

Elsevier Editorial System(tm) for Best
Practice & Research Clinical Obstetrics & Gynecology
Manuscript Draft

Manuscript Number:

Title: Preventing infant and child morbidity and mortality due to
maternal depression

Article Type: Issue 30.7

Keywords: Mental health, depression, anxiety, mothers, child, developing
countries

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Abstract: This review provides an overview of perinatal depression and its impacts on the health of mothers, their newborns, and young children in low- and middle- income countries (LMIC). We define and describe the urgency and scope of the problem of perinatal depression for mothers, while highlighting some specific issues such as suicidal ideation and decreased likelihood to seek healthcare. Pathways through which stress may link maternal depression to childhood growth and development (e.g. the HPA axis) are discussed, followed by a summary of the adverse effects of depression on birth outcomes, parenting practices, and child growth and development. Though preliminary studies on the association between maternal depressive symptoms and maternal and child mortality exist, more research on these topics is needed. We describe available interventions and suggest strategies to reduce maternal depressive symptoms in LMICs, including integration of services with existing primary healthcare systems.

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PREVENTING INFANT AND CHILD MORBIDITY AND MORTALITY DUE TO MATERNAL DEPRESSION

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Current word count: 8,658

Target word count: 7000 with references

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4 **ABSTRACT**
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8 mothers, their newborns, and young children in low- and middle- income countries (LMIC). We
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10 define and describe the urgency and scope of the problem of perinatal depression for mothers,
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12 while highlighting some specific issues such as suicidal ideation and decreased likelihood to seek
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14 healthcare. Pathways through which stress may link maternal depression to childhood growth
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16 and development (e.g. the HPA axis) are discussed, followed by a summary of the adverse
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18 effects of depression on birth outcomes, parenting practices, and child growth and development.
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Though preliminary studies on the association between maternal depressive symptoms and
maternal and child mortality exist, more research on these topics is needed. We describe
available interventions and suggest strategies to reduce maternal depressive symptoms in LMICs,
including integration of services with existing primary healthcare systems.

Abstract Word Count: 144

HIGHLIGHTS

- Perinatal mental health is an urgent issue in low- and middle-income countries
- It is a fundamental upstream cause of variety of adverse maternal and child outcomes
- Integration of mental and primary healthcare is needed in low-resource settings

KEYWORDS

Mental health, depression, anxiety, mothers, child, developing countries

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4 **INTRODUCTION**
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7 Maternal depression is an urgent priority in the global health agenda [1]. The World
8 Health Organization (WHO) identifies major depression as the primary cause of years lived with
9 a disability and the second leading cause of disability-adjusted life years in women of
10 reproductive age worldwide [2]. Common perinatal mental disorders (CPMD), referring
11 primarily to depression and anxiety, is estimated to occur in nearly one out of six pregnant
12 women and one out of five women in the postpartum period in LMICs [3]. Maternal depression
13 in LMICs is not only harmful to the women’s wellbeing, but also often adversely impacts child
14 health and development [4, 5]. The high prevalence of perinatal depressive symptoms presents
15 particular challenges for families in LMICs, where mental health services are scarce [6].
16 Although LMICs have a higher prevalence of maternal depression, most research on the
17 consequences of perinatal depression on mothers and children is concentrated in high income
18 countries (HIC). For these reasons, we have chosen to focus this review primarily on the
19 correlates of perinatal depression and its impacts on the health of mothers, newborns, and young
20 children in LMICs. Where data are not available in LMIC settings, we report evidence from high
21 income settings that may provide insight into the respective phenomenon in LMICs.
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45 ***Scope of Problem of Maternal Depression***
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47 ***Definitions and correlates***
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49 Maternal depression can broadly be divided by the time of occurrence: during the
50 pregnancy (in the “prenatal period”) or after the delivery of a child (in the “postnatal period”). A
51 recent systematic review suggests that prevalence of postnatal CPMD (19.8%) is higher than the
52 prevalence of prenatal CPMD (15.6%) in LMICs [3]. Just as with depression outside the
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4 perinatal period, there is no universally accepted definition for screening or diagnosis of
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7 postnatal depression. Definitions vary in their method of assessment and specified length of the
8
9 “postnatal period”. For example, the DSM-IV defines “postpartum depression” to have a window
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11 of onset within 4 weeks of delivery, while the ICD-10 defines the window to be up to 6 weeks
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13 from delivery [7]. Postnatal depression may encompass postpartum depression [8], and
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15 definitions have spanned from anywhere from 1 week to 1 year after the delivery of a child [9-
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Available data suggest that postnatal depression is higher in LMICs than HICs,[8, 11] though prevalence estimates vary substantially and range from 0-60% depending on the setting [13]. In addition to varying time periods of interest and different cultural and socioeconomic contexts of motherhood across studies, this wide range of prevalence may be due to inconsistent measurement tools (e.g., measures of depressive symptoms versus a diagnostic measure) or sampling designs (e.g., clinical versus community samples) [13].

In a cross-cultural qualitative study in eleven countries, respondents universally acknowledged the phenomenon of morbid unhappiness after delivery and also universally recognized social support from family partners as a possible remedy [14]. Similarly, several quantitative studies have confirmed that social stressors or economic hardships are risk factors for postnatal depression [8, 10, 15, 16]. Intimate partner violence is another risk factor for prenatal or postnatal depression across culturally and economically diverse settings [10, 17, 18]. Psychological violence alone or psychological, physical and sexual partner violence together during pregnancy were predictive of postnatal depression (ORs 1.58 and 1.76, respectively) among women in Brazil [17]. Women in rural Pakistan who experienced domestic violence were three times more likely to be depressed three months after the birth of a child [10]. In addition,

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4 history of depression or mood disorders during and prior to pregnancy has consistently been
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6 related to postnatal depression [15, 19]
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9 Depression during pregnancy has been less studied than postnatal depression [15]. Much
10 of the research in the prenatal period focuses on the third trimester, a time when risk of
11 depression is higher than that observed in the general population [20, 21]. Although our best
12 pooled estimate of prenatal CPMDs, of which depression is the most common disorder, in LMICs
13 is 15.6% [3], several studies of rural women report higher estimates (e.g., 18%, 25% and 47% in
14 rural areas of Bangladesh [22], Pakistan [23], and South Africa [21], respectively).
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23 Many social, family and socioeconomic factors have been linked to prenatal depression.
24 Several studies have found that being single/unmarried at the time of pregnancy is related to
25 prenatal depressive symptoms [24, 25], in addition to having negative attitudes towards the
26 pregnancy [25, 26]. Socioeconomic correlates of depressive symptomology during pregnancy
27 included, being in debt [26], having fewer years of schooling [22] and employment insecurity or
28 participating in casual (as opposed to salaried) work [27]. Poor family relationships and hostile
29 home environments are also consistently linked with prenatal depression. Partner violence [28],
30 lack of support from husbands or mothers-in-law [24, 28], and lack of decision making power in
31 major decisions [27] were each more likely to be reported by depressed compared with non-
32 depressed women.
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48 ***Perinatal depression and suicidal ideation*** 49

50 Suicide ideation is a major concern among mothers who experience depression. Data
51 from a confidential Enquiry into Maternal Death in the United Kingdom demonstrate that suicide
52 rates in the postnatal period may be as high as other times in a woman's life, challenging the
53 notion that maternity protects against suicidal behavior [29]. Several studies have examined
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4 suicidality measured as thoughts of self-harm during depression screening, for example a single-
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7 item (item 10) on the Edinburgh Postnatal Depression Scale (EPDS) [28, 30, 31] or a single item
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9 on the Patient Health Questionnaire (PHQ) [32].

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11 Previous or concurrent depression, economic hardship, interpersonal violence, and lack
12
13 of social support appear to play an important role in suicidal ideation during the prenatal period
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15 [28, 31, 32]. In rural Bangladeshi women at 34-35 weeks into their pregnancy, 14% who were
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17 classified as depressed reported thoughts of self-harm, and in qualitative follow-up, the authors
18
19 found that suicidal thoughts were in particular associated with spousal violence [28]. Nearly one-
20
21 quarter of pregnant women receiving antenatal care in Brazil had “current suicide risk”;
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24 investigators found depressive symptomology (OR=4.44) and years of education (OR=0.45) to
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26 be significant correlates of current suicide risk [33]. Another study of pregnant women in Brazil
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28 found the prevalence of suicidality to be 8%, and lack of education, low socioeconomic class,
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30 being single, and symptoms of anxiety and depression were all significantly higher in women
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32 who reported suicidality compared with those who did not [30]. Among Peruvian women,
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34 symptoms of depression, lifetime intimate partner violence, history of childhood abuse, and
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36 difficulty paying for basic needs were significantly higher among women who had thoughts of
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38 self-harm measured using both the PHQ-9 and the EPDS [32].
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45 In the postnatal period, the prevalence of suicidal variation has varied from 4% in Nepal
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47 to 8% in South Africa [9, 31]. In South African women three months after delivery,
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49 experiencing food insecurity was associated with higher likelihood of probably depression
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51 (adjusted risk ratio [RR] =1.05, p<.05) and suicidality (adjusted RR = 1.15, p<.05) [9].
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56 ***Health care seeking during pregnancy among depressed women***
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4 Women who are depressed during pregnancy do not often seek treatment for their
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6 depression [34]. This may be in part due to the scarcity of mental health services in LMICs [35].
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8 As mental health conditions are stigmatized in many LMICs [36], the desire to acknowledge or
9
10 seek treatment may also be culturally sensitive. There are several reports that depressed women
11
12 tend to express their symptoms somatically in non-Western settings.[37] From a clinical
13
14 standpoint, physicians in these settings should be sensitized to diagnosing/detecting women who
15
16 present with somatic symptoms. Migrant women from non-Western cultures have been observed
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18 to be more reluctant to discuss mental problems outside the household [38]. Furthermore,
19
20 pharmaceutical treatment during the pregnancy may be undesirable to women.
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26 Beyond care for depression, depressed mothers may be less likely to seek prenatal care
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28 [39]. One Taiwanese study found that within a sample of women with a depressive disorder
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30 within two years of their delivery, those that had seven or fewer prenatal visits were at
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32 approximately a four-fold five-fold and two-fold higher risk for low birthweight (LBW), preterm
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34 birth (PTB), and small-for-gestational age (SGA), respectively [40].
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38 ***Stress Pathways Linking Maternal Depression with Fetal and Child Growth and Development***

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41 Depression may be considered an expression of psychosocial stress, and research suggests
42
43 several potential pathways linking chronic stress to negative perinatal outcomes. The effects of
44
45 prenatal depression may result from both physiological changes in the mother (i.e. altered
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47 maternal hypo-pituitary axis [HPA] and catecholamine function; early evidence on epigenetics)
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49 that affect the developing fetus directly as well as stress-related health behaviors that impact the
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51 infant [41, 42]. In utero and postnatal period when the fetus is developing at an extraordinary
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53 rate, environmental stressors such as experience of depressive symptoms can have an especially
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55 pronounced impact [43]. Given that women are the primary caretakers of infants and children
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4 globally [44], and stress associated with antenatal depression and anxiety tend to endure across
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6 the prenatal and postnatal periods [45, 46], depression and anxiety may have a cumulative impact
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8 in the postnatal period when maternal-child interactions are critical for child growth and
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10 development [4, 47]. Although measurement of stress in pregnancy may differ and results may
11
12 depend on variation in the response to stressful events and interactions with other factors that
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14 modify it (e.g. underlying anxiety as well as support and coping mechanisms)[48], we
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16 summarize what is known about impacts of maternal stress on fetal and infant growth and
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18 development.
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24 During fetal development, growing evidence suggests that maternal stress and depression
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26 affect nutrition, maternal-fetal communication [49], and may result in neurobehavioral
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28 dysregulation [50]. One study showed that fetuses of depressed compared to non-depressed
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30 mothers had elevated baseline heart rates, had attenuated response to induced vibroacoustic
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32 stimulation, and longer recovery time to return to baseline heart rates [51]. Another similar study
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34 did not find differences at baseline but showed increased heart rate reactivity in fetuses of
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36 depressed mothers compared to both non-depressed women and women with anxiety disorders
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38 when mothers were exposed to a standardized laboratory challenge paradigm [52]. In terms of
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40 fetal activity, fetuses of women with high levels of depressive symptoms have been found to be
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42 more active between the 5th and 7th months of pregnancy [53]. Maternal cortisol levels may in
43
44 part mediate the relation between maternal prenatal depression and fetal weight; fetuses of
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46 mothers with elevated maternal cortisol levels had approximately 13 times higher odds of having
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48 fetuses with below average estimated fetal weight [54]. Dysregulation of cortisol is additionally
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50 expected to adversely affect the mother and child through cardiometabolic (e.g., elevated
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4 cholesterol) and inflammatory (e.g., elevated cytokines) responses that may increase risk of
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6 preterm birth [42].
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10 The effects of exposure to cortisol in utero appear to carry over into the postnatal period
11 for infants. Mothers with higher urinary cortisol levels at 20 weeks of gestation reported higher
12 depressive symptoms; their fetuses had smaller head circumference, abdominal circumference
13 biparietal diameter and fetal weight; and after birth, their newborns persisted to have indicators
14 of growth restriction [55]. It has also been suggested that this neurobehavioral dysregulation
15 developed prenatally subsequently interacts with depressed mothers' poor interaction styles,
16 potentially compounding growth and developmental problems over time [50]. Among infants of
17 depressed mothers, studies have found elevated cortisol and norepinephrine levels like their
18 mothers [54, 56] and greater relative right frontal EEG symmetry [54], which is associated with
19 high cortisol levels in infants [57]. Poorer performance on the Brazelton assessment
20 (administered within the first day after birth) has been observed in newborns of depressed
21 mothers, on a number of assessments including irritability, less activity and interest, lower
22 endurance and robustness, as well as lower orientation and motor scores.[58]
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41 Maternal stress may also have physiological effects leading to PTB, including (1) increases
42 in corticotrophin-releasing hormone (CRH) caused by stress leading to upregulation of
43 inflammatory cytokine release that stimulates myometrial contractions leading to preterm labor,
44 (2) stress-related down regulation of functions of T and B lymphocytes that increase
45 susceptibility to infections that act as co-factors triggering PTB, and (3) stimulation of a low-
46 grade inflammation reflected in increased levels of cytokines and C-reactive protein caused by
47 chronic stress.[59]
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4 Although research on epigenetic mechanisms linking in utero maternal stress to fetal DNA
5 methylation changes is in its infancy, the effects of depression and anxiety in pregnancy on
6 epigenetic changes is one potential pathway through which pregnancy outcomes may be
7 affected.[60] Social stressors such as intimate partner violence [61], psychological stress [62],
8 such as in response to natural disaster [63] or post-traumatic stress disorder [64] have shown
9 differential methylation in CpG sites. Likewise, infants of depressed mothers have shown
10 differential methylation of CpG sites compared to unexposed infants.[65] However evidence is
11 mixed, with not all studies finding such an association.[66]
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26 ***Maternal depression, pregnancy and birth outcomes***

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28 Several recent reviews summarize the impact of stress and symptoms of depression and
29 anxiety during pregnancy and birth outcomes. Grote et al pooled 29 research studies on the
30 impact of depressive symptoms and depression in pregnancy and birth outcomes including PTB,
31 LBW and intrauterine growth restriction (IUGR).[67] Maternal depressive symptoms predicted
32 between a 39-49% higher risk of these three outcomes in studies with a categorical maternal
33 depression/depressive symptom variable.[67] Weaker non-significant or marginally significant
34 effects were observed for a small number of studies with continuous depression measures for
35 these same outcomes. [67] Of the 29 studies only three were conducted in LMICs, all of which
36 tended to show relatively strong relationships. Prenatal psychiatric morbidity, comparing the top
37 to the lower three quartiles of the General Health Questionnaire (GHQ), was associated with a
38 3.5 times higher likelihood of LBW in India [68]. Maternal antenatal depression was associated
39 with 2.1 times higher risk of LBW in Pakistan.[69] In Brazil, the associations (RRs) of antenatal
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4 maternal depressive symptoms with PTB, LBW, and IUGR were 2.3, 2.0, and 1.6,
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6 respectively.[70]
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9 Another recent meta-analysis conducted by Grigoriadis et al (2013) found prenatal maternal
10 depression or depressive symptoms significantly associated with 37% higher odds of premature
11 delivery, but showed a non-significant association with LBW, except among studies conducted
12 with low socio-economic groups [71]. Only two studies included in the review were conducted
13 in LMICs (one of the two in Hong Kong, resembling more closely a high-income economy). The
14 study conducted in a low-income setting, in Pakistan, reported significant associations between
15 maternal depressive symptoms with PTB, LBW, lower mean APGAR scores, and obstetric
16 complications[72]. Although that study lacked sample size to control for potential confounders,
17 strong associations were reported.
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30 Accortt et al (2015) also published a review focused on prenatal depression diagnosis or
31 depressive symptoms and PTB or LBW [73]. It included both observational studies and case-
32 control studies, but did not pool results in a formal meta-analysis. Authors reported the
33 proportion of studies with significant results for each outcome, concluding that evidence exists
34 for a stronger relationship between preterm depressive symptoms and LBW (and birthweight)
35 than with PTB (and gestational age). However, similar to the other reviews, few studies were
36 conducted in LMICs[73].
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48 Another meta-analysis of prospective cohort studies by Ding et al published in 2014 focused
49 on the same outcomes, PTB and LBW, but specifically studied maternal antenatal symptoms of
50 anxiety and anxiety disorder as the exposure of interest.[74] Based on 9 and 6 studies included in
51 their meta-analyses, they reported overall significant increased risks of 1.5 and 1.8 for PTB and
52 LBW births for mothers with prenatal anxiety, respectively. However, no studies with PTB as an
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4 outcome included in the meta-analysis were from LMICs. For the studies with LBW as an
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7 outcome, the association appeared stronger in the two Asian countries included than the three
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9 studies conducted in Europe [74].

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11 Finally, Bussières et al in a 2015 meta-analysis of 88 studies report associations between
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13 maternal prenatal stress – e.g. including subjective stress, anxiety disorder, pregnancy-related
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15 anxiety, cortisol, life events, exposure to disaster, etc. – and infant birthweight and gestational
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17 age.[75] Type of stress appeared to be related to the magnitude of the association, with strongest
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19 effects observed for pregnancy-related anxiety, compared to other stress indicators. Both high
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21 risk samples and studies conducted outside of Europe and North America also showed larger
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23 effect sizes. Only four of 88 studies were from LMICs, indicating an apparent paucity of
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25 research from those settings. [75]

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27 Littleton et al 2009, conducted a review of 35 studies focusing birth outcomes and four
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29 categories of stressors: number of stressful events, hassles or minor stressors, perceived stress,
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31 and appraised stressful life events.[76] Although associations were small in magnitude, authors
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33 found significant associations between psychosocial stress in pregnancy and birth outcomes such
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35 as LBW and lower neonatal weight. Like Bussières et al, they noted that the strength of the
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37 associations differed depending on the type of stress, e.g. minor stressors were more weakly
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39 associated with negative outcomes than major stressors. [76] Apart from these reviews, two
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41 studies in Africa (Ethiopia and Ghana) found that antenatal depression was associated with
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43 higher risk for prolonged labor [26, 77].

52 ***Maternal depression and early parenting practices***

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55 In addition to poor maternal-child interactions, aspects of parenting such as health-care
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57 seeking and parenting may also be affected by maternal depression [78]. The impact of
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4 depression on specific parenting practices beyond feeding behaviors is not well-described in
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6 LMIC settings, and evidence for this pathway largely comes from HIC. Reviews of maternal
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8 depression and early parenting practices in HIC identified the domains of infant feeding, sleep
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10 routines, preventive health care such as well-child visits and vaccinations, and negative
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12 coercive behaviors [78, 79].
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16 Of parenting practices, breastfeeding has been best studied in relation to depressive
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18 symptoms in LMICs. In a study of mothers in rural Pakistan, depressed mothers breastfed for
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20 a shorter duration than non-depressed mothers [80]. Authors suggest that this association
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22 between depression and truncated breastfeeding may be mediated by perceived insufficient
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24 milk [80]. Another study in rural Ethiopia found that depressed mothers delayed initiation of
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26 breastfeeding compared with non-depressed mothers [26]. Similarly, in U.S. studies, depressed
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28 mothers were less likely to continue breastfeeding 2-4 months after delivery [81], and an
29
30 international meta-analysis of mothers largely in high-income countries found that maternal
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32 depression was associated with a lower odds of breast feeding initiation [71] Another study
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34 found that mothers with more symptoms of depression, anxiety and stress was related to non-
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36 responsive feeding in low-income US children.[82] Although there is mixed evidence
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38 regarding whether mothers with depression engage in unsafe parenting practices (e.g., mothers
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40 with depression were no more or less likely to put their to sleep in an unsafe position or fail to
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42 lower the water temperature during bathing), practices to encourage child development may be
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44 compromised among depressed mothers [81]. After adjusting for demographics and
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46 socioeconomic factors, depressed mothers in the U.S. were less likely to engage in any of the
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48 four examined practices related to child development: setting routines, showing their infant a
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4 book daily, talking to their infant while working, and playing with their infant daily [81]. We are
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6
7 not aware of comparable studies in LMICs.
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9 Health-care seeking for the child – both preventive and curative – is another important
10 parenting responsibility that often falls on mothers. In the U.S., there is evidence of increased use
11 of acute care and decreased vaccination in children under 3 years for children of depressed
12 mothers [83]. However, a study of children under the age of two in Brazil did not find an
13 association with maternal depressive symptoms and time to completion of recommended
14 vaccination.[84] Other research showed an increased odds of a “problem visit” to the hospital
15 among infants <5 months of depressed mothers, but no significant association with well-child
16 visits [85]. Although preventive care and vaccination may be particularly relevant in LMICs—
17 where the burden of infectious disease remains high—the lack of well-developed health care
18 systems in LMICs may preclude the relevance of unnecessary emergency department visits/acute
19 care. Other poor parenting practices associated with maternal depression in HICs [78, 86]
20 such as reduced odds of car seat usage, storage of medicines, and water heat regulation may
21 similarly be less relevant among the poor and lower-middle class in many LMIC settings.
22 Finally, it is important to acknowledge that no population within or outside LMICs is
23 homogenous, and there may be different concerns in different communities and cultural
24 groups. In a multi-ethnic longitudinal study of child behavior problems in the U.S., maternal
25 depression significantly and negatively impacted parental provision of emotional support and
26 cognitive stimulation among White and Latino children; among Black/African-American
27 children, there was no relation between maternal depression and parenting practices [87].
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55 Negative coercive behaviors have included a broad range of practices such as hitting,
56 using an unpleasant voice, and expressing hostility toward the child [79]. In a review of 46
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4 studies, Lovejoy and colleagues reported that maternal depression was strongly related to
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6 negative coercive behaviors, especially among mothers who were currently depressed [79],
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8 and the link between maternal depression and harsh or physical disciplining has also been
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10 confirmed in more recent studies in the U.S. [86, 88]. Another study among U.S. families
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12 reported that although there is a strong cross-sectional relation between maternal depression
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14 and negative parenting behaviors such as physical assault and psychological aggression, there
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16 was no evidence that a change in maternal depression (i.e., a new episode of depression)
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18 negatively impacted parenting behavior [89].
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23 ***Postpartum depressive symptoms and child growth***

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26 Physical growth is considered one of the best indicators of child health status, with
27
28 stunting (short stature-for-age relative to reference growth curves) reflecting more chronic
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30 nutritional and health insults, while other indicators such as wasting reflect more acute
31
32 undernutrition or disease. [90] A meta-analytic review of studies in LMICs mostly including
33
34 children up to the age of two years found maternal depression or depressive symptoms associated
35
36 with approximately a 40% and 50% higher overall estimated risk of child stunting and
37
38 underweight, respectively.[91] Inconsistencies across studies may be attributable to either
39
40 cultural/contextual differences or heterogeneity in the measurement of depressive symptoms and
41
42 anthropometric indices, age of the child and time to follow-up. For stunting, half of the 12
43
44 studies found significant impact of maternal depression or depressive symptoms, while the other
45
46 half of the studies did not.[91] Interestingly, all four of the studies in the review that were
47
48 conducted in South Asia (India, Bangladesh, and Pakistan) found positive effects of postpartum
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50 depression/depressive symptoms on stunting [69, 92-94]. While with the exception of one
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52 Nigerian study [95], no other study from the African continent (including Ethiopia, South Africa
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4 and Malawi) confirmed this association with stunting.[93, 96, 97] Among studies published since
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6 that review, Nasreen et al documented a relation between antenatal but not postnatal depressive
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8 symptoms with stunting in Bangaldeshi infants at 6-8 months of age.[98]
9

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11 Regarding underweight during the first year of life, four of the six South Asian studies
12
13 (conducted in India and Pakistan) in the review showed significant associations with maternal
14
15 depression or depressive symptoms [69, 92, 99, 100], though no association was observed in any
16
17 of the studies from the African continent [93, 95-97]. Supporting the South Asian findings, a
18
19 subsequent Bangladeshi study reported maternal depressive symptoms at 2-3 months postpartum
20
21 were associated with underweight in infants 6 to 8 months old.[98] Some of the strongest effect
22
23 estimates have been observed in South Asia; in Pakistan a community-based study found
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25 approximately a three-fold higher risk for underweight and stunting at six and twelve month
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27 follow-ups (OR range 2.8-3.5).[69]
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34 The particularly strong associations between maternal depression and child growth failure
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36 in South Asia has led some authors to conclude that maternal depression particularly impacts
37
38 infant growth in Asia compared to in Africa or South America [101-103]. Reasons for these
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40 differences have been put forward; Harpham et al 2005 suggested that women in Asia may be
41
42 disempowered and face particular social pressure, such that depressed mothers in these contexts
43
44 have more difficulty in making sure a child is adequately nourished.[93] Stewart conjectured that
45
46 the ‘Asian Enigma’, of higher rates of malnutrition on the Indian subcontinent than would be
47
48 predicted from food availability, might be in part due to maternal mental health.[101]
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53 54 ***Studies of maternal depressive symptoms and maternal and child mortality***

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56 Very few studies have empirically examined the association between depressive symptoms
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58 among mothers and subsequent mortality risk among mothers or children in LMICs or
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4 elsewhere. Even HIC studies of mortality related to mental health, which have mostly focused on
5
6 schizophrenia rather than depression, have been generally limited by weak study design and lack
7
8 of statistical power [104]. With respect to antenatal depression, neither of the two prospective
9
10 cohort studies conducted on this topic in LMICs—specifically, rural Ghana [77] or rural Ethiopia
11
12 [26]—found an association between antenatal depression and neonatal mortality, although the
13
14 Ethiopian study may have been underpowered to detect an association. Maternal depressive
15
16 symptoms and stillbirth were not statistically significantly associated among adolescent mothers
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18 in urban Brazil [105]. Similarly, in the high-income setting of the Netherlands, antenatal
19
20 depression was not associated with child loss defined as miscarriages, fetal deaths, and neonatal
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22 deaths [106]. A study conducted in Taiwan which examined mortality of children up to age 5
23
24 years found that children were at a 1.47 times greater risk of death if their mother was depressed
25
26 [107]. In contrast, in a cohort of Ghanaian mothers probable postnatal depression was found to
27
28 be highly and significantly associated with infant mortality, with an adjusted mortality rate ratio
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30 of 2.86 (95%CI: 1.58 to 5.19) [108]. Collectively, these findings suggest that postnatal
31
32 depression may be more critical for child survival outcomes than antenatal depression.
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40 41 ***Strategies to reduce maternal depressive symptoms in LMICs***

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43 A dearth of funding exists for mental health services in LMICs, impacting both
44
45 community and human resources, with the poorest countries tending to allocate the smallest
46
47 proportion of their overall health budgets for mental health problems.[35] Part of the inability to
48
49 overcome barriers to improving mental health services in low-resource settings may be due to
50
51 lack of mental health leadership in LMICs and the lack of a population-oriented perspective
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53 [109]. Regardless of the cause, this treatment gap in which globally the most socio-economically
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55 needy populations have the least access to care for mental health conditions [35, 110] has
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4 important implications for the prevention and treatment of perinatal depression in these settings.
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7 Recognition of this situation has led to calls for an increase the involvement of a range of
8
9 appropriately trained non-specialist providers [111].

10
11 Research suggests interventions for common perinatal mental disorders in LMICs using
12 supervised non-specialist health and community workers can be feasible and effective [112].
13
14 One program, an effective evidence-based intervention based on Cognitive Behavior Therapy
15 implemented in the late prenatal and early postpartum period, the *Thinking Health Program*
16 (*THP*), more than halved maternal depression and the effects were sustained until at least a year
17 postpartum [113]. THP has been adopted as model program by the WHO as an effective low-
18 intensity psychological intervention for perinatal depression in LMICs [114]. A meta-analysis of
19 thirteen randomized trials summarized the effects of maternal mental health interventions on
20 maternal depressive symptoms, mother-infant relationships and infant developmental outcomes
21 between three weeks to three years after delivery [112]. The pooled intervention effect suggested
22 on average approximately a 0.4 standardized effect size reduction in maternal depressive
23 symptom score attributable to the intervention. Regarding the content of these interventions, four
24 trials focused directly on symptoms of depression, while others centered on topics such as
25 parenting education and child development. Notably, almost all of studies reviewed were
26 conducted with low-income participants.[112]

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48 Another review focused on the content of nine psychological interventions for perinatal
49 depression delivered by non-specialist health workers in LMICs.[115] The authors highlighted
50 key features of such successful interventions in LMICs included that they: were community
51 based, involved other family members in addition to the mother, extended from the prenatal to
52 postnatal period, and addressed larger psychosocial issues (e.g. empowerment, domestic
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4 violence).[115] Further study on the type of psychosocial intervention that may be most effective
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6 for common perinatal mental health disorders in LMICs in these settings was carried out in a
7
8 pooled analysis by Clarke et al, showing significantly larger effect size associated with
9
10 psychological interventions compared to health promotion interventions [116]. Others have
11
12 suggested that while interventions vary in their approach and level of training of personnel
13
14 implementing the programs, one crosscutting finding is that social support provided to
15
16 participants at home has been a successful strategy across diverse studies [117]. This finding is
17
18 supported by research from a study of largely multi-ethnic immigrant women the US suggesting
19
20 that enhanced social support and social networks are independently inversely associated with
21
22 postpartum depressive symptoms [118].
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28 ***Future directions and recommended approaches***

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31 Regarding the importance of different types of psychosocial factors, more research is
32
33 needed to understand their relative impact in specific socio-cultural settings, as these may vary.
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35 A pooled analysis, including both LMICs and HICs, highlighted that among longitudinal studies
36
37 partner violence during pregnancy was associated with a three-fold higher risk of high levels of
38
39 postnatal depressive symptoms.[119] Though a body of randomized trials has now evaluated the
40
41 effectiveness of using lay or non-mental health workers to address mental health disorders in
42
43 LMICs [120, 121], Mutumba et al noted that lay health worker interventions have almost
44
45 exclusively focused on secondary or tertiary prevention, rather than taking a more population
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47 approach to prevention [120], which is has been suggested as the most sustainable approach to
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49 reducing the burden of mental disorders.
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56 Because of its interconnectedness to other disorders, addressing mental health issues (like
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58 maternal depression) is key to addressing a wide range of physical health disorders and mental
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4 health awareness needs to be integrated into all aspects of delivery of healthcare generally [122].

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7 A promising approach to improve perinatal depression in LMICs could be through the
8
9 integration of services for these women into maternal and child health programs [123, 124]. Use
10
11 of non-specialized health care workers, e.g in the context of an integrated CBT intervention,
12
13 demonstrated success was enhanced through their training in: emphatic listening, family
14
15 engagement, guided discovery by use of pictures, behavioral activation and through problem
16
17 solving [125].
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21 An integrated approach of mental health and primary care services has the advantage of
22
23 providing a holistic approach towards treating the patient while reducing stigma associated with
24
25 mental health specialist care, and may foster long-term relationships with families that can
26
27 improve the care of the family and perhaps can also have spillover effects, by predisposing
28
29 mothers to be receptive to other maternal and child health programs [124]. Furthermore, because
30
31 of the population-based nature of many such programs, mental health initiatives integrated into
32
33 maternal and child health programs may facilitate access to rural and hard to reach populations
34
35 compared to other strategies [124]. Some necessary steps in order to integrate maternal mental
36
37 health with child health programs include improving collaboration between sectors and bringing
38
39 mental health screening and other services into routine primary healthcare [123]. Regarding lay
40
41 health workers, research is needed to develop a larger number of effective treatments that they
42
43 can deliver, which relates to a need for increased capacity building for mental health research,
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45 education and training in LMICs [123].
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55 **Conflicts of interest: None**
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Practice Points

- Maternal depression is an urgent global health priority in LMICs that adversely affects both maternal and child health
- Depressed mothers are at risk for self-harm due to suicidal ideation
- Prenatal depressive symptoms may impact the developing infant through fetal dysregulation and lead to adverse birth outcomes
- Postpartum depressive symptoms can lead to poor parenting and child developmental problems
- Interventions for perinatal mental health implemented by non-specialized healthworkers can be effective in LMICs

Research Agenda

- Additional study of consequences of maternal depression on mother’s health and well-being in LMICs
- Causes for regional variation on maternal depression and child growth
- Effect of maternal depression on specific maternal behaviors related to child care beyond breastfeeding in LMICs
- Strategies to screen and manage depression among new mothers in LMICs
- Implementation science research to integrate mental health programs into primary care

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HIGHLIGHTS

- Perinatal mental health is an urgent issue in low- and middle-income countries
- It is a fundamental upstream cause of variety of adverse maternal and child outcomes
- Integration of mental and primary healthcare is needed in low-resource settings

***Practice Points**

Practice Points

- Maternal depression is an urgent global health priority in LMICs that adversely affects both maternal and child health
- Depressed mothers are at risk for self-harm due to suicidal ideation
- Prenatal depressive symptoms may impact the developing infant through fetal dysregulation and lead to adverse birth outcomes
- Postpartum depressive symptoms can lead to poor parenting and child developmental problems
- Interventions for perinatal mental health implemented by non-specialized healthworkers can be effective in LMICs

***Research Agenda**

Research Agenda

- Additional study of consequences of maternal depression on mother's health and well-being in LMICs
- Causes for regional variation on maternal depression and child growth
- Effect of maternal depression on specific maternal behaviors related to child care beyond breastfeeding in LMICs
- Strategies to screen and manage depression among new mothers in LMICs
- Implementation science research to integrate mental health programs into primary care

Multiple Choice Questions

Question 1

Commonly used approaches to measure perinatal depression in large research studies in LMICs include:

- (a) Edinburgh Postnatal Depression Scale
- (b) Patient Health Questionnaire
- (c) Psychiatrist' diagnosis
- (d) General Health Questionnaire
- (e) Depression Scale for Low Income Women

Answers to Question 1

- (a) T (b) T (c) F (d) T (e) F

Explanations for answers to Question 1

- (a) The Edinburgh Postnatal Depression Scale is one of the most common measures used for postnatal depression.
- (b) Patient Health Questionnaire is a general mental health questionnaire that is used to assess symptoms of common mental disorders, including depressive symptoms in women around the time of pregnancy.
- (c) Psychiatric diagnosis is not commonly employed in large research studies because of cost. Instead, survey questionnaires of depressive symptoms are more common due to feasibility of implementation at scale.
- (d) The General Health Questionnaire is a general mental health questionnaire that is used to assess depressive symptoms in women during pregnancy and in the postnatal period.
- (e) There is no such questionnaire.

Question 2

Risk factors for perinatal depression in low- and middle-income settings include:

- (a) There are no known risk factors
- (b) Exposure to intimate partner violence
- (c) High family income
- (d) Previous history of depression
- (e) Poor family relationships

Answers to Question 2

- (a) F (b) T (c) F (d) T (e) T

Explanations for answers to Question 2

- (a) Maternal depression is not randomly distributed in the population. Several psychosocial and economic correlates have been identified across multiple settings.
- (b) Exposure to intimate partner violence is a risk factor for higher depressive symptoms in both the prenatal and postnatal period.
- (c) Evidence indicates that women with fewer economic resources are at higher risk for depression or depressive symptoms.

- (d) Previous history of depression or other mental disorders is related to depressive symptoms around the time of child birth.
- (e) Poor relationships with family members, including spouse and mother-in-law, are correlates of perinatal depression.

Question 3

There is research suggesting that the following are associated with perinatal depression:

- (a) Infant low birthweight
- (b) Preterm infant birth
- (c) Decrease in breastfeeding initiation
- (d) Child stunting
- (e) Practices and behaviors compromising child development

Answers to Question 3

(a) T (b) T (c) T (d) T (e) T

Explanations for answers to Question 3:

- (a) See a meta-analytic reviews: Grote et al 2010 for prenatal depression; Grigoriadis et al 2013 reported a relation only among low-socio-economic groups.
- (b) See the meta-analytic review by Grigoriadis et al 2013
- (c) See the meta-analytic review by Grigoriadis et al 2013
- (d) See the meta-analytic review by Surkan et al 2012 in LMICs
- (e) Much of this work has been conducted in high-income settings. There evidence pointing to suboptimal parenting practices among mothers with high levels of depressive symptoms (see reviews: Field 2010 and Lovejoy et al 2000; McLern et al. 2006).

Question 4

The following statements are true regarding interventions to reduce perinatal depression

- (a) Employing non-specialists health workers is considered a feasible strategy to address maternal depression
- (b) Cognitive behavioral therapy is not effective at reducing maternal depression
- (c) Health promotion is as effective as psychological intervention
- (d) Involving other family members is a key a feature of effective interventions
- (e) Interventions cannot target upstream factors such as empowerment

Answers to Question 4

(a) T (b) F (c) F (d) T (e) F

Explanations for answers to Question 4:

- (a) Recent research such as the Thinking Healthy Program in Pakistan (See Rahman et al 2008) has highlighted the feasibility of successfully using non-specialist health workers in low-resource settings; also see Chowdhary et al 2014.
- (b) Cognitive behavioral therapy is indicated for reducing maternal depressive symptoms
- (c) See Clarke et al for a meta-analysis based on 10 studies.
- (d) Based on guidelines from Zafar et al 2014, family engagement and assuring their support is important to the success of such interventions.

- (e) Although it may be costly and difficult to change cultural norms to improve empowerment, such upstream factors may be key to ultimately improving peri-natal depressive symptoms