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Authors
Stewart, Robert C
Ashorn, Per
Umar, Eric
et al.

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Associations between antenatal depression and neonatal outcomes in Malawi

Robert C. Stewart[1] [iD] | Per Ashorn[2,3] | Eric Umar[4] | Kathryn G. Dewey[5] | Ulla Ashorn[2] |
Francis Creed[6] | Atif Rahman[7] | Barbara Tomenson[6] | Elizabeth L. Prado[5] [iD] | Ken Maleta[4]

[1] Department of Mental Health, College of
Medicine, University of Malawi and Division
of Psychiatry, University of Edinburgh,
Edinburgh, UK

[2] Centre for Child Health Research, University
of Tampere Faculty of Medicine and Life
Sciences, Tampere, Finland

[3] Department of Pediatrics, Tampere
University Hospital, Tampere, Finland

[4] School of Public Health and Family Medicine,
College of Medicine, University of Malawi,
Blantyre, Malawi

[5] Department of Nutrition, University of
California, Davis, California, USA

[6] Neuroscience and Mental Health, University
of Manchester, UK

[7] Institute of Psychology, Health and Society,
University of Liverpool, UK

Correspondence
Robert C Stewart, Department of Mental
Health, College of Medicine, University of
Malawi, Mahatma Ghandi Road, Blantyre 3,
Malawi.
Email: robcstewart@mac.com

Abstract

Studies from several low- and middle-income countries have shown that antenatal
depression may be a risk factor for poor neonatal outcomes. However, those studies
conducted in sub-Saharan Africa have not consistently demonstrated this association.
We set out to investigate whether antenatal depression is associated with shorter
duration of pregnancy and reduced newborn size in rural Malawi. Pregnant women
recruited from four antenatal clinics to the International Lipid-Based Nutrient Supple-
ments Project-DYAD-Malawi (iLiNS-DYAD-M) randomised controlled trial of nutrient
supplementation were screened for antenatal depression in the second or third tri-
mester using a locally validated version of the Self Reporting Questionnaire (SRQ).
Outcomes were duration of pregnancy, birthweight, newborn length for age z-score
(LAZ), head circumference z-score, and mid-upper arm circumference (MUAC). Other
potential confounding factors and predictors of birth outcome were measured and
adjusted for in the analysis. 1,391 women were enrolled to the trial. 1,006/1,391
(72.3%) of these women completed an SRQ and gave birth to a singleton infant whose
weight was measured within 2 weeks of birth. 143/1,006 (14.2%) scored SRQ $\geq$ 8,
indicating likely depression. Antenatal depression was not associated with birth
weight, duration of pregnancy, newborn LAZ, or head-circumference Z-score. There
was an inverse association with newborn MUAC (adjusted mean difference − 0.2 cm
(95% CI −0.4 to 0, p = 0.021) the significance of which is unclear. The study was
conducted within a randomised controlled trial of nutritional supplementation and
there was a high proportion of missing data in some enrolment sites; this may have
affected the validity of our findings.

KEYWORDS

depression, fetal growth, low income countries, Malawi, maternal mental health, pregnancy
outcome

1 | INTRODUCTION

Preterm birth (PTB) and intrauterine growth retardation (IUGR) are
both common in low- and middle-income countries (LMIC). Both
prematurity and IUGR are associated with neonatal death, childhood
morbidity, poor postnatal growth, and delayed psychomotor develop-
ment (Howson et al., 2013). Depression occurring in the antenatal

period is an important health problem globally, including in LMIC. A
systematic review found a weighted mean prevalence of antenatal
common mental disorders in LMIC of 15.6% (Fisher et al., 2012).

Antenatal depression has been shown to be a predictor of poor
neonatal outcomes although there is considerable heterogeneity
between studies. A meta-analysis of 29 studies showed that antenatal
depression is associated with both PTB and IUGR, with associations

more likely to be found in studies from LMIC, socio-economically deprived populations in the US, and in studies that used categorical versus continuous measures of depressive symptoms (Grote et al., 2010). Antenatal depression may affect foetal growth through poor maternal self-care, nutrition and healthcare-seeking, or through a direct effect of stress-related physiological changes on the intrauterine environment (Glover, 2014; Stewart, 2007).

In studies from LMIC outside Africa, antenatal depression (or a high level of depressive and anxious symptoms) was found to be a risk factor for IUGR or low birth weight in prospective studies from Pakistan (Rahman, Iqbal, Bunn, Lovel, & Harrington, 2004), Brazil (Rondo et al., 2003), India (Patel & Prince, 2006), Bangladesh (Nasreen, Kabir, Forsell, & Edhborg, 2010), and Vietnam (Niemi, Falkenberg, Petzold, Chuc, & Patel, 2013); and a risk factor for PTB in Brazil (Rondo et al., 2003) and Vietnam (Niemi et al., 2013). Results from sub-Saharan African studies have been mixed with associations found only in some studies and for varying neonatal outcomes. Antenatal depression was inversely associated with infant birth weight in a study conducted in rural Ethiopia (Wado, Afework, & Hindin, 2014) and with lower newborn head circumference in a South African study (Brittain et al., 2015). In a large prospective cohort study in Ghana, there was a marginal association with PTB but no association with low birth weight (Weobong et al., 2014). In a prospective case-control study of HIV+ pregnant women in Zambia, Collin et al. (2006) found an association between high levels of depressive and anxious symptoms and lower birth length (but not birth weight or PTB). In a prospective cohort study in Ethiopia, Hanlon et al. (2009) found no association between high levels of depressive and anxious symptoms antenatally and either birth weight or gestational age at delivery. A study restricted to women with low risk pregnancies in Ghana and Cote D'Ivoire also showed no significant associations (Bindt et al., 2013).

Malawi is a low-income country in sub-Saharan Africa. The estimated rate of PTB in Malawi is 18.1% (Blencowe et al., 2012) and 37.4% of children under 5 years are stunted (National Statistical Office [Malawi] & ICF, 2017). The prevalence of antenatal major depressive episode has been estimated as 10.7% (Stewart, Umar, Tomenson, & Creed, 2014a). No previous studies have investigated whether antenatal depression is associated with poor neonatal outcomes in Malawi.

In this prospective study, conducted as part of a randomised controlled trial of lipid-based nutrient supplements (LNS) in rural Malawi, we set out to determine whether a high level of antenatal depressive symptoms was an independent predictor of shorter duration of pregnancy and reduced neonatal size after adjustment for likely confounders.

2 | METHOD

The International Lipid-Based Nutrient Supplements Project - DYAD - Malawi (iLiNS-DYAD-M) trial was a randomised controlled trial designed to study the impact on child growth and development of providing a lipid-based nutrient supplement to women during the perinatal period. The trial methodology is described in full elsewhere (Ashorn et al., 2015). The trial is registered at the clinical trial registry at the National Institute of Health (USA) under identifier NCT01239693 (https://clinicaltrials.gov/ct2/show/NCT01239693).

Key messages

- Studies from several low- and middle-income countries have shown that antenatal depression may be a risk factor for poor neonatal outcomes. However, those studies conducted in sub-Saharan Africa have not consistently demonstrated this association.

- In this study, in rural Malawi, we did not find antenatal depression to be associated with duration of pregnancy or measures of newborn size other than inversely with mid-upper arm circumference.

- The study was conducted within a randomised controlled trial of nutritional supplementation and there was a high proportion of missing data in some enrolment sites; this may have affected the validity of our findings.

The trial was conducted in Mangochi District, a predominantly rural area situated at the southern end of Lake Malawi. Key economic activities in the district are subsistence farming, fishing, and small-scale business. The two most widely spoken languages are Chichewa and Chiyao. Participants were recruited from the population of women attending antenatal clinics in the government-run Mangochi District Hospital, a part-private hospital (Malindi), and two government-run health centres (Lungwena and Namwera). Consenting participants were randomly allocated to one of three study arms; the intervention arm (lipid-based nutrient supplements, LNS) or one of two comparator arms (iron–folic acid [IFA] and multiple micronutrients [MMN]). Supplements were delivered fortnightly to each participant. The study participants attended antenatal and under-5 clinics according to the same schedule as all other Malawian pregnant women and infants and received all normal preventive services provided by the national health system. Participants were refunded for any medical costs incurred during the study period.

Inclusion criteria were: pregnancy of no more than 20 completed gestation weeks (confirmed by ultrasound), being resident in the defined catchment area and available during the study period, and giving informed consent (signed or thumb print). Exclusion criteria were: age less than 15 years, a chronic health condition requiring regular medical attention, asthma (formally diagnosed and on treatment), a severe illness requiring referral to hospital or emergency medical care, peanut allergy, history of any serious allergic reaction, significant pregnancy complications at enrolment visit, previous recruitment to the trial (during a previous pregnancy), or current enrolment in another clinical trial.

2.1 | Measurement of antenatal depression

Maternal antenatal depressive symptoms were measured in the second or third trimester using the Self Reporting Questionnaire (SRQ). The SRQ was designed by the World Health Organisation as a screen for common mental disorders that could be used internationally and particularly in LMIC (WHO, 1994). It consists of 20 questions with yes/no answers exploring symptoms of depression, anxiety, and somatic manifestations of distress experienced over the previous

4 weeks. Scores are obtained by totalling the number of yes answers, with higher scores indicating higher number of depressive symptoms (possible score range 0–20). The SRQ was validated in a local sample of women attending an antenatal clinic at one of the study sites (Stewart, Umar, Tomenson, & Creed, 2013). At a cut-off score of SRQ ≥ 8 (a cut-off commonly chosen in previous studies (Harpham et al., 2003), the SRQ Chichewa version had sensitivity 50.4%, specificity 88.4%, and positive predictive value of 41.2% for detection of Diagnostic and Statistical Manual of Mental Disorders 4th edition, major depressive episode. The test characteristics of the Chiyao translation of the SRQ were similar (unpublished data).

Data collectors were trained in the administration of the SRQ by a clinical psychologist fluent in English, Chichewa, and Chiyao (EU) and given written instructions for later reference. At interview, any participant answering "yes" to the item about suicidal thoughts was asked further questions regarding suicidal ideation. Any participant reporting active or persistent suicidal ideas was referred to local mental health care services (nurse-led outpatient clinics). During the study, no participants fulfilled this criterion.

2.2 | Other variables

We measured the following maternal variables at, or shortly following, enrolment: age, number of years of education completed, number of previous pregnancies, household ownership of a set of assets (combined into an index with a mean of zero and standard deviation of one, using principal components analysis [Vyas & Kumaranayake 2006]), household food insecurity access scale (a 9-item measure with higher scores indicating greater food insecurity), and season of enrolment (divided into quarters: Jan-Mar, Apr-Jun, Jul-Sept, and Oct-Dec). The Multidimensional Scale of Perceived Social Support (MSPSS) was administered at the same time as the SRQ. The MSPSS is a measure of the perception of the adequacy of support from others that was translated and locally validated; higher scores indicate greater perceived support (Stewart, Umar, Tomenson, & Creed, 2014b).

At enrolment, trained anthropometrists measured the participants' weight, height, and MUAC. All measurements were done in triplicate, using scales with a reading increment of 50 g (SECA 874 flat scale; Seca GmbH & Co.), stadiometers with a reading increment of 1 mm (Harpenden stadiometer; Holtain Limited), and plastic tapes with a reading increment of 1 mm (Shorrtape; Weigh and Measure LLC).

To estimate the duration of gestation, research nurses measured fetal abdominal circumference, biparietal diameter and femur length (all taken in duplicate, measured in millimetres) with ultrasound imagers with inbuilt Hadlock tables (EDAN DUS 3 Digital Ultrasonic Diagnostic Imaging System; EDAN Instruments Inc.). They measured participants' malaria parasitaemia in peripheral blood using rapid tests (Clearview Malaria Combo; British Biocell International Ltd.) and haemoglobin concentration using on-site cuvette readers (HemoCue AB; Angelholm). After providing pretest counselling, nurses employed in the health facility tested for HIV infection (whole-blood antibody rapid test; Alere Determine HIV-1/2; Alere Medical Co, Ltd.) in all participants except those who opted out or were already known to be HIV infected. If the result was positive, the test was checked using another rapid test (Uni-Gold HIV; Trinity Biotech plc).

2.3 | Outcome measures

All participating women were provided with mobile phones so that they could promptly inform the study team about deliveries. On notification of a delivery, a member of the study team visited the woman, interviewed her about delivery time and measured the infant's birth weight with an electronic infant weighing scale with a reading increment of 20 g (SECA 381 baby scale; Seca GmbH & Co.). One to 2 weeks postnatally, mother and infant were brought to the study clinic where study anthropometrists measured (in triplicate) the infant's length (recorded to the nearest 1 mm) with a length board (Harpenden Infantometer; Holtain Limited), weight with electronic scales as used at immediate postnatal visit, and head circumference and MUAC (recorded to the nearest 1 mm) with plastic tapes (Shorrtape; Weigh and Measure LLC). Further details of quality control are fully described elsewhere (Ashorn et al., 2015). Data collectors made tracing home visits if a participant did not come for the scheduled visit within 14 days of the appointment.

The duration of pregnancy was calculated by adding the time interval between enrolment and delivery to the ultrasound-determined gestational age at enrolment. Birth weight was used directly if measured within 48 hr of delivery or back-calculated from data collected between 6 and 13 days after delivery by using the WHO z-scores. If birth weight was first measured between 2 and 5 days after delivery (when weight loss is typical), it was calculated as a percentage of the actual measured weight (Cheung, 2013). Age- and sex-standardised anthropometric indices (length-for-age, and head circumference z-scores) were calculated by using the WHO Child Growth Standards (Fall et al., 2009).

2.4 | Statistical analysis

The mean of the first two readings of anthropometric measurements (that were done in triplicate) was used if those two readings did not differ by more than a prespecified tolerance limit. If the difference exceeded the limit, the third measurement was compared with Measurements 1 and 2, and the mean was calculated from the pair of measurements with the smallest difference. When only one or two repeated measurements were done, the mean of those was used.

The characteristics of the sample included in the analysis versus those excluded because of missing data were compared using the t-test for continuous data, and chi-squared or Fishers exact test for categorical data. Prevalence of antenatal depression (SRQ ≥ 8) was calculated. Mean (SD) neonatal outcomes (gestational age at delivery, birth weight, LAZ, head circumference z-score, and MUAC) in the two groups (maternal depressed vs not depressed) were compared in univariate (t-test) and multivariate (linear regression) analyses. Variables entered into the adjusted analyses were child sex, number of previous pregnancies, maternal MUAC and height, maternal HIV status, haemoglobin concentration and malaria test result at enrolment, gestational age at enrolment, marital status, season of enrolment (entered as 3 dummy variables), study site (entered as 3 dummy variables), trial intervention group (entered as 2 dummy variables), and language (Chichewa vs. Chiyao).

We conducted an exploratory analysis to investigate whether associations between antenatal depression and birth/neonatal

outcomes were moderated by other variables. Interaction terms were created for depression by child sex, maternal height, MUAC, malaria at enrolment, haemoglobin, years of education, site of enrolment, season of enrolment, trial intervention group, MSPSS score, food insecurity (HFIA) score, assets score, and number of previous pregnancies. These were added separately to the linear regression analysis for each of the outcomes. If the interaction term was significant ($p < 0.05$), then we examined the association of antenatal depression with the outcome stratified by the moderator.

3 | RESULTS

3.1 | Participant flow and sample characteristics

Participant flow is shown in Figure 1. Between February 2011 and August 2012, 9,304 women were approached at the antenatal clinics of the four study sites. Of these, 4,449 were excluded and 3,470 were not interested in participating. 1,391/9,304 (15.0%) were enrolled to the trial. The enrolled participants and those who refused or were not eligible were similar in mean age, number of completed school years, marital status, home building material, and ownership of phones in the household. See Ashorn et al. (2015).

Out of 1,391 enrolled, 1,006 (72.3%) women completed the SRQ and gave birth to a singleton infant whose weight was measured within 2 weeks of birth. All analyses were restricted to this group. A comparison of those with and without data is shown in Table 1. Compared with those included in the analysis ($n = 1006$), those with

missing data ($n = 385$) were younger, were later in gestation at enrolment, had higher asset score, had had fewer previous pregnancies, and were more likely to have a positive malaria test. They had higher antenatal SRQ scores, lower haemoglobin and were more likely to be enrolled in Q3/Q4 and from a site other than Malindi.

For the 1,006 participants the following neonatal outcomes were recorded: LAZ in 911 (90.6%), MUAC in 919 (91.4%) and head circumference in 913 (90.8%).

3.2 | Prevalence of depression and infant outcomes

143/1,006 (14.2%) of participating women scored SRQ ≥ 8 indicating likely antenatal depression. For the total sample, mean (SD) values for birth outcomes were birth weight 2,977 (441g), gestational age 39.6 (1.9weeks), neonatal LAZ -0.97 (1.10), head-circumference Z-score − 0.13 (1.06), and MUAC 10.6 (0.9) cm. The incidence of low birth weight (<2,500 g) was 12.3%, low newborn length (z-score < −2.0) was 15.1%, and preterm delivery (<37 weeks gestation at birth) was 6.6%.

3.3 | Associations between antenatal depression and birth outcomes

Table 2 shows associations between antenatal depression and birth outcomes in adjusted analyses. Antenatal depression was not associated with birth weight, gestational age, neonatal LAZ, or head-circumference Z-score but was inversely associated with MUAC (mean difference − 0.2 cm [95%CI −0.4 to 0.0, $p = 0.021$]).

3.4 | Exploratory analysis of factors that may moderate the associations between antenatal depression and birth/newborn outcomes

In exploratory analyses of moderation, for birth weight, there were interactions between antenatal depression and number of previous pregnancies (dichotomised at median; $p = 0.039$), number of years of education (dichotomised at median; $p = 0.017$), and trial intervention group (LNS-vs.-comparator arms dummy variable $p = 0.044$). Table 3 shows associations between antenatal depression and birth weight in adjusted analyses stratified by these variables. For newborn LAZ, there were interactions between antenatal depression and season of enrolment (in quarters; Q1-vs.-Q2,3,4 dummy variable [p = 0.021]; Q3-vs-Q1,2,4 dummy variable [p = 0.013]) and site of enrolment (Malindi-vs.-other sites dummy variable, [p = 0.037]). In Malindi, adjusted mean difference (95% CI) in newborn LAZ between infants born to mothers with antenatal depression versus those without depression was −0.48 (−0.97 to −0.09), $p = 0.016$; in other sites it was 0.075 (−0.162 to 0.313), $p = 0.535$.

4 | DISCUSSION

In this prospective study, conducted in a predominantly rural area in a low-income country in sub-Saharan Africa, antenatal depression was not associated with duration of pregnancy, birthweight, newborn
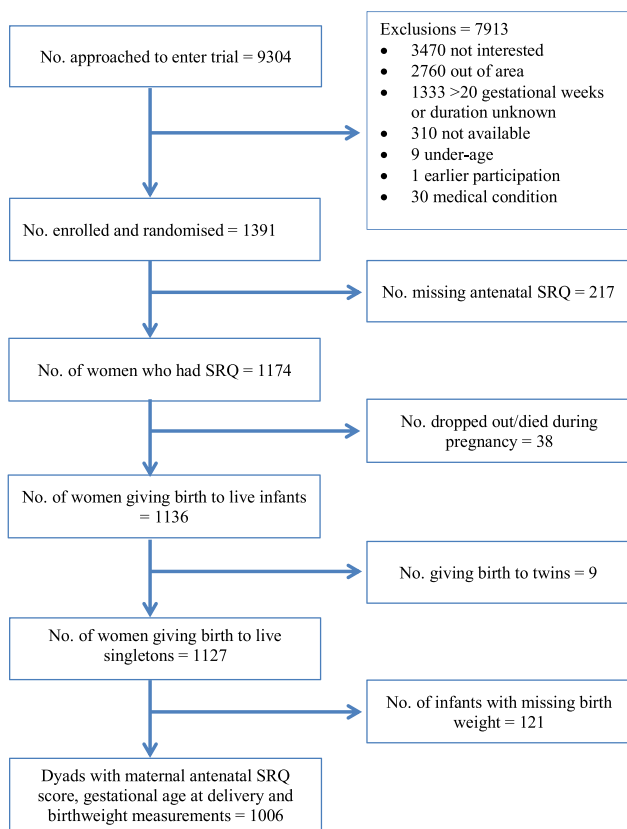

FIGURE 1 Participant flow

TABLE 1 Characteristics of participants enrolled to the trial (n = 1,391) who completed the SRQ and gave birth to a singleton infant whose gestational age and birth weight were recorded (n = 1,006), versus those missing these data (n = 385)

		Included n = 1006 (72.3%)	Missing n = 385 (27.7%)	P-value [a]
Maternal age (years; mean [SD])		25.3 (6.1)	24.0 (6.3)	<0.005
Maternal education (completed years; mean [SD])		4.1 (3.4)	3.8 (3.6)	0.130
Household asset score (mean [SD])		−0.1 (1.7)	0.2 (2.0)	0.008
Gestational age at enrolment (weeks; mean [SD])		168 (2.2)	17.0 (2.0)	0.043
Number of previous pregnancies (mean [SD])		2.2 (1.7)	1.8 (1.8)	<0.005
Height, cm (mean [SD])		156.2 (5.7)	155.7 (5.5)	0.141
Weight, kg (mean [SD])		54.0 (7.8)	54.4 (8.5)	0.354
MUAC, cm (mean [SD])		26.3 (2.6)	26.4 (2.8)	0.666
BMI, kg/m2 (mean [SD])		22.1 (2.8)	22.4 (2.9)	0.088
Blood haemoglobin concentration, g/L (mean [SD])		112.5 (15.9)	108.9 (17.1)	<0.005
MSPSS score (mean [SD])		37.1 (8.5)	37.1 (8.2)	0.979
Positive HIV test (%)		13.9	13.3	0.802
Positive malaria test (RDT; %)		21.6	27.3	0.024
SRQ completed in Chichewa (%)		55.9	58.4	0.497
Trial arm (%)	IFA	33.8	31.9	0.789
	MMN	33.1	34.5	
	LNS	33.1	33.5	
Season of enrolment (%)	Jan-Mar	24.9	19.5	<0.005
	Apr-June	30.2	21.8	
	July-Sept	27.0	32.5	
	Oct-Dec	17.9	26.2	
Site of enrolment (%)	Lungwena	35.7	40.5	<0.005
	Malindi	22.0	5.5	
	Namwera	15.9	15.8	
	Mangochi	26.4	38.2	

Note. BMI: body mass index; IFA: iron–folic acid; LNS: lipid-based nutrient supplements; MMN: multiple micronutrients; MUAC: mid-upper arm circumference; RDT: rapid diagnostic test; SD: standard deviation; SRQ: Self Reporting Questionnaire

[a]Comparison used the t-test for continuous data, and chi-squared or Fisher's exact test for categorical data.

TABLE 2 Adjusted associations between antenatal depression and birth/newborn outcomes

Outcome variable (number of women without depression, number of women with depression)	Women without depression Mean (SD)	Women with depression Mean (SD)	Adjusted group comparison[a]	
			Diff. In means (95% CI)	P-value
Birth weight, g (n = 863,143)	2,990 (440)	2,920 (450)	−40 (−120 to 30)	0.259
Duration of pregnancy, weeks (n = 863,143)	39.6 (1.9)	39.4 (1.9)	0.2 (−0.2 to 0.5)	0.335
Length for age z-score (n = 783,128)	−0.96 (1.10)	−1.04 (1.09)	−0.09 (−0.29 to 0.12)	0.416
Head circumference z-score (n = 786, 127)	−0.13 (1.06)	−0.13 (1.07)	0.03 (−0.18 to 0.23)	0.777
Mid-upper arm circumference, cm (n = 790,129)	10.6 (0.9)	10.4 (0.9)	−0.2 (−0.4 to 0.0)	0.021

Note. SD: standard deviation.

[a]Adjusted for child sex; number of previous pregnancies; maternal MUAC and height; maternal HIV status, haemoglobin concentration and malaria test result at enrolment; gestational age at enrolment; marital status; season of enrolment; enrolment site; trial intervention group; and language.

length, or head circumference. This study adds to those studies from the sub-Saharan African literature that have not found antenatal depression to be a risk factor for prematurity or low birthweight. There was an isolated finding of an inverse association between antenatal depression and newborn MUAC, with a mean difference of 0.2 cm, the significance of which is unclear. In addition, several limitations of the study may have affected the validity of our findings.

Strengths of the study included the prospective design, the dating of gestational age at recruitment by USS, and quality-controlled infant anthropometry conducted by trained data collectors. We measured a range of potential confounders of any association

between antenatal depression and birth outcomes and adjusted for these in multivariate analyses.

On the other hand, there were a number of limitations to the study. We conducted the study within a trial of nutritional supplementation that was not specifically designed to answer the study question, and no a priori sample size calculation was conducted. All the participants received some form of nutritional supplement (iron/folate, multi-micronutrient tablets, or a lipid-based nutritional supplement), which could all have had a beneficial effect on maternal health including reduced levels of antenatal depression and anxiety. Maternal dietary supplements could also have had a beneficial effect on fetal

TABLE 3 Associations between antenatal depression and infant birth weight stratified by number of previous pregnancies, number of years of education and trial intervention group

Stratified by:	Strata (number of women without depression, number of women with depression)	Mean birthweight (SD)		Adjusted group comparison[a]	
		Women without depression	Women with depression	Diff. In means (95% CI)	P-value
Number of previous pregnancies	0–2 previous pregnancies (n = 508, 78)	2,940 (440)	2,920 (480)	40 (−70 to 150)	0.490
	3 or more previous pregnancies (n = 354, 65)	3,060 (420)	2,920 (410)	−120 (−240 to −10)	0.035
No. of years of education	0–3 years of education (n = 420, 58)	3,000 (410)	2,840 (390)	−140 (−260 to −30)	0.011
	4 or more years of education (n = 439, 84)	2,980 (460)	2,980 (490)	40 (−70 to 150)	0.446
Trial intervention group	Iron/folate (IFA; n = 290, 50)	2,970 (410)	2,900 (470)	−60 (−190 to 70)	0.389
	Multi-micronutrients (MMN; n = 284, 49)	2,960 (460)	2,970 (450)	40 (−100 to 180)	0.554
	Lipid-based nutrient supplements (LNS; n = 289, 44)	3,030 (450)	2,890 (430)	−120 (−260 to 30)	0.109

Note. SD: standard deviation. Number of previous pregnancies analysis also adjusted for number of years of education and trial intervention group. Number of years of education analysis also adjusted for number of previous pregnancies and trial intervention group. Trial arm analysis also adjusted for number of previous pregnancies and number of years of education

[a]All analyses adjusted for child sex; maternal MUAC and height; maternal HIV status, haemoglobin concentration and malaria test result at enrolment; gestational age at enrolment; marital status; season of enrolment; enrolment site; and language.

growth, which may have swamped any impact of symptoms of depression and anxiety. It should be noted, however, that the LNS intervention was not effective at significantly improving neonatal size (Ashorn et al., 2015), or maternal depression at 6 months postpartum (Stewart et al., 2016). The high refusal rate for inclusion in the trial and the missing SRQ and birth outcome measurements may have led to a biased sample not representative of the population as a whole. Of note, in exploratory analysis, we found that in the site with a high proportion of complete data (91.3%), depression was inversely associated with LAZ, whereas no such association was found in the remaining sites that had less complete data (68.3%). However, this was an exploratory analysis only and the sites also differed on a number of other variables.

Although we used an adapted version of the SRQ that had been locally validated for use in the antenatal period (Stewart et al., 2013), the SRQ is only a screening tool and does not provide a formal diagnosis of depressive disorder. At the chosen cut-off, the SRQ had high specificity but low sensitivity so there will have been some misclassification of cases, although this non-differential misclassification is more likely to have led to Type 2 rather than Type 1 error. Screening tools such as the SRQ may be more likely to detect self-limiting distress states that may not have the same implications for fetal development as major depressive disorder. Of note, most previous studies investigating antenatal depression and birth outcomes in sub-Saharan Africa have also used screening tools rather than diagnostic interviews.

We measured and adjusted for a wide range of potential confounders; however, the possibility of residual confounding remains. The heterogeneity in the results of studies investigating antenatal depression and birth outcomes in sub-Saharan Africa may be accounted for, in part, by differences in the completeness of adjustment for confounders. Bindt et al. (2013) argue that some studies did not adjust for the effect of physical morbidity during pregnancy that might be expected to confound the association between antenatal symptoms of depression and anxiety and birth outcomes. To overcome this, they restricted their sample to women with low-risk pregnancies and found no association between antenatal depression and birth outcomes.

In this study, we used a range of measures of birth size (i.e., weight, length, MUAC, and head circumference) and only found a consistent association with MUAC. Other studies have also shown associations

with only selected outcome measures, for example, of a range of outcomes, Brittain et al. (2015) only found an association with head circumference. Our use of multiple outcome measures will have increased the risk of positive findings occurring by chance, but different anthropometric measures can reflect different nutritional states resulting from differing intrauterine nutritional deficits and their timings.

Finally, a possible cause of heterogeneity in the results of studies of antenatal depression and birth outcomes in sub-Saharan Africa is that the study sites differed in the prevalence of other risk factors for poor birth outcomes. The effects of nutritional deficiencies, infectious disease (including HIV), and restricted access to reproductive health services may swamp any effect of antenatal depression and/or influence the functional impact that being depressed has on the ease of maintaining health and nutrition during pregnancy. Sociocultural factors that influence reproductive and mental health may also differ between settings. In our exploratory analysis of moderating factors, we found that antenatal depression was associated with lower birth weight in women with three or more previous pregnancies and those with less than 4 years of education. These analyses were exploratory and we did not adjust the significance level for the multiple comparisons made, so it is possible that the findings occurred by chance.

5 | CONCLUSION

In this study in rural Malawi, we did not find antenatal depression to be associated with duration of pregnancy or measures of newborn size other than inversely with MUAC. Given its limitations, the study does not resolve the conflicting findings regarding the association between antenatal psychiatric morbidity and prematurity and/or low birth weight in sub-Saharan Africa. It has, however, highlighted the role that methodological differences and limitations (that are often encountered when conducting research in low resource settings) may have in explaining the heterogeneous findings. Given the high prevalence of both poor birth outcomes and perinatal mental health problems in Malawi and other sub-Saharan African countries, further community based cohort studies are warranted to further understanding of this important public health issue.

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CONFLICTS OF INTEREST

CONTRIBUTIONS

The authors' responsibilities were as follows: KM, PA, KD, UA, EU, RS, FC, and AR designed the research; KM, PA, KD, UA, RS, EU, and EP conducted field research; RS and BT analysed data; RS wrote the manuscript, with critical input and comments from all other authors; and RS had primary responsibility for final content. All authors read and approved the final manuscript. The findings and conclusions contained within the article are those of the authors and do not necessarily reflect positions or policies of the Bill & Melinda Gates Foundation, USAID, the US government, or the other funders.

ORCID

Robert C. Stewart http://orcid.org/0000-0002-0413-1388
Elizabeth L. Prado http://orcid.org/0000-0002-5388-081X

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