot [1]
 - Yes, sometimes [2]
 - No, not much [3]
 - No, not at all [4]
-

28.7 MHQ - Things on Top

Have things have been getting on top of you?

Expects a single option response (**required**)

- Yes, most of the time you haven't been able to cope at all [1]
 - Yes, sometimes you haven't been coping as well [2]
 - Yes, most of the time you have coped quite well [3]
 - No, you have been coping as well as ever [4]
-

28.8 MHQ - Difficulty Sleeping

Have you been so unhappy that you have had difficulty sleeping?

Expects a single option response (**required**)

- Yes, most of the time [1]
 - Yes, sometimes [2]
 - Not very often [3]
 - No, not at all [4]
-

28.9 MHQ - Miserable

Have you felt sad or miserable?

Expects a single option response (**required**)

- Yes, most of the time [1]
 - Yes, sometimes [2]
 - Not very often [3]
 - No, not at all [4]
-

28.10 MHQ - Crying

Have you been so unhappy that you have been crying?

Expects a single option response (**required**)

- Yes, most of the time [1]
 - Yes, quite often [2]
 - Only occasional [3]
 - No, never [4]
-

28.11 MHQ - Self-harm

Has the thought of harming yourself occurred to you?

Expects a single option response (**required**)

- Yes, quite often [1]
 - Sometimes [2]
 - Hardly ever [3]
 - Never [4]
-

28.12 MHQ - Concentration

Have you been able to concentrate on whatever you're doing?

Expects a single option response (**required**)

- Worse than usual [1]
 - Same as usual [2]
 - Better than usual [3]
-

28.13 MHQ - Lost Sleep

Have you recently lost much sleep over worry?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.14 MHQ - Useful Part

Have you recently felt that you are playing a useful part in things?

Expects a single option response (required)

- Less useful than usual [1]
 - Same as usual [2]
 - More so than usual [3]
-

28.15 MHQ - Capable of Decision Making

Have you recently felt capable of making decisions about things?

Expects a single option response (required)

- Less so than usual [1]
 - Same as usual [2]
 - More so than usual [3]
-

28.16 MHQ - Under Strain

Have you recently felt constantly under strain?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.17 MHQ - Overcome Difficulties

Have you recently felt you couldn't overcome your difficulties?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.18 MHQ - Enjoy Daily Activities

Have you recently been able to enjoy your normal day - to - day activities?

Expects a single option response (required)

- Less so than usual [1]
 - Same as usual [2]
 - More than usual [3]
-

28.19 MHQ - Face up to Problems

Have you recently been able to face up to your problems?

Expects a single option response (required)

- Less able than usual [1]
 - Same as usual [2]
 - More than usual [3]
-

28.20 MHQ - Depressed

Have you recently been feeling unhappy and depressed?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.21 MHQ - Losing Self Confidence

Have you recently been losing confidence in yourself?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.22 MHQ - Worthless

Have you recently been thinking of yourself as a worthless person?

Expects a single option response (required)

- Rather more than usual [1]
 - No more than usual [2]
 - Not at all [3]
-

28.23 MHQ - Happiness

Have you recently been feeling reasonably happy, all things considered?

Expects a single option response (required)

- Less so than usual [1]
 - About same as usual [2]
 - More than usual [3]
-

Section 29. CHW Visits

29.1 Visited by CHW

When you were pregnant were you visited by a Good Start III Community Health Worker?

Expects a single option response (**required**)

Yes [1]

No [2]

Section 30. Dry Blood Spot Collection

Prerequisites

Skip when *HIV Status Hospital Records (11.1)* Equals 'Yes [1]'

30.1 DBS Required

A DBS is required for HIV positive mothers. Did the mother indicate she was HIV positive?

Expects a single option response (required)

- Yes [1]
- No [2]
- She didn't know [3]

Branches

If response **Not Equal 'Yes [1]'** then skip to *Baby Weight (31.1)*

30.2 Child DBS Permission Obtained

Did you obtain the mother's signed consent to take a DBS from **Child's Name (9.1)**?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

Prerequisites

Skip when *Child DBS Permission Obtained (30.2)* Equals 'No [2]'

30.3 Child DBS Obtained

Did you obtain a DBS from **Child's Name (9.1)**?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

30.4 Mother DBS Permission Obtained

Did you obtain the mother's signed consent to take a DBS from her?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

Prerequisites

Skip when *Mother DBS Permission Obtained (30.4)* Equals 'No [2]'

30.5 Mother DBS Obtained

Did you obtain a DBS from the mother?

Expects a single option response (required)

- Yes [1]
 - No [2]
-

Section 31. Anthropometry

31.1 Baby Weight

Enter the baby's weight (in kg):

Expects a decimal response (required)

Constraints

Response must be **Greater Than or Equal '2'**

Response must be **Less Than or Equal '15'**

31.2 Baby Length

Enter the baby's length (in cm):

Expects a decimal response (required)

Constraints

Response must be **Greater Than or Equal '20'**

Response must be **Less Than or Equal '100'**

Section 32. End of Survey

32.1 Voucher Given

Was the voucher given to the mother?

Expects a single option response (**required**)

Yes [1]

No [2]

32.2 End

You have reached the survey. You can go back and review previous responses or select Next to complete the section.

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- Authors
- Affiliations
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Examples:

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- Middle names (or initials, if used), and
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Each author should list an associated department, university, or organizational affiliation and its location, including city, state/province (if applicable), and country. If the article has been submitted on behalf of a consortium, all author names and affiliations should be listed at the end of the article.

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All persons designated as authors should qualify for authorship, and all those who qualify should be listed. Each author must have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Those who contributed to the work but do not qualify for authorship should be listed in the acknowledgments.

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- Not exceed 300 words

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- Note any relevant controversies or disagreements in the field
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Acknowledgments

People who contributed to the work but do not fit the [PLOS ONE authorship criteria](#) should be listed in the acknowledgments, along with their contributions. You must ensure that anyone named in the acknowledgments agrees to being so named.

Funding sources should **not** be included in the acknowledgments, or anywhere in the manuscript file. You will provide this information during the manuscript submission process.

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References

Only published or accepted manuscripts should be included in the reference list. Manuscripts that have been submitted but not yet accepted should not be cited. Limited citation of unpublished work should be included in the body of the text only as "unpublished data."

References must be listed at the end of the manuscript and numbered

in the order that they appear in the text. In the text, citations should be indicated by the reference number in brackets. Journal name abbreviations should be those found in the [NCBI databases](#). A number of reference software companies supply PLOS style files (e.g., [Reference Manager](#), [EndNote](#)).

Proper formatting of the references is crucial; some examples are shown below.

- **Published papers.** Hou WR, Hou YL, Wu GF, Song Y, Su XL, et al. (2011) cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda (*Ailuropoda melanoleuca*). *Genet Mol Res* 10: 1576-1588. Note: Use of a DOI number for the full-text article is acceptable as an alternative to or in addition to traditional volume and page numbers.
- **Accepted, unpublished papers.** Same as above, but “In press” appears instead of the page numbers
- **Electronic journal articles.** Huynen MMTE, Martens P, Hilderlink HBM (2005) The health impacts of globalisation: a conceptual framework. *Global Health* 1: 14. Available: <http://www.globalizationandhealth.com/content/1/1/14>. Accessed 25 January 2012.
- **Books.** Bates B (1992) *Bargaining for life: A social history of tuberculosis*. Philadelphia: University of Pennsylvania Press. 435 p.
- **Book chapters** Hansen B (1991) New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. *AIDS and the historian*. Bethesda: National Institutes of Health. pp. 21-28.

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Tables

Tables should be included at the end of the manuscript. All tables should have a concise title. Footnotes can be used to explain abbreviations. Citations should be indicated using the same style as outlined [above](#). Tables occupying more than one printed page should be avoided, if possible. Larger tables can be published as [Supporting Information](#). Please ensure that table formatting conforms to our [Guidelines for table preparation](#).

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Figure Legends

Figures should **not** be included in the manuscript file, but figure legends should be. Guidelines for preparing figures can be found [here](#).

Figure legends should describe the key messages of a figure. Legends should have a short title of 15 words or less. The full legend should

have a description of the figure and allow readers to understand the figure without referring to the text. The legend itself should be succinct, avoid lengthy descriptions of methods, and define all non-standard symbols and abbreviations.

Further information about figure legends can be found in the [Figure Guidelines](#).

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3. Specific Reporting Guidelines

Human Subject Research

Methods sections of papers on research using human subject or samples must include ethics statements that specify:

- The name of the approving institutional review board or equivalent committee(s). If approval was not obtained, the authors must provide a detailed statement explaining why it was not needed
- Whether informed consent was written or oral. If informed consent was oral, it must be stated in the manuscript:
 - Why written consent could not be obtained
 - That the Institutional Review Board (IRB) approved use of oral consent
 - How oral consent was documented

For studies involving humans categorized by race/ethnicity, age, disease/disabilities, religion, sex/gender, sexual orientation, or other socially constructed groupings, authors should:

- Explicitly describe their methods of categorizing human populations
- Define categories in as much detail as the study protocol allows
- Justify their choices of definitions and categories, including for example whether any rules of human categorization were required by their funding agency
- Explain whether (and if so, how) they controlled for confounding variables such as socioeconomic status, nutrition, environmental exposures, or similar factors in their analysis

In addition, outmoded terms and potentially stigmatizing labels should be changed to more current, acceptable terminology. Examples: "Caucasian" should be changed to "white" or "of [Western] European descent" (as appropriate); "cancer victims" should be changed to "patients with cancer."

For papers that include identifying, or potentially identifying, information, authors must download the [Consent Form for Publication in a PLOS Journal](#) (PDF), which the individual, parent, or guardian must sign once they have read the paper and been informed about the terms of PLOS open-access license. The signed consent form should not be submitted with the manuscript, but authors should securely file it in the individual's case notes and the methods section of the manuscript should explicitly state that consent authorization for publication is on file, using wording like:

- **The individual in this manuscript has given written informed consent (as outlined in PLOS consent form) to publish these case details.**

For more information about *PLOS ONE* policies regarding human subject research, see the [Publication Criteria](#) and [Editorial Policies](#).

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Clinical Trials

Authors of manuscripts describing the results of clinical trials must adhere to the [CONSORT](#) reporting guidelines appropriate to their trial design, available on the [CONSORT Statement website](#). Before the paper can enter peer review, authors must:

1. Provide the registry name and number in the methods section of the manuscript
2. Provide a copy of the trial protocol as approved by the ethics committee and a completed [CONSORT checklist](#) as Supporting Information (which will be published alongside the paper, if accepted)
3. Include the [CONSORT flow diagram](#) as the manuscript's "Figure 1"

Any deviation from the trial protocol must be explained in the paper. Authors must explicitly discuss informed consent in their paper, and we reserve the right to ask for a copy of the patient consent form.

The methods section must include the name of the registry, the registry number, and the URL of your trial in the registry database for each location in which the trial is registered.

For more information about *PLOS ONE* policies regarding clinical trials, see the [Editorial Policies](#).

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12. Table Guidelines

Tables submitted for publication should be included at the very end of the article file (.doc, .rtf, .tex). Supporting Information tables should be submitted as separate files in any of the following formats (although authors should aim to ensure that the file type is most appropriate to the information displayed): Word (.doc), Excel (.xls), PDF, PPT, JPG, EPS, or TIFF.

Title and Footnotes Each table needs a concise title of no more than one sentence, placed above the table with the table number (e.g., Table 1). The legend and footnotes should be placed below the table. Footnotes may be used to explain abbreviations.

Specifications Tables that do not conform to the following requirements may give unintended results when published. Problems may include the movement of data (rows or columns), loss of spacing, or disorganization of headings. Note: Multi-part tables with varying numbers of columns or multiple footnote sections should be divided and renumbered as separate tables. In the published version, tables will be formatted in PLOS style. This includes alternate row shading, content left-aligned in cells, title above the table and legend/footnotes below the table.

Tables must:

- Be cell-based (e.g., created in Word with Tables tool (preferred) or in Excel).
- Be editable (i.e., not a graphic object).
- Have heading/subheading levels in separate columns.
- Be no larger than one printed page (7 in x 9.5 in). Larger tables can be published as online supporting information. Note: some wide tables may be printed sideways in the PDF.

• Tables must *not*:

- Use returns or tabs within a cell.
- Have color or shading.
- Use lines, rules, or borders.
- Contain spaces within cells to align text.
- Have *vertically* merged cells; horizontally merged cells are fine.
- Have inserted text boxes or pictures.

Have tables within tables.
 Include empty columns, rows, or cells to create spacing.
 Include hyperlinked text.

If your submitted table contains any of these elements, they will be returned for adjustments.

Problem: Using rules to specify layout.

Incorrectly formatted submission

		Package 1		Package 2	
PDB	Time	Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

Incorrectly formatted result

		Package 1		Package 2	
PDB	Time	Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

Correctly formatted submission - Notice the use of horizontally merged cells.

		Package 1		Package 2	
PDB	Time	Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

Correctly formatted result

		Package 1		Package 2	
PDB	Time	Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

Problem: Using returns to create rows.

Incorrectly formatted table

Category	Subcategory	Result¶ (%)
Sex	Female	350¶ (49)
	Male	362¶ (51)
Age	<10 y	202¶ (28)
	10-15 y	419¶ (59)
	>15 y	91¶ (13)

Incorrectly formatted result - Notice that the paragraph returns create new rows.

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)

Correctly formatted table

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)

Correctly formatted table results

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)

Problem: Use of shading to convey grouping.

Incorrectly formatted table

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)
Height	< 140 cm	142 (20)
	140-150 cm	382 (54)
	>150 cm	188 (26)

Incorrectly formatted result - Notice that the submitted shading pattern is lost.

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)
Height	< 140 cm	142 (20)
	140-150 cm	382 (54)
	>150 cm	188 (26)

Problem: Footnotes included in table.

Incorrectly formatted table

PDB	Time	Package 1		Package 2	
		Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns ^a	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

^a 3ns of equilibration were not used for the analysis.

Correctly formatted table

PDB	Time	Package 1		Package 2	
		Protocol 1	Protocol 2	Protocol 1	Protocol 2
1E56	10ns ^a	3.65	3.45	2.90	2.86
3MB5	10ns	2.67	2.86	1.78	1.76
1Q03	10ns	2.56	2.43	2.13	2.05

^a 3ns of equilibration were not used for the analysis.

Problem: Vertically merged cells.

Incorrectly formatted table

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)

Correctly formatted table

Category	Subcategory	Result (%)
Sex	Female	350 (49)
	Male	362 (51)
Age	<10 y	202 (28)
	10-15 y	419 (59)
	>15 y	91 (13)

Problem: Multi-part table.

Incorrectly formatted table

A.	PDB	Catalytic residues	Distance
	1F6G	123GLU 393ASP	5.2
	4D90	328HIS 476ASP	3.4
	2MX8	186LYS 373GLU	4.3
B	Complex	Time	Distance
	Receptor	Ligand	
	1D34	3E45	20ns
	2MD1	2MD3	30ns
	3LX3	5LY3	25ns

Solution: Separate into two tables.

Problem: LaTeX Table - Use of "\\" within a cell.

Incorrectly formatted table

```

\begin{tabular}{|c|c|c|}
\hline
Head1 & Head2 & Head3 \\
Unit1 & Unit 2 & Unit3 \\
\hline
Row1 & Row1 & Row1\\
\hline
Row2 & Row2 & Row2\\
\hline
Row3 & Row3 & Row3\\
\hline
Row4 & Row4 & Row4\\
\hline
\end{tabular}

```

Incorrectly formatted result - Notice the Unit cells are on a separate row from the Head cells.

Head1	Head2	Head3
Unit1	Unit2	Unit3
Row1	Row1	Row1
Row2	Row2	Row2
Row3	Row3	Row3
Row4	Row4	Row4

Correctly formatted table - Allows text within a cell to wrap.

```

\begin{tabular}{|c|c|c|}
\hline
Head1 Unit1 & Head2 Unit2 & Head3 Unit3 \\
\hline
Row1 & Row1 & Row1 \\
\hline
Row2 & Row2 & Row2 \\
\hline
Row3 & Row3 & Row3 \\
\hline
Row4 & Row4 & Row4 \\
\hline
\end{tabular}

```

Correctly formatted table

Head1	Head2	Head3
Unit1	Unit2	Unit3
Row1	Row1	Row1
Row2	Row2	Row2
Row3	Row3	Row3
Row4	Row4	Row4

13. Getting Help

If you have questions about your figures after reading the guidelines, you can e-mail **figures [at] plos.org**.