Maternal Depression: The potential role of nutrition in prevention and treatment

INTRODUCTION
Depression during pregnancy and after delivery affects women around the globe. It is associated with increased maternal morbidity, poorer self-care, and it has significant harmful consequences for infants and children. The potential role of nutrition in preventing or contributing to maternal depression has been gaining attention. Nutrition is important for brain development and synthesis of mood regulators (such as serotonin, dopamine, and norepinephrine), which play a role in the pathophysiology of depression.

Mothers who are depressed during pregnancy are less likely to seek prenatal care, they may have a greater risk of pregnancy and labor complications, and their risk of suicide is higher. For children, the effects begin while they are still in the womb, with increased likelihood of low fetal weight, pre-term birth, and low birthweight. Caregiving compromised by maternal depression also affects physical growth and cognitive development. Studies have linked maternal depression to developmental delays demonstrated by a recent meta-analysis that found approximately 4.2 lower cognitive scores in children of depressed mothers 6-8 weeks postpartum compared with children of mothers without depressive symptoms. While the majority of studies have analyzed data from high-income countries (HICs), a meta-analytic study specifically focused on low- and middle-income countries (LMICs) found a 50 percent higher risk for underweight and 40 percent for stunting in children with mothers who had high levels of depression.

This brief by Pamela J. Surkan, Farah Behbehani, and Alive & Thrive presents what we know about the role of nutrition in predicting and preventing maternal depression. It also discusses interventions and platforms to address maternal depression within healthcare systems. Finally, it identifies areas for future research and action in understanding nutrition’s impact on maternal depression and identification of preventative nutrition interventions.

WHAT IS MATERNAL DEPRESSION?
- Maternal depression, also known as perinatal depression, is defined as depression occurring during pregnancy or up to the first year postpartum.
- Symptoms of depression include low mood, loss of interest or pleasure, disturbed sleep or appetite, low energy, and poor concentration.

* Definitions vary. The period after delivery is shorter in some clinical definitions. (e.g., Diagnostic and Statistical Manual definition of peripartum onset is only up to four weeks post-delivery). This brief uses the broader public health definition for perinatal depression that includes up to a year postpartum.

In LMICs, maternal depression is experienced by:

1 IN 6 PREGNANT WOMEN and 1 IN 5 WOMEN AFTER DELIVERY
FIGURE 1. Prevalence of postpartum depression in low and middle-income countries

From Parsons et al. British Medical Bulletin 2012; vol 101; page 61

PREVALENCE OF MATERNAL DEPRESSION

While high-quality studies of maternal depression are available for HICs indicating that about 10 percent of pregnant women and 13 percent of those who have given birth experience some degree of depression, the prevalence for women living in low- and lower-middle-income countries has only recently become the subject of research. Data are available from only 8 percent (9/112) of low- and lower-middle-income countries for prenatal depression, and from 15 percent (17/112) of low- and lower-middle-income countries for postpartum depression (Figure 1). Furthermore, these limited data do not allow for comparisons across countries—either within low-and middle-income group or with high-income countries—since the settings, recruitment strategies, inclusion and exclusion criteria, and other factors affect the representative adequacy of the samples, and assessment measures varied widely. Only broad comparisons are possible. However, rates are substantially higher than in HICs; in LMICs about 16 percent of pregnant women and about 20 percent of women who have recently given birth are experiencing maternal depression.

Depressive symptoms can occur throughout pregnancy and far beyond delivery. The variability of the timing of the condition was illustrated in a study from Côte d’Ivoire and Ghana that found distinct patterns in the prevalence of maternal depressive symptoms in different groups of women. In one group, depressive symptoms increased close to birth and
DETERMINANTS OF MATERNAL DEPRESSION

• Prior depression
• Prenatal anxiety
• Poverty
• Lack of control in reproductive health decisions
• Intimate partner violence
• Genetic predisposition
• Maternal illness
• Poor birth outcomes
• Large family size

As the consequences of maternal depression become better known, more research is focusing on identifying risk factors. Twin and sibling studies have shown that maternal depression is strongly influenced by both genetic disposition and the social environment. Social determinants of maternal depression, including poverty, maternal illness, large family size, poor birth outcomes, and women’s lack of control in reproductive health decisions are common in LMICs, possibly explaining why the prevalence of maternal depression is higher in LMICs compared to HICs.

Factors including social support and having a larger network of friends appear to be protective; both are inversely related to postpartum depression. Intimate partner violence has been linked to maternal depression across culturally diverse settings. Also, prior depression strongly predicts both prenatal and postnatal depression. Prenatal anxiety has also been identified as a major risk factor for postpartum depression. The mechanisms involved and the ways in which these risk factors for depression interact in LMICs are still not well understood.
Nutritional deficiencies are another potential risk factor for maternal depression. Different nutrients are needed for the synthesis of mood regulators, known as neurotransmitters (such as serotonin, dopamine, and norepinephrine), and thus may be involved in the regulation of one’s mood. Emerging evidence is expanding our understanding of the potential role that specific nutrients may play as biological risk or protective factors for maternal depression. This section looks at what we know about the biological function of depression, the extra burden women experience during pregnancy, and recent research on the role of key nutrients in maternal depression.
**BIOLOGICAL FUNCTION OF KEY NUTRIENTS**

Deficiencies in key nutrients affect the production and function of neurotransmitters, which are implicated in the development of depression. Some of the vitamins that have been proven to be vital to brain function include vitamin B-12, folate, and vitamin B-6. These vitamins are involved in several biological processes involving neurotransmitters.\(^3\)

Other nutrients that have been linked to altered mood include vitamin D and zinc. The link to vitamin D is thought to occur through its role in protecting the neurons of the hippocampus—the part of the brain that is associated with emotions.\(^40,41\) Zinc has been found to modulate the overall excitability of the brain through its influence on serotonin uptake and may explain reported associations between zinc and depression.\(^42\)

A deficiency in omega-3 fatty acids is thought to alter the brain's ability to transfer signals that regulate one's mood.\(^3\) While research has begun to examine the role of individual nutrients in the synthesis, metabolism, and function of hormones and neurotransmitters, there is a need for further research to improve our understanding of their role in the development of depression.\(^3,41\)

**THE EXTRA NUTRITIONAL BURDEN IN THE PERINATAL PERIOD**

Pregnant women are at increased risk for nutrient deficiencies, potentially increasing their chances of developing maternal depression. Additional nutrient requirements are higher during pregnancy and lactation\(^3\) in order to support the mother's metabolic needs related to reproduction as well as the baby's specific energy and nutrient needs for appropriate growth and development in the womb and after birth.\(^43\) For example, compared to non-pregnant and non-lactating women, pregnant women need 60 percent more folate and 170 percent more iron to meet the demands of fetal development (Figure 3).\(^44,45\)

The body’s requirements for additional nutrients in pregnancy can lead to nutrient depletion by the end of the pregnancy, especially when preceded by inadequate pre-pregnancy nutrient intake.\(^3\) Nutrient levels tend not to recover in the postpartum period.\(^46\) For example, maternal reserves of docosahexaenoic acid (DHA), a type of omega-3 fatty acid vital to fetal brain development, start to decline by the second trimester (as the fetus’s need for these nutrients increases). Maternal DHA stores are depleted by the end of most pregnancies and need around six months to restore themselves.\(^47\) Therefore, a lack of omega-3 supplementation in the diet can lead to essential fatty acid deficiency, which has

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**FIGURE 3. Increased nutrient requirements during pregnancy**

- **60% MORE FOLATE**
- **170% MORE鐵**
been linked to major depressive disorders. Other factors such as hormonal and lifestyle changes that occur during the perinatal period may in themselves increase the risk of maternal depression, and may also affect nutrient levels (influencing maternal depression through that pathway).

**RESEARCH ON DIETARY INTAKE OF KEY NUTRIENTS**

Recent studies have explored the relationship between key nutrients and maternal depression. Two systematic reviews of these studies are highlighted below.

**SUMMARY (REVIEW 1)**

**Type of studies**
- 35 articles:
  - Cross-sectional (n=16)
  - Cohort (n=12)
  - Case-control (n=1)
  - RCT (n=6)

**Results**
- 22 studies found some protective effects from dietary intake on maternal depression (e.g. on fish and PUFA intake, vitamin supplements, calcium, vitamin D, zinc, and selenium):
  - 11 demonstrated clear protective effects.
  - The other 11 could have been due to chance as they were observed in certain groups, but not as a trend.
- 13 studies found no association between dietary intake and maternal depression

**Conclusions**

These inconsistent results, due in part to methodological problems and weak study design, suggest the need for more research in order to reach a conclusion regarding the association with nutritional factors and maternal depression.

**SYSTEMATIC REVIEW 1: The role of diet and nutritional supplementation in perinatal depression**

A systematic review by Sparling, Henschke et al. synthesized evidence on whether dietary intake influences the risk of depression in the perinatal period. While 13 studies did not find evidence of an association, 22 studies indicated some protective effects from healthy dietary patterns, the intake of polyunsaturated fatty acids (PUFA) and fish, multivitamin supplements, vitamin D, calcium, zinc, and selenium. See Table 1 for detailed results.

Some of the studies with a clear protective effect include a study in Greece and another study conducted in Brazil, which found healthy dietary patterns were protective against depressive symptoms when compared with less healthy patterns.

When assessing total nutrient intakes, Paoletti et al. found that women taking full multivitamin supplements had lower levels of depression one month postpartum compared to women taking vitamin D and calcium supplements only. However, Miyake et al. also found benefits of dietary intake of vitamin D—observing a lower prevalence of antenatal depression in women who consumed the highest intakes of vitamin D compared to those with the lowest intake of vitamin D. In addition, two studies found that higher calcium intake was associated with lower depressive symptoms.

When examining the effects of PUFA supplementation, one in four randomized controlled trials (RCT) found that women receiving DHA in fish oil had lower levels of postpartum depressive symptoms compared to women taking the placebo. Two of four cohorts examining the effect of fish and essential fatty acid intake found a protective effect against depressive symptoms. In addition, a cross-sectional study in Japan showed that higher fish, DHA, and eicosapentaenoic acid (EPA) consumption was associated with lower prevalence of depression during pregnancy.
TABLE 1. Detailed findings from Sparling, Henschke et al. (2017)\textsuperscript{50}

<table>
<thead>
<tr>
<th>REVIEWED</th>
<th>MAIN FINDINGS</th>
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<tbody>
<tr>
<td><strong>Dietary Patterns</strong></td>
<td>Eight studies found healthy dietary patterns had protective effects against maternal depression.</td>
</tr>
<tr>
<td>(n=9)</td>
<td></td>
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<tr>
<td><strong>Total Nutrient</strong></td>
<td>Three studies found that a higher intake of the following nutrients had protective effects against maternal depression:</td>
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<tr>
<td>Intake</td>
<td>• Multivitamin supplementation (vs. calcium and vitamin D supplementation)</td>
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<tr>
<td>(n=6)</td>
<td>• High (vs. low) intake of selenium</td>
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<td></td>
<td>• High (vs. low) intake of total calcium, plant calcium, plant iron, potassium, dietary folate, and total folate</td>
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<td></td>
<td>One study found that higher intake of calcium was associated with more depressive symptoms.</td>
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<tr>
<td><strong>B Vitamins</strong></td>
<td>In one study, Riboflavin intake had protective association against maternal depression in the third-highest quartile, but not in the highest quartile.</td>
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<tr>
<td>(n=4)</td>
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<td><strong>Calcium</strong></td>
<td>In both studies, there was an association between calcium intake and decreased prevalence of depression.</td>
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<td>(n=2)</td>
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<tr>
<td><strong>Vitamin D</strong></td>
<td>One study found lower odds of depression among women in the highest quartile of vitamin D consumption compared to those in the lowest quartile.</td>
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<tr>
<td>(n=1)</td>
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<tr>
<td><strong>Zinc</strong></td>
<td>Lower zinc consumption was associated with increased prevalence of maternal depression.</td>
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<tr>
<td>(n=1)</td>
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<tr>
<td><strong>Fish and PUFAs</strong></td>
<td>One of four RCTs on supplementation with PUFAs found it affected maternal depression.</td>
</tr>
<tr>
<td>(n=12)</td>
<td>Two of four cohort studies on fish and essential fatty acid intake showed a protective effect against depression.</td>
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<tr>
<td></td>
<td>Two of four cross-sectional studies on fish and PUFA intake found evidence of protective effects on depressive symptoms during pregnancy.</td>
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**SYSTEMATIC REVIEW 2: Nutrients and perinatal depression\textsuperscript{49}**

The same authors conducted a separate systematic review focused on the relationship between blood nutrient levels and the risk of maternal depression (Table 2).\textsuperscript{49} In this review, 14 studies found evidence of an association between maternal depression and lower levels of vitamin D, fats and fatty acids, iron, selenium, zinc, and folate, while two studies found associations between maternal depression and higher levels of nutrients, and eight studies found no associations.

Of the nutrients reviewed, there was inconsistent but stronger evidence for vitamin D having a protective effect on maternal depression (based on mostly high-quality studies). Out of the 10 studies on vitamin D (which were predominately prospective cohort studies with sample sizes <200), six not only reported protective associations but found linear trends between vitamin D concentrations and depression. For fats and PUFA, there is some evidence for a protective effect, based on a cohort study examining high-density lipoprotein concentrations\textsuperscript{61} and three other studies focused on PUFA levels.\textsuperscript{62-64}
SUMMARY (REVIEW 2)

Type of studies
24 articles:
- Cross-sectional (n=5)
- Cohort (n=16)
- Case-control (n=2)
- RCT (n=1)

Results
- 14 studies found an association between maternal depression and lower levels of vitamin D, fats and fatty acids, iron, selenium, zinc, and folate.
- 2 studies found associations between maternal depression and higher levels of nutrients.
- 8 studies found no associations.

Conclusions
- Blood levels of specific nutrients potentially play a protective role in preventing maternal depression, but the results were inconsistent. Currently, the evidence is stronger for vitamin D compared with B vitamins or minerals.
- Because of paucity of data (only one study for many nutrients) and methodological limitations, findings are not conclusive.
- Causal inferences between nutrient levels and perinatal depression cannot be made.
- High-quality studies in populations with high prevalence of nutrient deficiencies are needed.

Of the five studies examining iron and maternal depression, only one reported a protective association. However, it was the study with the lowest risk of bias, a prospective cohort with sufficient power to detect an association. The four other studies on iron had cross-sectional or case-control study designs, the majority of which had small sample sizes (<200) and overall higher risk of bias.

Little evidence exists regarding other minerals as only a single study has examined each nutrient. Although studies that examined selenium, zinc, and magnesium had smaller sample sizes, they found that higher nutrient levels were associated with lower maternal depression.

There was also weak evidence for a protective effect of B vitamins on maternal depression. One study showed increased folate levels were protective against antenatal depression, but there was little evidence for any association between folate or vitamin B12 and maternal depression in three other studies focused on those nutrients.

However, it is unclear whether the study populations and methodologies of these studies were appropriate for detecting associations; for example, three of the four studies on B vitamins did not report the prevalence of nutrient deficiency and the last study reported a low prevalence (<5 percent).

<table>
<thead>
<tr>
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<tr>
<td>Vitamin B (n=4)</td>
<td>One study showed increased folate levels were protective against depression only in the antenatal period.</td>
</tr>
<tr>
<td>Vitamin D (n=10)</td>
<td>Six studies showed protective associations with linear trends between vitamin D concentrations and depression.</td>
</tr>
<tr>
<td>Iron (n=5)</td>
<td>One study showed anemia was protective against depression in the first trimester while another study showed iron deficiency and iron depletion were both associated with higher odds of developing postpartum depression at 32 weeks.</td>
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<tr>
<td>Selenium (n=1)</td>
<td>The study found significantly lower average Edinburgh Postpartum Depression Scale scores in the selenium supplement group compared to a control group.</td>
</tr>
<tr>
<td>Zinc and Magnesium (n=1)</td>
<td>The study showed decreased zinc concentrations (but not magnesium) were associated with more severe postpartum depressive symptoms.</td>
</tr>
<tr>
<td>Fats and fatty acids (n=4)</td>
<td>Three studies showed increased levels of omega-3 fatty acids were protective against depression. One study showed higher HDL concentrations were significantly associated with lower risk of antenatal depression.</td>
</tr>
<tr>
<td>All nutrients (n=1)</td>
<td>The study did not find any associations between essential fatty acids, micronutrients or carotenoids and depression.</td>
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RESEARCH ON INTERVENTIONS ADDRESSING MATERNAL DIET

Some research has focused on interventions to address the relationship between nutrient intake and postpartum depression, although research has not sufficiently advanced to offer nutrition-focused interventions as effective preventative measures.

SYSTEMATIC REVIEW 3: Perinatal nutrition interventions and postpartum depressive symptoms

Gould et al. reviewed studies focused on nutrition interventions of either omega-3 PUFAs, vitamin D, or overall diet during pregnancy and/or lactation and their effects on postpartum depressive symptoms (Table 3).

Of the 11 trials that studied PUFA supplementation, nine did not find a significant benefit of supplementation administered either antenatally, postpartum, or during a combination of both periods. Two small trials (including a study conducted in Iran) that included pregnant women with at least mild depression found a significant reduction in depressive symptoms in the PUFA supplemented group. The majority of these trials were considered to be low-to-moderate quality due to their small sample size (<100) and high risk of bias, and there was considerable heterogeneity between studies.

Conversely, no relevant RCTs were identified for vitamin D, however seven observational studies (one based in Turkey) of maternal vitamin D levels with postpartum outcomes showed inconsistent associations. Two Australian RCTs with dietary advice interventions in pregnancy had mixed results. One of the RCTs, conducted by Crowther et al., aimed to decrease maternal complications in women who were at risk of developing gestational diabetes. While the intervention reduced the risk of maternal complications including symptoms of postpartum depression, the study did not report whether or not the diets of participating mothers improved.

Conclusions

- Evidence is inconclusive for the role of perinatal nutrition in the prevention of postpartum symptoms.
- Further high-quality research is needed to determine whether nutritional interventions during pregnancy are protective against postpartum depression.
- Future prenatal nutritional interventions should include postpartum depression as an outcome.

### TABLE 3. Detailed findings from Gould et al. (2017)

<table>
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<tr>
<th>REVIEWED</th>
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<tbody>
<tr>
<td>Fish oil (n=11)</td>
<td>Two RCTs showed positive effects of omega-3 on postpartum depressive symptoms.</td>
</tr>
<tr>
<td>Vitamin D (n=7)</td>
<td>No relevant RCTs were identified. Of the seven observational studies assessing the relationship between vitamin D status and postpartum depression, four showed an association between low maternal serum vitamin D levels and postpartum depression.</td>
</tr>
<tr>
<td>Diet (n=2)</td>
<td>One study that randomized pregnant women at risk of developing gestational diabetes to receive individualized lifestyle and dietary advice vs. standard care, found less likelihood of postpartum depression in the intervention compared to the control group.</td>
</tr>
</tbody>
</table>
The other RCT enrolled overweight women with the aim of reducing gestational weight gain to improve maternal and infant outcomes.78 Contrary to Crowther et al.’s findings, the authors concluded that although women in the intervention group improved their diets, postpartum depressive symptoms were not different between the groups.78 Although there are similarities between these two large Australian RCTs, such as use of the Edinburgh Postpartum Depression Scale, the trials were not designed with postpartum depression as a main outcome.74

Based on these findings, evidence is inconsistent regarding the influence of dietary intake on the risk for maternal depression, with stronger support for some nutrients over others.49 The weakness of the evidence to support a protective association between nutrients and maternal depression include the limited number of studies in this area as well as their methodological limitations (rather than lack of true associations). Identification of the limitations shared by studies on this topic offer some pathways for conducting future high-quality studies.
GAPS IN THE EXISTING NUTRITION RESEARCH AND RECOMMENDATIONS FOR FUTURE STUDIES

To better understand whether certain diets and nutrients influence the risk of maternal depression, several methodological limitations need to be addressed in future studies. Many studies to date have used a single food frequency questionnaire (FFQ) to estimate average nutrient intake, which can be imprecise and suffer from reporting bias. On the other hand, some studies measured nutrient biomarkers (i.e. blood levels of nutrients) which are generally precise indicators of nutrients made available by the body. However, nutrient blood analysis is costly and only available for a few nutrients.

A more robust approach would be to collect multiple records of food intake to get at average nutrient intake and to couple this with measures of specific nutrient biomarkers.

Specific to pregnant women, measuring nutritional status at multiple times in pregnancy and at similar stages of pregnancy is important; levels measured at the beginning of pregnancy may not be comparable with nutrient levels around the time of birth, even within the same woman, as pregnancy and lactation deplete nutrient levels throughout the perinatal period. Ideally, dietary intake should be measured at several time points to adequately assess the magnitude of change over time.

As the majority of studies to date have been cross-sectional (where both nutrient intake and depression were measured at the same time), longitudinal studies are needed to determine the directionality of these associations. It is important to measure depression with an appropriate time lag where one can reasonably expect to see an onset of depression after a nutritional deficiency.

Finally, most studies have had small sample sizes (<200 participants) limiting the power to detect an effect between nutrient deficiency and maternal depression. The majority of studies have also been conducted in HIC where the prevalence of nutrient deficiencies is typically low. More studies are needed in LMICs with larger samples sizes.

RECOMMENDATIONS

- Conduct more studies in LMICs.
- Conduct more randomized controlled trials.
- Measure dietary intake at several time points to adequately assess the magnitude of change over time.
- Collect multiple records of food intake to get at average nutrient intake.
- Couple assessments of dietary intake with measures of nutrient concentrations when possible.
- For pregnant women, measure nutritional status at multiple times in pregnancy and at similar stages of pregnancy.
- Carry out longitudinal studies to determine the directionality of associations between nutrient intake and maternal depression.
- Build an appropriate time lag in studies for detecting depression after nutritional deficiency.
CONCLUSION

Maternal depression is a debilitating condition for mothers that has serious potential consequences for them and their offspring. It is especially prevalent in LMICs, possibly because of socio-economic and other social-environmental conditions and cultural factors that disproportionately affect women in these settings. There is evidence that maternal depression affects fetal and neonatal development, as well as physical growth and cognitive development of the child when the mother’s caregiving is compromised. Policymakers can help relieve the burden of maternal depression by addressing depression in clinical care and including screening for maternal depression during pregnancy. 

The need to prevent and manage maternal depression as part of universal health care is becoming widely recognized. A substantial amount of the impact of maternal depression on children is probably related to parenting behaviors and practices. Responsive maternal-child interactions, including breastfeeding, form the foundation of healthy attachments that are critical in infancy and early childhood. Potential mediators between maternal depression and early childhood development include maternal responsiveness, parenting style, the quality of the home environment and maternal caregiving practices including infant and young child feeding. Although current research is still inconclusive, some researchers have suggested that both malnutrition and depression in pregnancy are associated with behavioral problems in offspring and may share biological mechanisms. Given that both malnutrition and maternal depression co-occur at high rates in LMICs, the synergy of these conditions is relevant in this context and should be investigated further.

While psychological interventions delivered by non-specialists may also be an immediate strategy to reduce the symptoms of maternal depression, there is a need to further understand the impact of nutrition in maternal depression, and the potential of interventions to address deficiencies. Available evidence suggests certain nutrients could play a role in the development of maternal depression. This current evidence appears to be stronger for vitamin D compared with B vitamins or minerals. While overall inconclusive, the potential for appropriate nutrition to prevent maternal depression warrants further research as nutritional interventions are stigma-free, address a potentially modifiable risk factor, and may offer a cost-effective approach with added benefits to various health outcomes. Future high-quality RCTs are needed in low-income settings with a higher prevalence of nutritional deficiencies to determine whether nutrition is an effective means of preventing maternal depression.
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