HHS Public Access

Author manuscript

Paediatr Perinat Epidemiol. Author manuscript; available in PMC 2024 August 01.

Published in final edited form as:

Paediatr Perinat Epidemiol. 2023 August ; 37(6): 489–504. doi:10.1111/ppe.12978.

Risks of adverse perinatal outcomes in relation to maternal depressive symptoms: A prospective cohort study in Kenya

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Abstract

Background: Evidence gaps remain regarding the influence of prenatal psychosocial factors on adverse pregnancy outcomes.

Objective: To evaluate relationships between psychosocial factors and adverse perinatal outcomes among Kenyan women.

Methods: We analysed data from a prospective cohort study enrolling HIV-negative women in pregnancy (NCT03070600) in 20 antenatal clinics in Western Kenya. Study nurses assessed depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CESD-10), social support using the Medical Outcomes Survey scale (MOS-SSS), intimate partner violence (IPV) with the Hurt, Insult, Threaten, Scream scale (HITS), and pregnancy outcomes at 6 weeks postpartum. Cox proportional hazards models were used to evaluate relationships between depressive symptoms (moderate-to-severe [MSD, CESD-10 ≥10] and mild-to-severe [Mild-SD, CESD-10 ≥5]), low social support (MOS-SSS <72), and IPV (HITS ≥10) with adverse perinatal outcomes of pregnancy loss, stillbirth, preterm birth (PTB), small for gestational age, and neonatal mortality. We also estimated the population attributable risk.

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Results: Among 4153 women, 23.9% (n = 994) had MSD, 54.7% (n = 2273) mild-SD, 37.3% (n = 1550) low social support, and 7.8% (n = 323) experienced IPV. Pregnancy loss was 5-fold higher among women with MSD (adjusted hazard ratio [HR] 5.04, 95% confidence interval [CI] 2.44, 10.42); 37.4% of losses were attributable to MSD. Mild-SD was associated with PTB (HR 1.39, 95% CI 1.03, 1.87). Stillbirth risk more than doubled among women reporting low social support (HR 2.37, 95% CI 1.14, 4.94).

Conclusions: Adverse perinatal outcomes were common and associated with prenatal depressive symptoms and low social support in this large cohort of Kenyan mother-infant pairs.

Keywords

Depression; preterm birth; pregnancy loss; perinatal; Kenya; social support

Background

Over 10% of pregnant women experience depression; the burden is higher in low- and middle-income countries (LMIC), particularly in sub-Saharan Africa (SSA) where a quarter of women are depressed during or after pregnancy.[1] Changes in reproductive hormones during gestation and innate genetic factors are compounded by stressors, such as inadequate social support and violence by an intimate partner, to impact mental distress during this period.[2–4] Maternal mental distress during pregnancy influences a range of adverse maternal and child health outcomes.[2] A meta-analysis utilising data from high-income countries (HICs) and LMICs (India and Pakistan) found an association between depression during pregnancy with preterm birth (PTB) and intrauterine growth restriction (which was more than doubled among women with antenatal depression in India and Pakistan).[5] Subsequent meta-analyses confirmed these relationships,[6,7] additionally identifying maternal depressive symptoms as a predictor of small for gestational age (SGA)[7,8] and infant death.[9]

Adverse perinatal outcomes including pregnancy loss, stillbirth, PTB, and SGA occur more frequently in LMICs and contribute to suboptimal neonatal survival.[10,11] However, relationships between psychosocial factors and adverse birth outcomes have been insufficiently evaluated in LMICs, particularly in sub-Saharan Africa where 43% of global neonatal deaths occur.[12] The high prevalence of maternal depression in sub-Saharan Africa (25%),[1,13] combined with slower gains in neonatal health, make understanding the potential linkages between maternal mental health and perinatal outcomes vital in this region. Routine maternal child health (MCH) services are well-attended in sub-Saharan Africa (>95%),[14] offering a high-impact setting for preventing and treating depression in pregnancy for dyadic benefit.[15]

A recent meta-analysis identified only 3 studies in sub-Saharan Africa (Ethiopia,[16] Ghana and Cote d'Ivoire,[17] and Kenya[18]) evaluating antenatal depression and birth outcomes.[19] Pooled results (n=1511 participants) indicated an increased risk of PTB with maternal depression in pregnancy.[19] These studies had relatively small sample sizes and evaluated few birth outcomes, limiting their scope.

We evaluated relationships between psychosocial factors during pregnancy (depression, low social support, intimate partner violence) and adverse perinatal outcomes of pregnancy loss, stillbirth, PTB, SGA, and neonatal mortality among perinatal women in Kenya.

Methods

Cohort selection

This analysis was nested in the PrEP implementation for Mothers in Antenatal Care study (PrIMA) which was a cluster randomized trial comparing two models for pre-exposure prophylaxis implementation among pregnant women in Western Kenya (NCT03070600).[20] Women attending antenatal care (ANC) between Jan 15, 2018, and July 31, 2019 in 20 MCH clinics were screened and enrolled. Eligible women were pregnant, HIV-uninfected, ≥15 years old and were able to provide consent.

Study nurses collected information about demographics, pregnancy history, partner characteristics, and psychosocial factors through questionnaires administered in Kiswahili, Dholuo, or English languages using REDCap surveys.

Exposures

Experience of depressive symptoms was collected during pregnancy (enrolment visit) using the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), which has been adapted and validated among perinatal and general populations in sub-Saharan Africa.[21,22] Participants rated each of 10 items from 0–3 based on past-week frequency (absolute score range: 0–30). Moderate-to-severe depressive symptoms (MSD) were defined as a validated cut-point of 10 or greater (CESD-10 score ≥ 10).[23] Mild-to-severe depressive symptoms (Mild-SD) were defined as a cut-point of 5 or greater (CESD-10 score ≥ 5) to identify differences between women with “any” versus “no” depressive symptoms. The 18-item Medical Outcomes Study Social Support Survey (MOS-SSS; range: 18–90), which has been previously used among African women, was used to assess social support.[24–26] This variable was dichotomized with a cut-point of <72 denoting low social support (LSS). Scores <72 indicate that women reported not having access “most of the time” to all forms of social support. The 4-item Hurt, Insult, Threaten, Scream Scale, which has been adapted for SSA populations, assessed intimate partner violence (IPV) based on a cut-point of 10 or greater (range: 4–20).[27,28]

Outcomes

Study nurses determined gestational age at enrolment by ascertainment of last menstrual period (LMP) or fundal height (if assessed). Data on birth outcomes were collected at the 6-week postpartum visit and abstracted from medical records. Information was collected about pregnancy loss (<20 weeks’ gestation), stillbirth (fetal death ≥20 weeks’ gestation), gestational age at delivery (weeks), and birthweight (kg). Late stillbirth was defined as fetal death ≥28 weeks’ gestation. PTB was defined as delivery <37 weeks’ gestation. Infant SGA was defined using the World Health Organization (WHO) Fetal Growth Standards to identify infants in the lowest 10th percentile for birthweight for respective gestational age week and

sex.[29] Verbal autopsies were performed by a study nurse with the mother or caregiver for pregnancy loss, stillbirth, or neonatal death (up to 28 days post-delivery).

Covariates

We hypothesized that multiple characteristics confound the relationships of interest. Household crowding,[30] defined as a ratio of people per room greater than the median (>2 people/room), was used as a marker of socioeconomic status. A validated risk score, developed to predict HIV acquisition among perinatal women in SSA, was used to define high HIV risk.[31] Self-perceived risk for HIV acquisition was measured by asking participants "What is your gut feeling about how likely you are to get infected with HIV?", with five Likert response options. We defined high self-perceived HIV risk as "somewhat likely", "very likely", or "extremely likely" compared to "very unlikely" or "extremely unlikely".[32]

Data were collected at study visits monthly during pregnancy and at 6 weeks, 14 weeks, 6 months, and 9 months postpartum.

Statistical analysis

Participants were included in the analysis if they had data on gestational age at pregnancy outcome (values >44 weeks were considered missing), did not acquire HIV, had a singleton birth, and had depressive symptom information during pregnancy. Incidence of pregnancy loss and stillbirth were evaluated among those enrolled <20 weeks' gestation to alleviate selection bias. Similarly, late stillbirth was assessed among those enrolled at <28 weeks, and PTB incidence among participants enrolled at <37 weeks gestation. The SGA analysis was limited to live births with infant birthweight data. Neonatal mortality was evaluated among all live births.

Two different definitions were used for "any adverse perinatal outcome" among different sub-groups. First, we estimated the risks of pregnancy loss, stillbirth, PTB, or neonatal death among all pregnancies ($n = 4153$) to evaluate the most inclusive number of pregnancies. Second, we separately assessed the occurrence of pregnancy loss, stillbirth, PTB, SGA, or neonatal death in a more restricted group of pregnancies enrolled <20 weeks gestation with birthweight data for live births ($n = 625$) (Figure 1). By evaluating the most- and least-inclusive groups, we offer a reasonable range of risk for any adverse perinatal outcome.

Cox proportional hazards models were used to assess relationships between psychosocial factors of depressive symptom score, mild-SD, MSD, LSS, and IPV with time to pregnancy loss, stillbirth, PTB, SGA, and neonatal death, clustered by the facility. When case counts were <5, regression analyses were not performed. Time from enrolment gestational age to gestational age at the adverse perinatal outcome was used for time-at-risk for cases, except for the neonatal death analyses which used the time from birth. Time-at-risk for non-cases was gestational age at the end of the at-risk period or gestational age at pregnancy end, whichever came first. Gestational age at enrolment served as the start time to account for left truncation.[33] Start time was set at 20 weeks gestation for the stillbirth analysis and 28 weeks gestation for the late stillbirth analysis based on the at-risk period. In the "any adverse

perinatal outcome" analyses, survival time to neonatal death was gestational age plus time from birth to death (cases) and gestational age plus 28 days postpartum (non-cases).

Variables hypothesized as confounders were included in multivariable models, per our conceptual model (Table 3, Figure 2).[2,13,34,35] In each model, the two psychosocial factors that were not being evaluated as the main exposure (MSD, LSS, and/or IPV) were included. Multivariable analyses were performed for relationships between psychosocial factors and adverse perinatal outcomes identified in univariable analyses. Population attributable risk percentages (PAR%) were estimated for each psychosocial risk factor; we did not estimate PAR for protective or continuous variables.

Missing data

For participants missing data in <5 out of 10 depressive symptom scale items (11.8%, 492/4185, Appendix 1), item-level scores were imputed as the median score across the participant's existing items (person-median imputation).[36] Person-median imputation has advantages over other scale imputation methods; it does not artificially reduce variability and has been shown to produce similar estimates to multiple imputations.[36] Among those missing <8 out of 16 social support scale items (2.6%, 108/4185, Appendix 2), we imputed item-level scores using person-median imputation. Scores were not analysed for participants missing over half of the scale items. Analyses were conducted using Stata 15 by StataCorp, LLC in College Station, Texas.

Ethics approval

The study protocol was approved by the Kenyatta National Hospital-University of Nairobi Ethics Research Committee and the University of Washington Human Subjects Review Committee. All participants provided written informed consent.

Results

Overall, 93.4% (n=4153) of the 4447 pregnant women enrolled in the parent study met the inclusion criteria for this analysis (Figure 1). The median maternal age was 24 years (Interquartile range [IQR]: 21–28) and the median educational attainment 10 years (Table 1). The median gestational age at enrolment was 24 weeks (IQR: 20–30), predominantly determined by LMP (fundal height was used for 2.2% [90/4153] of participants). Most participants were married or living with a partner (84.8%) and were multiparous (74.3%). Half of the women (50.5%) attended their first ANC visit during the second trimester, and most (88.0%) attended at least 4 ANC visits during pregnancy.

About a quarter (23.9%) of women reported MSD during pregnancy (median CESD-10 score: 5, IQR: 3–9). Over 50% of women reported mild SD. Over a third (37.3%) had low social support, and 7.8% reported IPV within two weeks prior to enrolment.

Pregnancy loss

Pregnancy loss was experienced by 1.5% (15/1005) of women enrolled <20 weeks gestation (Table 2), over 111.3 fetus-years of follow-up until 20 weeks gestation (incidence rate [IR]

13.5 pregnancy losses per 100 fetus-years) (Appendix 3). The median gestational age at pregnancy loss was 15.0 weeks (IQR 12.1, 17.7). Women reporting MSD were over twice as likely to experience pregnancy loss compared to those without MSD (Appendix 4). This relationship became stronger after confounding adjustment (Table 3). A ten-unit increase in CESD-10 score was associated with at least 70% higher risk of pregnancy loss (Table 3, Figure 3).

Stillbirth

Overall, 3.2% (32/990) of women enrolled <20 weeks gestation experienced stillbirth (Table 2) over 337.9 fetus-years of follow-up starting at 20 weeks gestation (IR: 9.5 stillbirths per 100 fetus-years) (Appendix 3). Stillbirths occurred at a median gestational age of 35.4 weeks (IQR: 25.6, 38.3). Women reporting low social support (LSS) had over double the risk of stillbirth (Table 3, Appendix 5). Late stillbirth occurred in 1.8% (47/2563) of women enrolled <28 weeks gestation over 542.1 fetus-years (IR: 8.7 per 100 fetus-years).

Preterm birth

PTB occurred among 19.1% (780/4084) of mother-infant pairs enrolled <37 weeks gestation (Table 2) over 1099.3 fetus-years of follow-up (IR 71.0 PTB per 100 fetus-years) and at median gestational age of 36.0 weeks (IQR 35.3, 36.0). Mild-SD was associated with increased risk for PTB (Table 3, Figure 3). There was a pattern for higher CESD-10 scores associated with higher risk of PTB, yet this estimate became only marginally more precise after adjustment (Table 3, Figure 3). IPV in pregnancy was inversely related to risk of PTB (Table 3, Appendix 6), yet this relationship did not persist after confounding adjustment.

Small for gestational age

Overall, 64.7% (2627/4055) of live births had birthweight data and were included in the SGA analyses. SGA occurred among 10% (263/2627) mother-infant pairs (Table 2) over 682.9 fetus-years of follow-up (IR 38.5 SGA births per 100 fetus-years). There was no evidence of relationships between psychosocial factors and SGA.

Neonatal death

Among 4,055 live births, 63 deaths occurred in the first 28 days postpartum (1.6%), for a cumulative mortality of 16 deaths per 1000 live births (Table 2). Neonatal deaths took place over 306.8 fetus-years (IR 20.5 cases per 100 fetus-years). The median age at neonatal death was 1 day (IQR 0, 7.5). There was no evidence of relationships between psychosocial factors and neonatal mortality.

Any adverse perinatal outcome

Over a quarter (27.3%, 1132/4153) of pregnancies resulted in at least one adverse perinatal outcome (Table 2), for an incidence rate of 63.8 per 100 fetus-years). Any adverse perinatal outcome was more likely with maternal mild-SD, and a 10-unit higher CESD-10 score (Table 3, Figure 3). In the subset of mother-infant pairs enrolled <20 weeks gestation with birthweight data, 32.2% (201/625) had any adverse perinatal outcome for an incidence

rate of 64.7 per 100 fetus-years. Risk of any adverse outcomes was higher among women reporting low social support than those with higher social support (Table 3, Appendix 5).

Population-level impact

Based on population attributable risk proportions, over a third of pregnancy losses were attributable to MSD (Table 3), and a third of stillbirth cases were attributable to low social support. About 17.3% of PTB and 17.6% of any adverse perinatal outcome cases were attributable to having mild SD. Among those enrolled <20 weeks gestation and with birthweight data, 14% of any adverse perinatal outcome cases were attributable to low social support.

Prior to imputing CESD-10 and MOS-SSS items for partial scores, 23.9% of women had MSD and 37.3% had low social support. Those with complete vs. partial CESD-10 data were not meaningfully different (Appendix 7).

Comment

Principal findings—In this large prospective analysis among mother-infant pairs followed from pregnancy through 28 days postpartum, mild- or moderate-to-severe depressive symptoms during pregnancy were common and associated with increased pregnancy loss and PTB. The risk of stillbirth was elevated among women with low levels of social support. Our results extend the global evidence base for the relationships between maternal mental distress and adverse perinatal outcomes, adding novel results on psychosocial factors and birth outcomes to the dearth of data on this topic from the African region. To our knowledge, this is the largest study to evaluate relationships between maternal mental health and >3 birth outcomes among African mother-infant pairs.[19] Our findings that maternal depressive symptoms are associated with increased risk of pregnancy loss and PTB, and that lack of social support was associated with increased risk of stillbirth, highlight the potential need for integrated mental health services within MCH settings.

Strengths of the study—Prospective data from a large cohort (>4000) of pregnant women enabled rigorous evaluation of relationships between multiple psychosocial factors and adverse birth outcomes.

Limitations of the data—Selection bias, which disproportionately excluded earlier pregnancy losses and stillbirths, is evident in the cohort since only 24% (1005/4153) of pregnancies were enrolled prior to 20 weeks' gestation and pregnancy losses were rare (1.5%) compared to the estimated 10–20% of pregnancies that result in spontaneous abortion.[37,38] This selection bias may be responsible for the lack of stronger associations with more specific exposure measurement – we had expected to see more of a "dose-response" relationship with higher depressive symptoms (MSD) and adverse pregnancy outcomes compared to Mild-SD.

Further, we found a counterintuitive trend of lower PTB among women with IPV in pregnancy in contrast to findings from other East African settings.[39,40] This finding was not retained in multivariable analyses and therefore may have been due to confounding. We also

suspect that selection bias played a role in the counterintuitive relationship between IPV and adverse perinatal outcomes, wherein those experiencing both IPV and adverse pregnancy outcomes were disproportionately underrepresented in our sample.

For particularly rare perinatal outcomes and infrequent exposures, our study had modest power to detect associations. We predominantly estimated gestational age as the time between last menstrual period (LMP) and pregnancy end. LMP tends to overestimate gestational age which may have biased our risk estimates.[41]

We calculated population attributable risk percentages to estimate the proportion of adverse perinatal outcome cases in the population that were potentially attributable to the exposure of interest. PAR% are not additive across risk exposures and, therefore, should be interpreted with that limitation in mind.[42]

Interpretation

We found about a quarter (24%) of women were depressed during pregnancy, which closely aligned with results from a recent meta-analysis of antenatal depression in Africa (26%).[1] Low social support (37%) and IPV (8%) during pregnancy were also similar to estimates from other studies among pregnant women in SSA (23%,[43] 13.5%,[44] respectively). Half of women enrolled in this study initiated ANC during the second trimester, similar to national findings for Kenya (median gestational month of initial ANC: 5.4).[14]

Pregnancy loss incidence is not routinely evaluated in sub-Saharan Africa. Our finding of 15 pregnancy losses per 1000 pregnancies was about double the estimate from a Kenyan study using the Nairobi Urban Health and Demographic Surveillance System,[45] likely due to underreporting and ascertainment challenges within the health system. Our estimate of pregnancy loss aligns with estimates from settings with more advanced monitoring systems for this outcome,[46] yet is substantially below the global estimate that 10–20% of pregnancies result in spontaneous abortion.[37,38] Our estimate of stillbirth risk was also higher than regional estimates.[11] In our study, PTB occurred in 19% of births, somewhat higher than the 12% estimated for SSA overall.[47,48] Our finding that 16 neonatal deaths occur per 1000 live births was slightly lower than a 2015 estimate of 22 deaths per 1000 live births.[49]

We used gestational age estimated by LMP, which has been previously shown to overestimate duration of gestation, yet a recent study in South Africa found LMP provided a reliable and valid estimate of gestational age compared to ultrasound (within 0.2 days).[50] We used person-median imputation for CESD-10 and MOS-SSS items among participants missing fewer than half of scale items (12% and 2% of participants, respectively). In simulation studies, this method performs indistinguishably from multiple imputation of item-level psychosocial scale missingness and is recommended to optimize analytic power.[36]

In this large cohort of mother-infant pairs, maternal depressive symptoms in pregnancy were associated with multiple adverse birth outcomes. To date, few studies have evaluated associations between depression during pregnancy and pregnancy loss,[51,52] likely due to challenges with statistical power and timing of measurement. The PrIMA study enrolled over 1000 pregnant women before 20 weeks gestation who were evaluated for pregnancy

loss, among whom pregnancy loss risk was substantially increased with MSD. We found nearly 40% of pregnancy losses could be potentially prevented if MSD in pregnancy was eliminated in this population. Pregnancy loss risk increased with higher depressive symptom scores, strengthening inference and suggesting a potential “dose-response” relationship.

As in similar studies, depressive symptoms were not associated with stillbirth in our study. However, stillbirth incidence was double among women reporting low social support. We are not aware of other studies identifying this relationship, though a study in Ethiopia found an association between low social support and low birthweight.[16] Social support is modifiable with low-intensity, evidence-based psychological interventions integrated in routine MCH care.[53]

There is strong global evidence for the influence of depression during pregnancy on PTB,[5–7] including one study from Kenya.[18] A study in Ghana also found a potential relationship, however the effect size was not substantial and the estimate had low precision.[17] We found an association between mild-SD and PTB. There is need for further study of depression and PTB in SSA where >25% of the world’s PTB occur.[47]

Maternal depressive symptoms may influence pregnancy loss and PTB through physiologic mechanisms like heightened stress hormone levels, and through behavioural responses to depressive symptoms such as inadequate nutrition or insufficient sleep, which can affect foetal growth and length of gestation.[54–56] Depressive symptoms may also adversely influence one’s health-seeking behaviour, potentially limiting opportunities for monitoring and early intervention.[54]

Psychosocial interventions in individual- or group-based formats, led by trained or lay counsellors, are effective in preventing and treating perinatal depression.[57–59] Approaches like cognitive behaviour therapy and interpersonal psychotherapy utilize multiple sessions with a counsellor to reduce negative thought processes, improve interpersonal relationships, promote problem-solving, and reduce stress – ultimately disrupting the bio-physiological underpinnings of perinatal depression.[57–59] Psychosocial interventions are increasingly evaluated in SSA settings, particularly those utilizing task-shifted models delivered by peer and lay counsellors integrated into well-attended public sector health settings (e.g., MCH or HIV care).[60–62] These interventions show promise in SSA,[60–62] yet further efforts are needed to rigorously identify successful approaches and expand access through integrated care models to support African perinatal women.

Conclusions

This study contributes new evidence for the relationships between maternal mental distress and birth outcomes contributing to high pregnancy loss and neonatal mortality in LMICs. Among this large cohort of Kenyan mother-infant pairs, we found that having mild- or moderate-to-severe depressive symptoms during pregnancy was common and associated with an elevated risk of pregnancy loss and preterm birth. Those with low social support also had higher risk of stillbirth. Closing the “last mile” in neonatal health should include integrating mental health services into MCH care to reduce maternal depression

and depression-related neonatal outcomes. Interventions that increase social support and alleviate depressive symptoms may substantially reduce pregnancy loss, stillbirth, and preterm birth ultimately improving linked mother-infant health.

Funding

This work was supported by the National Institute of Allergy and Infectious Disease (R01 AI125498 to GJS and P30AI027757), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (F31HD101149 to AL, 1F32HD108857 to AL, R01HD100201 to JP and R01 HD094630 to GJS). The funding agencies had no role in the writing of the manuscript or the decision to submit it for publication.

APPENDICES

Appendix 1.

Number of CESD-10 items missing among singleton births with pregnancy outcome data among women who did not acquire HIV by 9 months postpartum in the PrIMA study (n=4185)

Number of CESD-10 items missing	N (%)
0	3661 (87.5%)
1	259 (6.2%)
2	152 (3.6%)
3	67 (1.6%)
4	14 (0.3%)
5	7 (0.2%)
6	2 (0.1%)
7	1 (0.02%)
8	1 (0.02%)
9	0 (0.0%)
10	21 (0.5%)

Appendix 2.

Number of MOS-SSS items missing among singleton births with pregnancy outcome data among women who did not acquire HIV by 9 months postpartum in the PrIMA study (n=4185)

Number of MOS-SSS items missing	N (%)
0	4077 (97.4%)
1	80 (1.9%)
2	7 (0.2%)
3	3 (0.1%)
4	18 (0.4%)

Appendix 3.

Incidence of adverse perinatal outcomes by psychosocial factors among PrIMA study participants

					CESD-10 score[a]			
	Overall				Adverse perinatal outcome		Without adverse perinatal outcome	
Adverse perinatal outcomes	**Cases**	**Fetus-years**	**IR**	**95% Confidence interval (CI)**	**Mean**	**St. Dev. (SD)**	**Mean**	**SD**
Pregnancy loss (<20 weeks) (n=1005)	15	111.3	13.5	8.1, 22.4	8.6	6.5	6.2	5.4
Stillbirth (≥ 20 weeks) (n=990)	32	337.9	9.5	6.7, 13.4	5.2	4.1	6.2	5.5
Late stillbirth (≥28 weeks) (n=2566)	47	542.1	8.7	6.5, 11.5	6.8	5.4	6.3	5.4
Preterm birth (<37 weeks) (n=4084)	780	1099.3	71.0	66.1, 76.1	7.0	5.3	6.2	5.4
Small for gestational age (n=2627)	263	682.9	38.5	34.1, 43.5	6.8	5.5	6.6	5.6
Neonatal death (within 28 days of life) (n=4055)	63	306.8	20.5	16.0, 26.3	6.6	5.4	6.3	5.4
Any adverse perinatal outcome (n=625)[b]	201	310.7	64.7	56.3, 74.3	7.0	5.6	6.5	5.7
Any adverse perinatal outcome (n=4153)[c]	864	1355.1	63.8	59.6, 68.2	7.0	5.3	6.2	5.4

	Mild-SD in pregnancy				No Mild-SD in pregnancy			
	Cases	**Fetus-years**	**IR**	**95% CI**	**Cases**	**Fetus-years**	**IR**	**95% CI**
Pregnancy loss	10	57.1	17.5	9.4, 32.5	5*	54.1	9.2	3.8, 22.2
Stillbirth	15	175.1	8.6	5.2, 14.2	17	162.8	10.4	6.5, 16.8
Late stillbirth	28	297.7	9.4	6.5, 13.6	19	244.5	7.8	5.0, 12.2
Preterm birth	492	596.1	82.5	75.6, 90.2	288	503.2	57.2	51.0, 64.2
Small for gestational age	155	389.2	39.8	34.0, 46.6	108	293.8	36.8	30.4, 44.4
Neonatal death	38	167.4	22.7	16.5, 31.2	25	139.4	17.9	12.1, 26.5
Any adverse perinatal outcome (n=625)[b]	117	170.9	68.4	57.1, 82.0	84	139.7	60.1	48.5, 74.4
Any adverse perinatal outcome (n=4153)[c]	540	731.4	73.8	67.9, 80.3	324	623.7	51.9	46.6, 57.9

	MSD in pregnancy	No MSD in pregnancy

					CESD-10 score[a]			
	Overall				Adverse perinatal outcome		Without adverse perinatal outcome	
Adverse perinatal outcomes	**Cases**	**Fetus-years**	**IR**	**95% Confidence interval (CI)**	**Mean**	**St. Dev. (SD)**	**Mean**	**SD**
	Cases	**Fetus-years**	**IR**	**95% CI**	**Cases**	**Fetus-years**	**IR**	**95% CI**
Pregnancy loss	7	25.9	27.1	12.9, 56.8	8	85.4	9.4	4.7, 18.7
Stillbirth	4	73.6	5.4	2.0, 14.5	28	264.3	10.6	7.3, 15.3
Late stillbirth	11	126.7	8.7	4.8, 15.7	36	415.5	8.7	6.3, 12.0
Preterm birth	202	256.8	78.7	68.5, 90.3	578	842.5	68.6	63.2, 74.4
Small for gestational age	77	180.3	42.7	34.2, 53.4	186	502.7	37.0	32.1, 42.7
Neonatal death	14	73.3	19.1	11.3, 32.2	49	233.5	21.0	15.9, 27.8
Any adverse perinatal outcome (n=625)[b]	58	79.9	72.6	56.1, 93.9	143	230.8	62.0	52.6, 73.0
Any adverse perinatal outcome (n=4153)[c]	224	317.1	70.6	62.0, 80.5	640	1038.1	61.7	57.1, 66.6
	Low social support in pregnancy				**Not low social support in pregnancy**			
	Cases	**Fetus-years**	**IR**	**95% CI**	**Cases**	**Fetus-years**	**IR**	**95% CI**
Pregnancy loss	2	33.5	6.0	1.5, 23.9	13	77.7	16.7	9.7, 28.8
Stillbirth	16	110.9	14.4	8.8, 23.6	16	227.1	7.0	4.3, 11.5
Late stillbirth	21	189.0	11.1	7.2, 17.0	26	353.1	7.4	5.0, 10.8
Preterm birth	332	386.1	86.0	77.2, 95.8	448	713.2	62.8	57.3, 68.9
Small for gestational age	88	215.0	40.9	33.2, 50.4	175	467.9	37.4	32.2, 43.4
Neonatal death	24	114.9	20.9	14.0, 31.2	39	191.9	20.3	14.8, 27.8
Any adverse perinatal outcome (n=625)[b]	79	96.3	82.0	65.8, 102.3	122	214.4	56.9	47.7, 68.0
Any adverse perinatal outcome (n=4153)[c]	363	478.4	75.9	68.5, 84.1	501	876.7	57.1	52.4, 62.4
	IPV in pregnancy				**No IPV in pregnancy**			
	Cases	**Fetus-years**	**IR**	**95% CI**	**Cases**	**Fetus-years**	**IR**	**95% CI**
Pregnancy loss	1	9.0	11.1	1.6, 78.9	14	102.3	13.7	8.1, 32.1
Stillbirth	3	26.9	11.1	3.6, 34.5	29	311.0	9.3	6.5, 13.4
Late stillbirth	4	42.9	9.3	3.5, 24.8	43	498.4	8.6	6.4, 11.6
Preterm birth	48	86.7	55.4	41.7, 73.5	730	1011.3	72.2	67.1, 77.6
Small for gestational age	20	57.0	35.1	22.6, 54.3	243	625.3	38.9	34.3, 44.1

					CESD-10 score[a]			
		Overall			Adverse perinatal outcome		Without adverse perinatal outcome	
Adverse perinatal outcomes	**Cases**	**Fetus-years**	**IR**	**95% Confidence interval (CI)**	**Mean**	**St. Dev. (SD)**	**Mean**	**SD**
Neonatal death	3*	24.0	12.5	4.0, 38.8	60	282.4	21.2	16.5, 27.4
Any adverse perinatal outcome (n=625)[b]	13	23.8	54.7	31.7, 94.1	188	286.9	65.5	56.8, 75.6
Any adverse perinatal outcome (n=4153)[c]	55	107.5	51.2	39.3, 66.6	807	1246.1	64.8	60.4, 69.4

[a]CESD-10 score was re-scaled to reflect a 10-unit change in score

[b]Any adverse perinatal outcome: miscarriage, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data

[c]Any adverse perinatal outcome: miscarriage, stillbirth, preterm birth, or neonatal death; among all pregnancies

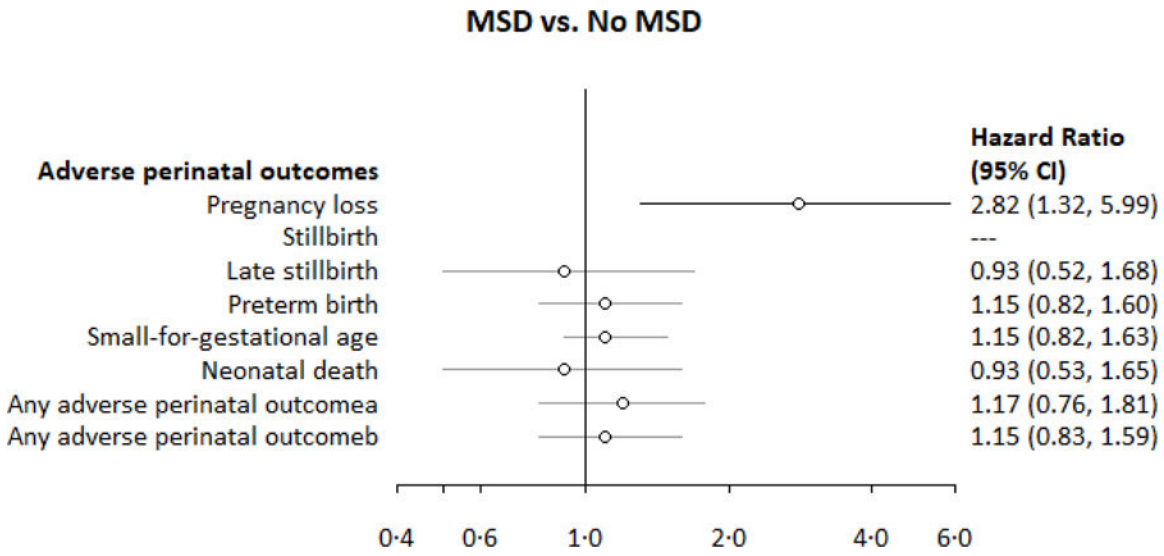
IR: Incidence rate per 100 fetus-years

Mild-SD: Mild-to-severe depressive symptoms

MSD: Moderate-to-severe depressive symptoms

LSS: Low social support

IPV: Intimate partner violence



Appendix 4. Associations between moderate-to-severe depressive symptoms and adverse perinatal outcomes among PrIMA study participants

[a]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births)

[b]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

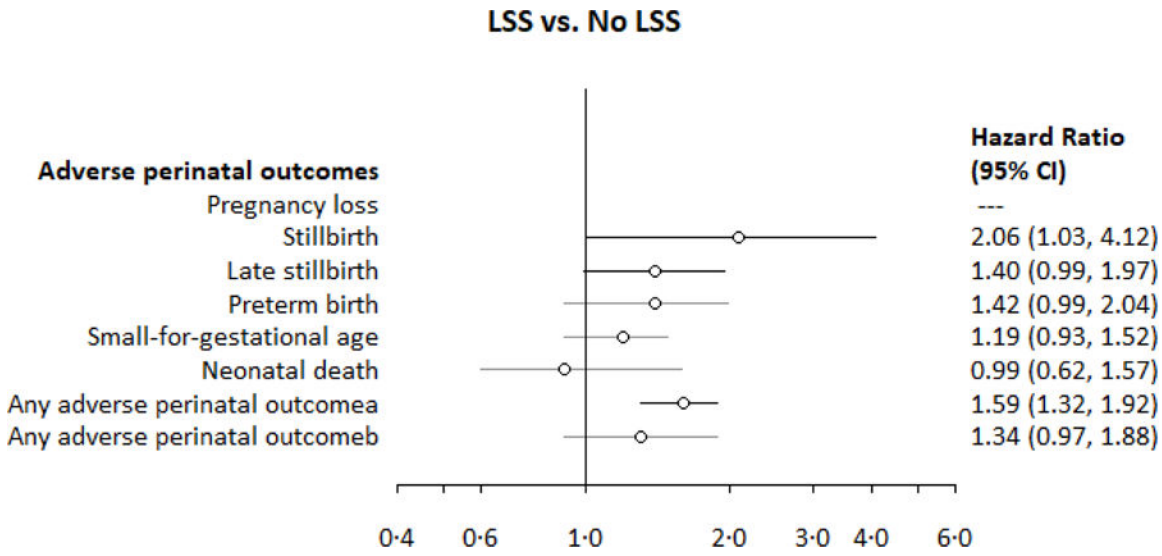
HR: Hazard ratios are from Cox Regression Models, clustered by facility used for outcomes of: pregnancy loss, stillbirth, late stillbirth, preterm birth, neonatal death, any adverse perinatal outcome

For instances with case counts ≤5 in an exposure group, we did not perform regression analyses

CESD-10 score was re-scaled to reflect a 10-unit change in score

CESD-10: Center for epidemiologic studies depression scale-10

MSD: Moderate-to-severe depressive symptoms



Appendix 5. Associations between low social support and adverse perinatal outcomes among PrIMA study participants

[a]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births)

[b]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

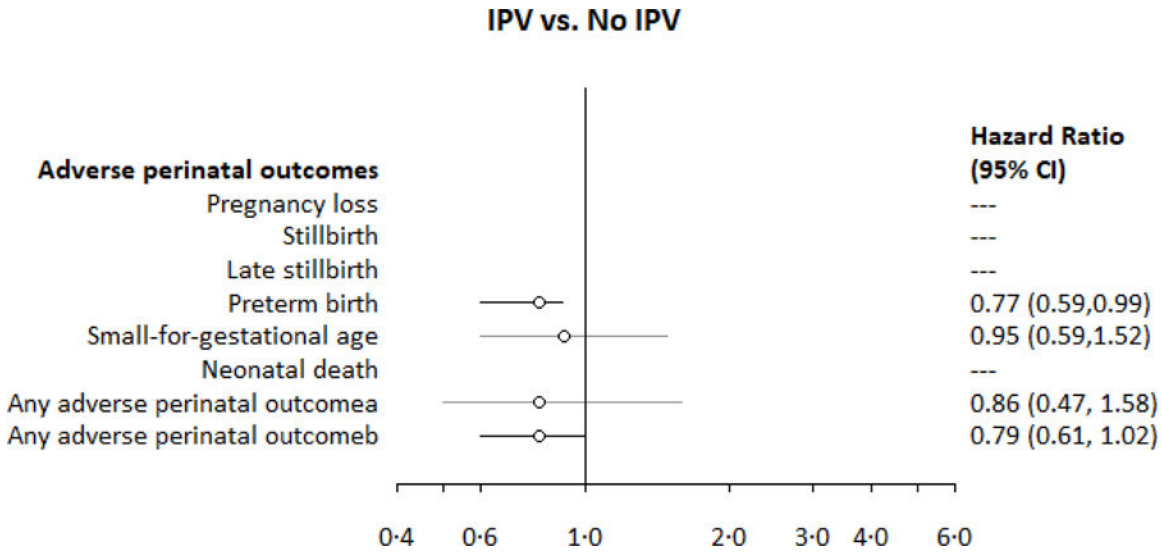
HR: Hazard ratios are from Cox Regression Models, clustered by facility used for outcomes of: pregnancy loss, stillbirth, late stillbirth, preterm birth, neonatal death, any adverse perinatal outcome

For instances with case counts ≤5 in an exposure group, we did not perform regression analyses

CESD-10 score was re-scaled to reflect a 10-unit change in score

CESD-10: Center for epidemiologic studies depression scale-10

LSS: Low social support



Appendix 6. Associations between intimate partner violence and adverse perinatal outcomes among PrIMA study participants

[a]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births)

[b]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

HR: Hazard ratios are from Cox Regression Models, clustered by facility used for outcomes of: pregnancy loss, stillbirth, late stillbirth, preterm birth, neonatal death, any adverse perinatal outcome

For instances with case counts ≤5 in an exposure group, we did not perform regression analyses

CESD-10 score was re-scaled to reflect a 10-unit change in score

CESD-10: Center for epidemiologic studies depression scale-10

IPV: Intimate partner violence

Appendix 7.

Baseline characteristics of PrIMA study participants among those with complete CESD-10 information versus partial (n=4153)

	Overall (N=4153)	Complete CESD-10 (N=3661)	Incomplete CESD-10 (N=492)
Demographic characteristics	n (%) or Median (IQR)	n (%) or Median (IQR)	n (%) or Median (IQR)
Age (years)	24 (21, 28) (n=4151)	24 (21, 29) (n=3659)	24 (21, 28) (n=492)
Adolescents and young women (<25 years)	2369 (57.0%)	2080 (56.8%)	289 (58.7%)
Missing	2 (<1%)	2 (0.1%)	0 (0.0%)
Gestational age (enrollment, weeks)	24 (20, 30) (n=4153)	24 (20, 30) (n=3661)	26 (18, 30) (n=492)
Married or living with a partner	3491 (84.1%)	3083 (84.2%)	408 (82.9%)

	Overall (N=4153)	Complete CESD-10 (N=3661)	Incomplete CESD-10 (N=492)
Missing	34 (0.8%)	33 (0.9%)	1 (0.2%)
Completed education (years)	10 (8, 12) (n=4072)	10 (8, 12) (n=3589)	10 (8, 12) (n=483)
Regularly employed	612 (14.7%)	517 (14.1%)	95 (19.3%)
Missing	52 (1.3%)	44 (1.2%)	8 (1.6%)
Household crowding (≥2 people/ room)	1995 (48.0%)	1771 (48.4%)	224 (45.5%)
Missing	27 (0.7%)	26 (0.7%)	1 (0.2%)
Pregnancy history & factors			
Multiparous	3083 (74.2%)	2735 (74.7%)	348 (70.7%)
Missing	5 (0.1%)	4 (0.1%)	1 (0.2%)
Prior pregnancy loss	539 (13.0%)	468 (12.8%)	71 (14.4%)
Missing	14 (0.3%)	12 (0.3%)	2 (0.4%)
Prior preterm birth	42 (1.0%)	35 (1.0%)	7 (1.4%)
Trimester of initial antenatal care (ANC) visit			
First	615 (14.8%)	523 (14.3%)	92 (18.7%)
Second	2098 (50.5%)	1894 (51.7%)	204 (41.5%)
Third	1440 (34.7%)	1244 (34.0%)	196 (39.8%)
Infant sex (female)	1842 (44.3%)	1633 (44.6%)	209 (42.5%)
Missing	534 (12.9%)	462 (12.6%)	72 (14.6%)
HIV risk factors			
Self-perceived high HIV risk	369 (8.9%)	320 (8.7%)	49 (10.0%)
Missing	7 (0.2%)	4 (0.1%)	3 (0.6%)
Lifetime sexual partners	2 (2, 3) (n=4148)	2 (2, 3) (n=3656)	2 (2, 3) (n=492)
Partner HIV-positive*	176 (4.2%)	149 (4.1%)	27 (5.5%)
Missing	52 (1.3%)	49 (1.3%)	3 (0.6%)
Sexually transmitted infection (enrollment)	104 (2.5%)	96 (2.6%)	8 (1.6%)
Missing	7 (0.2%)	5 (0.1%)	2 (0.4%)
Psychosocial characteristics			
Low social support (MOS-SSS score <72)	1504 (36.2%)	1372 (37.5%)	132 (26.8%)
Missing	90 (2.2%)	69 (1.9%)	21 (4.3%)
Intimate partner violence [c] (HITS score ≥10)	323 (7.8%)	289 (7.9%)	34 (6.9%)
Missing	5 (0.1%)	5 (0.1%)	0 (0.0%)

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Synopsis

Study question

Are psychosocial factors in pregnancy, including depression, low social support, and intimate partner violence associated with adverse perinatal outcomes among Kenyan mother-infant pairs?

What's already known

Depression in pregnancy is common and is associated with preterm birth and infant death. Yet, these relationships are understudied in sub-Saharan Africa—the region with the highest burden of adverse perinatal outcomes. It is unclear whether maternal psychosocial factors are associated with adverse perinatal outcomes in Kenya.

What this study adds

Our study is the largest to date to assess maternal mental health and >3 birth outcomes among African mother-infant pairs. Novel findings include the relationship between moderate-to-severe depressive symptoms in pregnancy and elevated risk of pregnancy loss, and the relationship between low social support in pregnancy and stillbirth in Kenya.

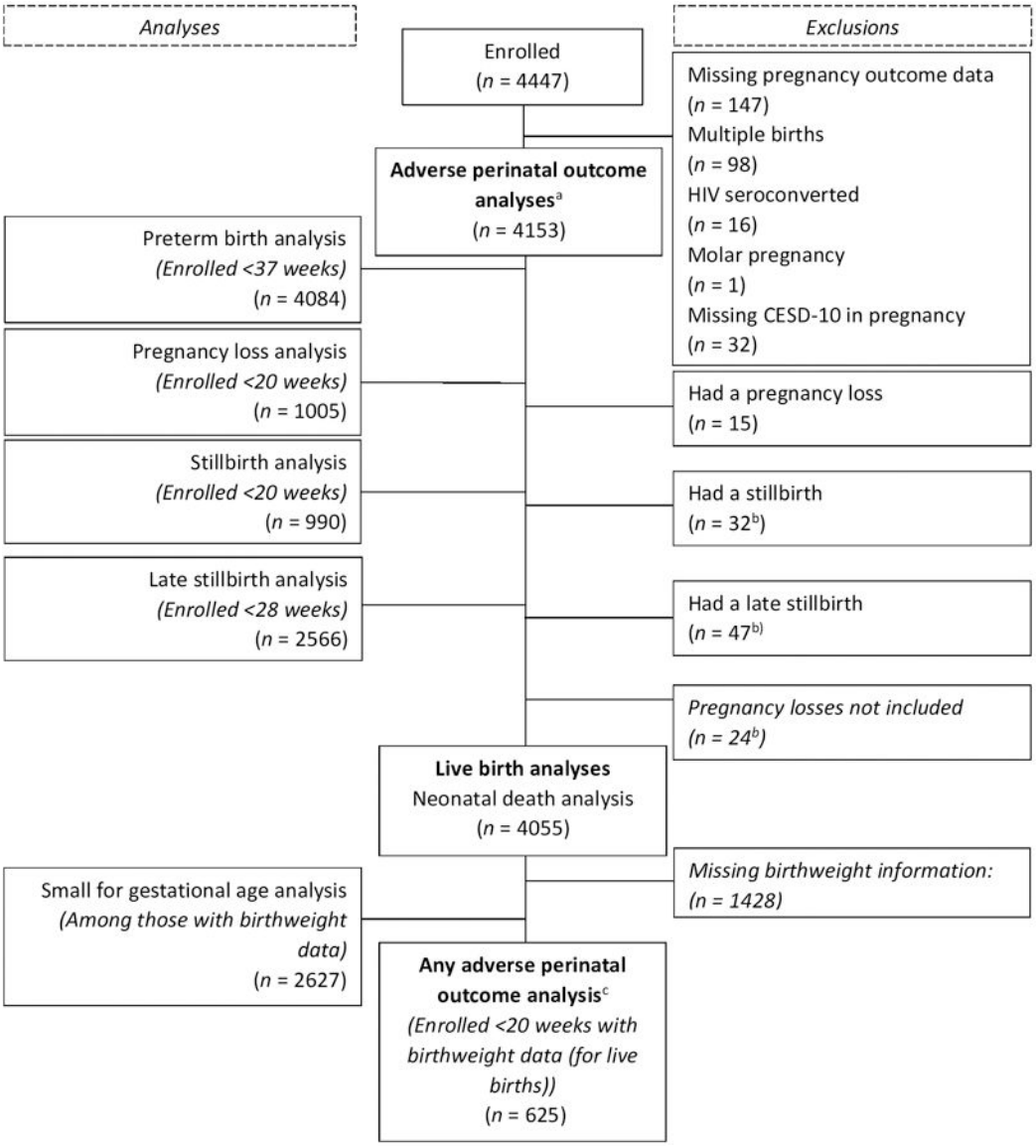

Figure 1. Flow diagram for PrIMA study population

[a]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births).

[b]The stillbirth cases included in the "stillbirth" analysis and "late stillbirth" analysis overlap by N = 20. There were N = 24 stillbirths not included in either stillbirth analysis based on ineligible enrollment age.

[c]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies.

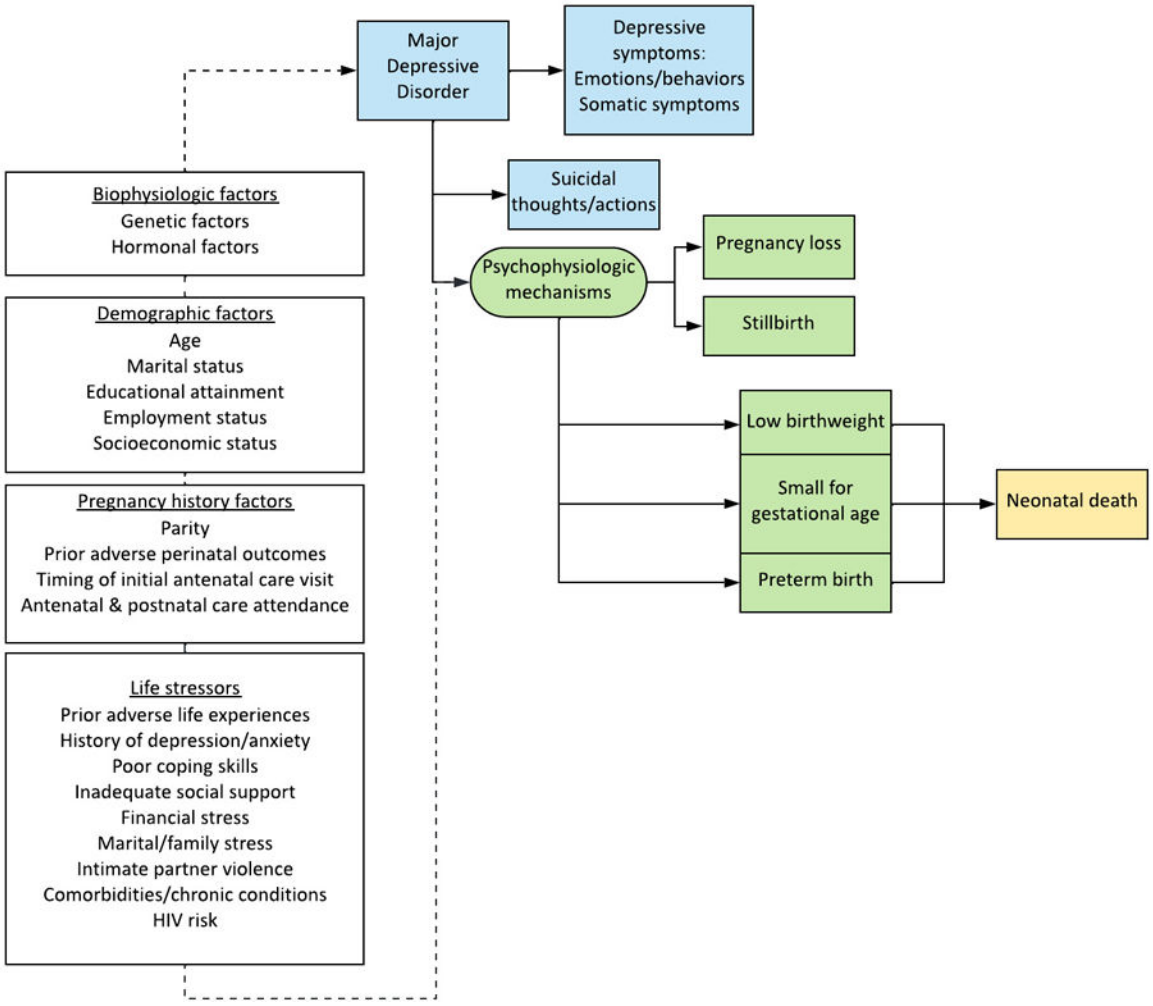

Figure 2. Conceptual model for depression and adverse perinatal outcomes

References for figure components:

Major depressive disorder, depressive symptoms:

Fisher J, Cabral de Mello M, Patel V, *et al.* Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bull World Health Organ* 2012; **90**: 139–149H.

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Small for gestational age:

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Preterm birth:

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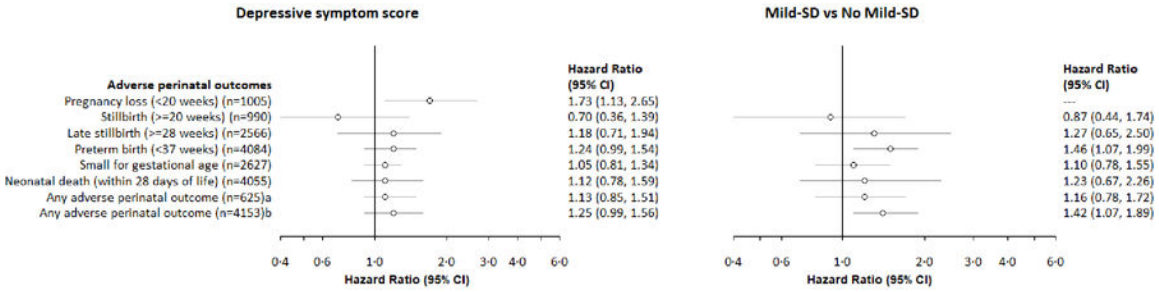

Figure 3. Associations between depressive symptoms and adverse perinatal outcomes among PrIMA study participants

[a]HR: Hazard ratios are from Cox Regression Models, clustered by facility used for outcomes of: pregnancy loss, stillbirth, late stillbirth, preterm birth, neonatal death, any adverse perinatal outcome

[b]For instances with case counts ≤5 in an exposure group, we did not perform regression analyses

[c]CESD-10 score was re-scaled to reflect a 10-unit change in score

[d]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births)

[e]Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

CESD-10: Center for epidemiologic studies depression scale-10

Mild-SD: Mild-to-severe depressive symptoms

MSD: Moderate-to-severe depressive symptoms

LSS: Low social support

IPV: Intimate partner violence

Table 1.

Baseline characteristics of PrIMA study participants included in MSD-birth outcomes analysis

	Overall (n=4153)			MSD (n=994)		No MSD (n=3159)	
Demographic characteristics	**N**	**n (%) or Median (IQR)**	**Missing n (%)**	**n**	**n (%) or Median (IQR)**	**n**	**n (%) or Median (IQR)**
Age (years)	4151	24 (21, 28)	2 (0.05%)	993	24 (21, 29)	3158	24 (21, 28)
Adolescents and young women (<24 years)	4151	2369 (57.1%)	2 (0.05%)	993	566 (57.0%)	3158	1803 (57.1%)
Gestational age (enrollment, weeks)	4153	24 (20, 30)	0 (0.0%)	994	24 (20, 30)	3159	24 (20, 30)
Married or living with a partner	4119	3491 (84.8%)	34 (0.8%)	987	812 (82.3%)	3132	2679 (85.5%)
Completed education (years)	4074	10 (8, 12)	81 (2.0%)	971	10 (8, 12)	3101	10 (8, 12)
Regularly employed	4101	612 (14.9%)	52 (1.3%)	982	121 (12.3%)	3119	491 (15.7%)
Household crowding (≥2 people/ room)	4126	1995 (48.4%)	27 (0.7%)	989	532 (53.8%)	3137	1463 (46.6%)
Pregnancy history & factors							
Primiparous	4148	1065 (25.7%)	5 (0.1%)	993	235 (23.7%)	3155	830 (26.3%)
Multiparous	4148	3083 (74.3%)	5 (0.1%)	993	758 (76.3%)	3159	2325 (73.7%)
No prior preterm birth	3083	3041 (98.6%)	0 (0.0%)	758	750 (98.9%)	2325	2291 (98.5%)
Prior preterm birth	3083	42 (1.4%)	0 (0.0%)	758	8 (1.1%)	2325	34 (1.5%)
No prior pregnancy loss	3083	2645 (85.9%)	0 (0.0%)	758	639 (84.3%)	2325	2008 (86.4%)
Prior pregnancy loss	3083	436 (14.1%)	0 (0.0%)	758	119 (5.1%)	2325	317 (13.6%)
Trimester of initial antenatal care (ANC) visit	4153		0 (0.0%)				
First	4153	615 (14.8%)	0 (0.0%)	994	128 (12.9%)	3159	487 (15.4%)
Second	4153	2098 (50.5%)	0 (0.0%)	994	500 (50.3%)	3159	1598 (50.6%)
Third	4153	1440 (34.7%)	0 (0.0%)	994	366 (36.8%)	3159	1074 (34.0%)
Attended at least 4 ANC visits (before pregnancy end)	4153	3655 (88.0%)	0 (0.0%)	994	876 (88.1%)	3159	2779 (88.0%)
HIV risk factors							
High HIV risk[a]	4153	1542 (37.1%)	0 (0.0%)	994	454 (45.7%)	3159	1088 (34.4%)
Self-perceived HIV risk	4146	369 (8.9%)	7 (0.2%)	993	124 (12.5%)	3153	245 (7.8%)
Lifetime sexual partners	4148	2 (2, 3)	5 (0.1%)	994	3 (2, 4)	3154	2 (2, 3)
Lifetime sexual partners (>2)	4148	3448 (83.1%)	5 (0.1%)	994	871 (87.6%)	3154	2577 (81.7%)
Partner age difference >10 years[b]	3182	497 (15.6%)	917 (23.4%)	736	118 (16.0%)	2446	379 (15.5%)
Partner HIV-positive[b]	4101	176 (4.3%)	0 (0.0%)	979	67 (6.8%)	3122	109 (3.5%)
Partner HIV status unknown[b]	4101	1296 (31.6%)	0 (0.0%)	979	370 (37.8%)	3122	926 (29.7%)
Sexually transmitted infection (enrollment)	4146	104 (2.5%)	7 (0.2%)	992	45 (4.5%)	3154	59 (1.9%)
PrEP Use in pregnancy	4153	551 (13.3%)	0 (0.0%)	994	192 (19.3%)	3159	359 (11.4%)
Psychosocial characteristics							
Ever drink alcohol	4135	168 (4.1%)	18 (0.4%)	985	50 (5.1%)	3150	118 (3.7%)

	Overall (n=4153)			MSD (n=994)		No MSD (n=3159)	
Demographic characteristics	**N**	**n (%) or Median (IQR)**	**Missing n (%)**	**n**	**n (%) or Median (IQR)**	**n**	**n (%) or Median (IQR)**
Social support score[c]	4153	75 (63, 88)	0 (0.0%)	994	70 (55, 81)	3159	78 (66, 89)
Low social support (MOS-SSS score <72)	4153	1550 (37.3%)	0 (0.0%)	994	521 (52.4%)	3159	1029 (32.6%)
Intimate partner violence[d] (HITS score ≥10)	4148	323 (7.8%)	5 (0.1%)	993	170 (17.1%)	3155	153 (4.8%)
CESD-10 score	4153	5 (3, 9)	0 (0.0%)	994	13 (11, 16)	3159	4 (2, 6)
Mild-to-severe depressive symptoms (CESD-10≥5)	4153	2273 (54.7%)	0 (0.0%)	994	994 (100.0%)	3159	1279 (40.5%)
Moderate-to-severe depressive symptoms (CESD-10≥10)	4153	994 (23.9%)	0 (0.0%)		--		--

[a] We evaluated HIV risk using the Pintye et al.[31] risk score (high HIV risk: score >6 = "Yes", score ≤6 = "No").

[b] Among those with current partners

[c] We evaluated social support using the 18-item Medical Outcomes Study social support score (MOS-SSS), defining low social support as scores below 72 (Low social support: MOS-SSS score score <72 = "Yes", MOS-SSS score ≥ 72 = "No").

[d] We evaluated intimate partner violence using the 4-item Hurt, Insult, Threaten, and Scream scale (HITS), defining intimate partner violence as scores of 10 and above (IPV: HITS score ≥10 = "Yes", HITS score <10 = "No").

CESD-10: Center for epidemiologic studies depression scale-10

MSD: Moderate-to-severe depressive symptom

Table 2.

Cumulative incidence of adverse perinatal outcomes among pregnant and postpartum women in Western Kenya in the PrIMA study

Adverse perinatal outcomes	Exposed	Cases	N	Cumulative incidence (CI) per 1000 pregnancies (95% Confidence interval [CI])	Unexposed	Cases	N	CI per 1000 pregnancies (95% CI)
Pregnancy loss (<20 weeks) **(n=1005)**	Overall	15	990	14.9 (8.1, 22.4)				
	MSD	7	223	31.4 (15.0, 64.6)	No MSD	8	782	10.2 (5.1, 20.3)
	Mild-SD	10	525	19.0 (10.3, 35.1)	No Mild-SD	5[a]	480	10.4 (4.3, 24.8)
	LSS	2[a]	333	6.0 (1.5, 23.8)	No LSS	13	672	19.3 (11.3, −33.1)
	IPV	1[a]	80	12.5 (1.7, 85.8)	No IPV	14	925	15.1 (9.0, 25.4)
Stillbirth (≥ 20 weeks) **(n=990)**	Overall	32	990	32.3 (22.9, 45.4)				
	MSD	4[a]	216	18.5 (6.9, 48.5)	No MSD	28	774	36.2 (25.1, 51.9)
	Mild-SD	15	515	29.1 (17.6, 47.8)	No Mild-SD	17	475	35.8 (22.3, 56.9)
	LSS	16	331	48.3 (29.8, 77.6)	No LSS	16	659	24.3 (14.9, 39.3)
	IPV	3[a]	79	37.9 (12.1, 113.0)	No IPV	29	911	31.8 (22.2, 45.5)
Late stillbirth (≥28 weeks) **(n=2566)**	Overall	47	2566	18.3 (13.8, 24.3)				
	MSD	11	599	18.3 (10.2, 32.9)	No MSD	36	1964	18.3 (13.2, 25.3)
	Mild-SD	28	1418	19.7 (13.6, 28.5)	No Mild-SD	19	1145	16.6 (10.6, 25.9)
	LSS	21	900	23.3 (15.2, 35.5)	No LSS	26	1663	15.6 (10.7, 22.9)
	IPV	4[a]	200	20.0 (7.5, 52.4)	No IPV	43	2359	18.2 (13.5, 24.5)
Preterm birth (<37 weeks) **(n=4084)**	Overall	780	4084	191.0 (179.2, 203.3)				
	MSD	202	975	207.2 (182.9, 233.8)	No MSD	578	3109	185.9 (172.6, 200.0)
	Mild-SD	492	2239	219.7 (203.1, 237.4)	No Mild-SD	288	1845	156.1 (140.2, 173.4)
	LSS	332	1522	218.1 (198.1, 239.6)	No LSS	448	2562	174.9 (160.6, 190.1)
	IPV	48	318	150.9 (115.5, 194.8)	No IPV	730	3761	194.1 (181.8, 207.1)
Small for gestational age **(n=2627)**	Overall	263	2627	100.1 (89.2, 112.2)				
	MSD	77	699	110.2 (89.0, 135.6)	No MSD	186	1928	96.5 (84.1, 110.5)
	Mild-SD	155	1486	104.3 (89.7, 120.9)	No Mild-SD	108	1141	94.7 (79.0, 113.1)
	LSS	88	881	99.9 (81.7, 121.5)	No LSS	175	1746	100.2 (87.0, 115.2)
	IPV	20	225	88.9 (57.9, 134.0)	No IPV	243	2400	101.3 (89.8, 114.0)

Adverse perinatal outcomes	Exposed	Cases	N	Cumulative incidence (CI) per 1000 pregnancies (95% Confidence interval [CI])	Unexposed	Cases	N	CI per 1000 pregnancies (95% CI)
Neonatal death (within 28 days of life) **(n=4055)**	Overall	63	4055	15.5 (12.8, 20.7)				
	MSD	14	967	14.5 (8.6, 24.3)	No MSD	52	3088	16.8 (12.9, 22.0)
	Mild-SD	40	2215	18.1 (13.3, 24.5)	No Mild-SD	26	1840	14.1 (9.6, 20.7)
	LSS	25	1516	16.5 (11.2, 24.3)	No LSS	41	2539	16.1 (11.9, 21.9)
	IPV	3^	315	9.5 (3.1, 29.2)	No IPV	63	3735	16.9 (13.2, 21.5)
Any adverse perinatal outcome **(n=625)**[b]	Overall	201	625	321.6 (286.1, 359.3)				
	MSD	58	163	335.8 (285.7, 432.8)	No MSD	143	462	309.5 (268.9, 353.3)
	Mild-SD	117	346	338.2 (290.1, 389.8)	No Mild-SD	84	279	301.1 (249.9, 357.7)
	LSS	79	201	393.0 (327.5, 462.6)	No LSS	122	424	287.7 (246.5, 332.8)
	IPV	13	49	265.3 (158.5, 409.0)	No IPV	188	576	326.4 (289.2, 365.9)
Any adverse perinatal outcome **(n=4153)**[c]	Overall	1132	4153	272.6 (259.2, 286.3)				
	MSD	297	994	298.8 (271.1, 328.0)	No MSD	835	3159	264.3 (249.2, 280.0)
	Mild-SD	694	2273	305.3 (286.7, 324.6)	No Mild-SD	438	1880	233.0 (214.4, 252.6)
	LSS	447	1550	288.4 (266.4, 311.5)	No LSS	685	2603	263.2 (246.6, 280.4)
	IPV	75	323	232.2 (189.2, 281.6)	No IPV	1055	3825	275.8 (261.9, 290.2)

[a] For instances with case counts ≤5 in an exposure group, we did not perform regression analyses

[b] Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births)

[c] Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

CESD-10: Center for epidemiologic studies depression scale-10

CI: Cumulative Incidence per 1000 pregnancies

Exposed/Unexposed: “Exposures” are psychosocial factors including mild-to-severe depressive symptoms (Mild-SD), moderate-to-severe depressive symptoms (MSD), low social support (LSS), and intimate partner violence (IPV)

Mild-SD: Mild-to-severe depressive symptoms

MSD: Moderate-to-severe depressive symptoms

LSS: Low social support

IPV: Intimate partner violence

Table 3.

Psychosocial correlates of adverse perinatal outcomes and population attributable risk percentages among PrIMA study participants

	Univariable Analysis	Multivariable Analysis	
	HR[d] (95% CI)	**aHR[e] (95% CI)**	**PAR (95% CI)**
Exposure: CESD-10 score [c]			
Pregnancy loss (n=1005)	1.73 (1.13, 2.65)	2.59 (1.71, 3.92)	
Preterm birth (n=4084)	1.24 (0.99, 1.54)	1.25 (1.01, 1.55)	
Any adverse perinatal outcome (n=4153)[a]	1.25 (1.00, 1.56)	1.28 (1.02, 1.60)	
Exposure: Mild-SD vs No Mild-SD			
Preterm birth (n=4084)	1.46 (1.07, 1.99)	1.39 (1.03, 1.87)	17.3% (2.6, 29.8)
Any adverse perinatal outcome (n=4153)[a]	1.42 (1.07, 1.89)	1.40 (1.02, 1.90)	17.6% (2.6, 30.3)
Exposure: MSD vs. No MSD			
Pregnancy loss (n=1005)	2.81 (1.32, 5.99)	5.04 (2.44, 10.42)	37.4% (30.3, 43.8)
Exposure: LSS vs. higher social support			
Stillbirth (n=990)	2.06 (1.03, 4.12)	2.37 (1.14, 4.94)	29.9% (12.0, 44.1)
Late stillbirth (n=2563)	1.40 (0.99, 1.97)	1.27 (0.88, 1.85)	
Any adverse perinatal outcome (n=625)[b]	1.59 (1.32, 1.92)	1.56 (1.24, 1.97)	14.0% (8.0, 19.6)
Any adverse perinatal outcome (n=4152)[a]	1.35 (0.97, 1.88)	1.34 (0.98, 1.85)	
Exposure: IPV vs. No IPV			
Preterm birth (n=4084)	0.77 (0.59, 0.99)	0.74 (0.54, 1.01)	
Any adverse perinatal outcome (n=4152)[a]	0.79 (0.61, 1.02)	0.77 (0.57, 1.05)	

[a] Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, small for gestational age, or neonatal death; among those enrolled <20 weeks and with birthweight data (for live births).

[b] Any adverse perinatal outcome: pregnancy loss, stillbirth, preterm birth, or neonatal death; among all eligible pregnancies

[c] CESD-10 score was re-scaled to reflect a 10-unit change in score

[d] Hazards Ratios (HR) estimated from Cox Regression, clustered by site

[e] Adjusted HRs were estimated from models including: the exposure of interest (CESD-10 score, Mild-SD, MSD, LSS, IPV) and maternal age (years, continuous), educational attainment (years, continuous), regular employment (yes/no), married/living with a partner (yes/no), household crowding (yes/no), multiparous (yes/no), prior adverse perinatal outcome (pregnancy loss, stillbirth, or preterm birth, yes/no), high HIV risk (yes/no), self-perceived high HIV risk (Extremely/very likely vs Somewhat/very/extremely unlikely), PrEP uptake in pregnancy (yes/no), ANC attendance (Total visits attended

by enrollment [pregnancy loss analysis], ≥4 ANC visits attended vs. <4 ANC visits [all other analysis]), and (the other psychosocial factors (MSD, low social support, or intimate partner violence).
CESD-10: Center for epidemiologic studies depression scale-10

Mild-SD: Mild-to-severe depressive symptoms

MSD: Moderate-to-severe depressive symptoms

LSS: Low social support

IPV: Intimate partner violence