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Maternal depression and mental health in early childhood: an examination of underlying mechanisms in low-income and middle-income countries

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Studies examining mechanisms underlying associations between maternal depression and adverse child outcomes (including behaviour, socioemotional adjustment, and emotion regulation) indicate that during pregnancy, maternal depression could affect child outcomes through altered placental function, epigenetic changes in the child, and stress reactivity. Infection and dietary deficiencies in the mother and the child, together with the child's genetic vulnerability, might also affect outcome. Postnatally, associations between maternal depression and child outcome are influenced by altered mother–child interactions, sociodemographic or environmental influences, and social support. Knowledge is scarce on mechanisms in low-income and middle-income countries where maternal depression is highly prevalent, and stressful factors that influence the development of perinatal maternal depression and adverse child outcome (eg, food insecurity, perinatal infections, crowded or rural living conditions, and interpersonal violence) are both more intense and more common than in high-income countries. We reviewed evidence and use the biopsychosocial model to illustrate risk factors, mediators and moderators underlying associations between maternal depression and child outcomes in low-income and middle-income countries.

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This is the second in a Series of two papers about maternal depression and child outcomes in low-income and middle-income countries

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Introduction

Depression is a leading cause of disability worldwide.[1] Since women are more likely to be affected than men,[2–4] particularly during the childbearing years,[5] maternal depression is highlighted as a global public health issue.[6] Maternal depression in the perinatal period is linked to a wide range of adverse child outcomes, including compromised physical and cognitive development, behavioural difficulties, and increased risk for later common mental disorders in the offspring.[7–9] A growing body of evidence points to common mental disorders (such as depression, anxiety, and stress) during pregnancy as conferring a specific risk to the developing fetus and affecting later child development, including associations with negative child temperament, anxiety, oppositional behaviour, and symptoms of attentional deficits.[10,11] Yet, to date, much of what is known on the links between perinatal depression (both prenatal and postnatal) and child outcome tends to come from studies done in high-income countries,[12,13] and much less is known about low-income and middle-income countries,[12,14] where most children live worldwide.[5] Prevalences of common perinatal mental disorders including depression and anxiety are substantially higher in low-income and middle-income countries, particularly in poorer rural areas.[12] Prevalences of maternal depression have been shown to vary among these settings, yet they are estimated to be two-to-three times higher than in high-income countries,[13] ranging from 5% in Ethiopia to up to 35% in South Africa.[15] In five low-income and middle-income countries (Ethiopia, India, Nepal, South Africa, and Uganda), prevalence during pregnancy was higher than reported postnatally.[15] Differences in prevalence might be partly because of the diversity in screening methods, lack of formal validation of these methods in the country or language against a gold standard (to establish appropriate cutoff scores for detecting symptoms meeting diagnostic criteria in that setting), cultural influences, and whether information is gathered from rural or urban settings.[12] There is increased exposure to known risk factors for depression in low-income and middle-income countries, namely, exposure to violence, particularly intimate partner violence; war; disasters; food insecurity; child maltreatment; sanitation deficiencies; shortage of accessible good quality health-care services, including difficult access to contraception (therefore contributing to unwanted pregnancy); and high prevalence of diseases such as tuberculosis, malaria, and HIV and other sexually transmitted diseases.[16–20] Although recent years have witnessed an increase in the number of studies examining maternal depression in low-income and middle-income countries, many of these studies have focused on outcomes pertaining to child physical health (ie, growth, stunting, birth complications),[21,22] or have examined risk factors for maternal antenatal and postnatal depression.[12,19,23–30] There is little information linking maternal depression with subsequent child behaviour and mental health.[31] We focused this report on the mechanisms that might explain associations between maternal depression and child outcome in low-income and middle-income countries within the first 5 years of the child's life. We focused on these early years given the child's increased dependence on the mother; however, we also drew from relevant studies of

older children including follow-up studies or those that are informative of mechanisms. Although maternal depression was the main exposure of interest, we acknowledge that anxiety disorders have not been as widely studied in low-income and middle-income countries as depression, despite high comorbidity, and not all psychological morbidity cited can be accurately construed as depression for the reasons we have mentioned. Thus, we used the term maternal depression more broadly to cover all of these conditions. The main child outcome of interest was mental health, yet given the focus on age 0–5 years, this outcome consists of more developmentally appropriate indices of temperament, behavioural difficulties, socioemotional development, attachment, and emotion regulation. When relevant to understanding mechanisms, we also refer to studies that include child cognitive outcome, given the rapid neurodevelopment during the first years of life and links between neurodevelopment and child mental health.

We used a biopsychosocial model to explain the intergenerational transfer of risk (figure), adapted to the context of low-income and middle-income countries. Although we expect that many of these mechanisms are likely to operate in a similar way in countries of all income levels, it is the context within which the depression occurs, including exposure to a multitude of risk factors at once, which is likely to differentiate high-income countries from low-income and middle-income countries. Knowledge of mechanisms is important for informing on the most appropriate and effective interventions that could be administered in such resource-constrained countries.

Potential mechanisms linking maternal depression in the prenatal period and child mental health

Fetal programming

There is considerable evidence from high-income countries that prenatal maternal depression and other forms of stress are associated with a range of adverse mental health outcomes for the child, including an increased risk of anxiety, depression, attention deficit hyperactivity disorder, and conduct disorder.[32] Although there is less research from low-income and middle-income countries, there are now several studies that show similar associations between prenatal maternal stress or depression and increased rates of adverse child outcomes.[30,33–36] These associations, found in large population studies that have taken into account a wide range of possible confounders such as smoking, alcohol consumption, paternal prenatal mood, and postnatal maternal mood and parenting, are likely to be partly due to fetal programming. The term fetal programming suggests that environmental influences during sensitive periods of gestation might alter the development of the fetus with long-lasting effects on the offspring. In one UK population cohort study,[37] if the mother was in the top 15% for symptoms of depression, following adjustment for confounders, her child had double the risk of a probable mental disorder at age 13 years. The effects were additive with those of postnatal depression. Fetal programming does not imply that the trajectory, started in utero, cannot be changed later. There is considerable evidence[38] that sensitive mothering can buffer the effects of prenatal stress, at least for some outcomes, and that insecure

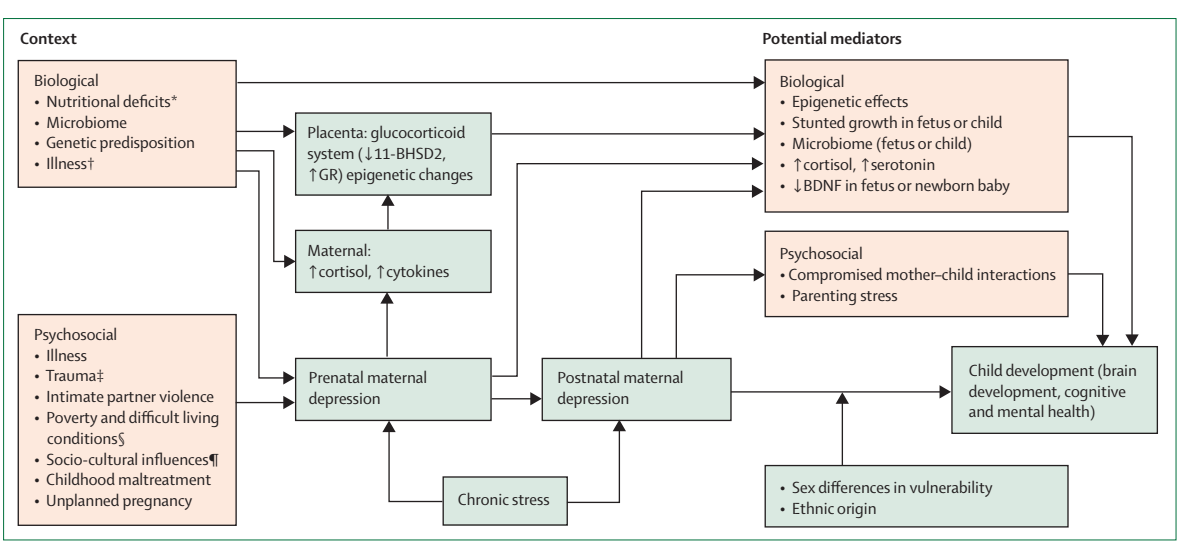

Figure: Model of mechanisms linking maternal depression and child mental health outcome: a focus on low-income and middle-income countries
Mechanisms underlying associations between maternal depression and child mental health outcomes are likely to be similar in high-income countries, and in low-income and middle-income countries. However, the context in which maternal depression occurs is likely to be different, with risk factors increased in low-income and middle-income countries. We expect such contextual risk factors might have both additive and interactive effects. Some risk factors could also be considered as both biological and psychosocial (eg, illness could have a biological and psychosocial effect on wellbeing). BDNF=brain derived neurotrophic factor. *For example, iodine or iron deficiency. †Include HIV, tuberculosis, malaria. ‡Includes war, natural disasters, and political and interpersonal violence. §Includes food insecurity and unmet needs. ¶Includes views of mental illness, family structure, gender roles, and maternal education.

attachment can exacerbate prenatal effects. Many of the studies have made use of different methods for measuring prenatal maternal mood; some have measured symptoms of depression, some anxiety, pregnancy-related anxiety, life events, or acute disasters such as a Canadian ice storm,[39] and few have made a clinical diagnosis of depression. We do not yet know whether these different types of mood change have different effects on child outcome, or whether they operate by different mechanisms. Post-traumatic stress disorder for example, can be associated with reduced cortisol output,[40] whereas other forms of anxiety, depression, and stress are often associated with increased cortisol concentrations.

The biological mechanisms underlying the fetal programming effects of prenatal maternal mood disturbance are just starting to be uncovered. The changes in the mother that induce changes in the development of the fetal brain are not clear. There is evidence that exposure to increased in-utero cortisol can affect fetal brain development in both rodent animal models and human beings.[38,41] However, in women, as pregnancy develops, the placenta produces large quantities of cortisol, and the mother's hypothalamic–pituitary–adrenal (HPA) axis becomes less sensitive to her own depression or external stress.[42] Prenatal stress and depression can still cause the fetus to be exposed to more cortisol, via alterations in the function of the placenta. Several studies have now revealed that there is altered expression of HPA-related genes in the placenta in association with maternal prenatal distress, including downregulation of the gene for 11-beta-HSD2,[43] the enzyme that metabolises cortisol, and upregulation of the gene for the glucocorticoid receptor NR3C1.[44] Several other biological systems are also likely to be involved. The placenta, for instance, is rich in serotonin and increased concentrations have been shown to alter fetal brain development.[45] There is considerable interest in the cytokines too, since several studies[46,47] have revealed that prenatal maternal depression, or a maternal history of early trauma, are associated with raised concentrations of prenatal maternal cytokines.

Genetic influences and gene–environment interactions

We know that not all children are affected by prenatal depression or other forms of stress, and those who are can be affected in different ways. This effect is partly due to the nature of the postnatal care, but also to the genetic make-up of the individual child, and gene–environment interactions.[48] Changes in the child are likely to be due, at least partly, to epigenetic changes. High pregnancy-specific anxiety has been associated with epigenetic changes in the promoter for the glucocorticoid receptor in the newborn baby.[49] Maternal exposure to intimate partner violence has been associated with epigenetic changes in the promoter for the same receptor in the blood of their adolescent children.[50] Increased exposure to trauma might also increase stress reactivity and lead to epigenetic changes in mothers and offspring. For instance, a study of 25 pregnant women exposed to the Tutsi genocide compared with 25 unexposed women reported increased methylation of the NR3C1 receptor and alterations of the HPA axis in mothers and their children,[34] which contributed to increased risk for offspring depression and post-traumatic stress disorder 20 years later.

Different genetic patterns in different populations could also alter the programming effects of prenatal depression. Teh and colleagues[51] have shown how the effects of the in-utero environment, including the effects of prenatal depression on the epigenetic pattern in the child, also depend on the genetic make-up of the child. The GUSTO cohort is comprised of the three major Singaporean ethnic groups, Chinese, Malay, and Indian. Analysis of the genotypes and DNA methylation patterns of neonates showed that approximately 25% of the variably methylated regions were explained by genotype, with the remaining 75% explained by the interaction of the genotype with different in-utero environments, including maternal smoking, maternal body mass index, infant birthweight, gestational age, birth order, and maternal depression.[51]

Environmental and nutritional influences

There are few studies of the possible mechanisms that could underlie the effects of prenatal maternal depression on child mental health in low-income and middle-income countries. However, there is evidence concerning several factors that are probably relevant, including social and environmental factors, which can contribute to maternal depression in these countries, and also the several biological factors such as nutrition, infection, and genetics, which could alter or exacerbate the effects on the fetus and the child. A review[52] of 31 studies in Latin America and the Caribbean examined the effect of intimate partner violence during pregnancy, and reported an increased risk for prenatal depression, unwanted pregnancy, obstetrical complications, and stress reactivity. Similarly, in rural Vietnam,[53] partner violence was associated with prenatal maternal depression. Some, but not all, of the evidence on mechanisms from studies in high-income countries might apply or guide thinking regarding mechanisms in low-income and middle-income countries.[10,14] However, key differences are likely to exist. In Vietnam, many pregnant women have low concentrations of vitamin D,[54] iron,[36] or iodine,[55] and these in turn can affect fetal and child neurodevelopment. An increased load of infection and different diets might also change the maternal microbiome (the pattern of bacteria, especially in the intestine), which is increasingly being related to health, including mental health.[56] One study[57] has indicated how prenatal stress can alter the pattern of the microbiome in the newborn baby. This pattern could potentially influence child neurodevelopment and later mental health.[58] Disruption of the microbiome in early life has the potential to influence neurodevelopment and mental health outcomes in the long term, particularly through

its interaction with the immune system and the gut–brain axis, which can involve both serotonin and cytokines.[59] The pattern of the vaginal microbiome has been found to differ between white and non-white women.[60]

Prenatal influences on the developing hypothalamic–pituitary–adrenal (HPA) axis

Some of the effects of prenatal depression or stress on the child could be mediated by an alteration of the function of the HPA axis. In a study in India, Fernandes and colleagues[61] showed an association between maternal prenatal depression and alterations in cortisol reactivity in the infant, with a U-shaped pattern of response. However, there might also be ethnic group differences in the function or reprogramming of the HPA axis. A study by Ward and colleagues[62] suggests that, compared with white populations, participants of south Asian origin are more likely to display HPA axis hyperactivity as a result of sensitivity to the effects of glucocorticoids, an effect amplified by adiposity. It is well established that the content and distribution of body fat is markedly different in different ethnic groups.[63]

Potential mechanisms linking maternal depression in the postnatal period and child mental health

Studies from high-income countries have indicated associations between maternal depression in the postnatal period and a range of adverse childhood outcomes.[8,11] Within the context of low-income and middle-income countries, there is a larger body of literature examining maternal depression postnatally compared with the prenatal period. Postnatal maternal depression might be affected by continuity of earlier depression, in addition to new challenges associated with parenting. Many of the studies examining postnatal maternal depression and child outcome in low-income and middle-income countries have tended to focus on child growth and morbidity. Far fewer studies have linked maternal depression with indices of child mental health such as temperament, socioemotional development, emotion regulation, or behaviour.[31] One examination[64] of child adversities and mental health in 21 countries from the World Health Survey (including 12 low-income and middle-income countries) indicated that childhood adversity and later common mental disorders are likely to be linked through more general mechanisms, and maladaptive family functioning (including parent mental disorders) was the strongest predictor of common mental disorders in offspring. Within a study of five low-income and middle-income countries, economic and social adversity, including marital and interpersonal difficulties and poverty, were highlighted to play an important role.[15]

The early caregiving environment

Many studies, from countries of all income levels, have pointed to the early mother–infant relationship, including parenting and mother–child interactions, as a key mechanism underlying the association between maternal depression and child outcome. An investigation in Vietnam[35] followed up women from the second trimester of pregnancy until 6 months post partum and examined the influence of mental health difficulties such as maternal depression on child socioemotional development at age 6 months. Results indicated that neither antenatal nor postnatal (at 6 weeks) depression were associated directly with infant socioemotional development at 6 months, but rather this association was mediated by parental efficacy and early parenting practices. Other work from South Africa[65,66] has highlighted how mother–child interactions (such as maternal intrusiveness and coerciveness) mediate associations between maternal postnatal depression and early childhood attachment. Similarly, a longitudinal study in Bangladesh[67] has indicated how the caregiving environment (assessed with the Home Observation Scale) mediates associations between maternal depression scores and irritable infant temperament and cognitive development between 6 and 12 months of age. Implications of such findings for developing and targeting interventions are discussed later.

Child maltreatment, physical punishment, and the familial context

The familial context has been shown to affect both maternal depression and child development, and familial adversity has been linked to later child mental health problems across 21 countries in the World Health Survey.[64] Research from various low-income and middle-income countries identifies intimate partner violence as an important factor contributing to maternal depression in the perinatal period.[12,25,68–70] Another study[71] has revealed links between antenatal and postnatal maternal depression (but not necessarily anxiety) and increased parenting stress. A study[72] in children aged 13–55 months and their mothers in Uruguay indicated that parenting stress, particularly parental distress and dysfunctional parent–child interactions, was associated with high depression scores in mothers. Although child behaviours were not specifically assessed, findings indicated the importance of considering that multiple risk factors could work together. Depression has also been linked to a more stressful living environment. A study[73] in 370 children aged 5–10 years living in an urban slum in India reported that maternal depression was associated with child emotional and behavioural problems, but that odds ratios for maternal depression were smaller than the influence of having an alcoholic father or conflicts in the family. Another potential mechanism could work through parenting methods, more specifically, harsh punishment.[74] Research in high-income settings has shown that depressed mothers might be less sensitive to their child and could be more likely to resort to harsh parenting.[75,76] Both intimate partner violence and maternal depression

have been linked to harsh maternal parenting practices.[77] A study in Brazil[78] assessed data from 480 participants aged 6–17 years, and showed that maternal depression was a risk factor for child internalising problems, but not necessarily externalising problems. This association was altered by exposure to harsh physical punishment and the presence of a father figure.[78] A follow-up of these children 5 years later[79] indicated that both physical punishment, and to a slightly lesser extent maternal depression and anxiety, contributed to mental health problems in adolescents. Another study[80] from Brazil examined the longitudinal associations between maternal depression and child mental health assessed at age 6 years. Both antenatal and postnatal depression at 3 months were associated with increased odds of a child psychiatric disorder at age 6 years. This odds ratio was reduced slightly once the authors tested for mediation by duration of breastfeeding or admission to hospital in the first year of life. Another longitudinal study[81] assessed maternal anxiety and depression and anxiety in offspring as they transitioned into adulthood. The authors reported that female offspring were particularly susceptible to the effects of maternal depression, and suggested that during the transition to adulthood, girls might be more likely to turn toward their mothers for support, which could be compromised in the case of increased symptoms of maternal depression.

Infant and child growth

Some studies have revealed associations between maternal depression and compromised child growth and physical development in low-income and middle-income countries,[21,82] and one investigation[21] reported that this effect persisted to age 8 years in India and Vietnam. There is evidence that the association between maternal depression and poorer child growth could operate through the caregiving environment. An investigation in Bangladesh[22] found that maternal depression was associated with stunted growth between 6–12 months of age, with effects partly mediated by the caregiving environment. The authors cautioned that it was difficult to establish whether maternal depression preceded stunted growth.

Child growth, particularly in the first years of life characterised by rapid neurodevelopment, can have implications for child behavioural and socioemotional development. A study from Ethiopia[83] indicated that stunting was associated with decreased developmental scores in 437 children aged 3–24 months, yet once stunting was taken into account, symptoms of maternal depression, more than anxiety, were associated with child developmental outcome. Although this study did not explicitly examine mechanisms, it was suggested that factors such as poverty and food insecurity might contribute to maternal depression and anxiety, which in turn could partly mediate associations between child developmental outcome and insecurities of poverty and food acquisition. A study in Soweto-Johannesburg, South Africa,[84] examined symptoms of maternal depression at 6 months post partum and child behaviour at 2 years in 635 mother–infant dyads participating in the Birth to Twenty cohort. Maternal depression was associated with a range of child behaviour difficulties at an age of 2 years (including sleep and eating difficulties, hyperactivity, temper tantrums, and relational difficulties), after adjusting for socioeconomic status and child characteristics such as gender and preterm delivery. However, the contribution of maternal depression did not reach significance once stunted growth was taken into account. This finding suggests that child stunting might mediate the association between maternal depression and child outcome. Longitudinal cohort studies, with measures started prenatally, are necessary to elucidate these associations.

As indicated earlier, nutritional factors such as iron deficiency and anaemia might be tightly linked to child neurodevelopment and behaviour,[85] as well as to symptoms of maternal depression. An investigation in the deprived South African community of Khayelitsha[86] indicated that iron deficiency in mothers could contribute to poorer mother–infant interactions. More specifically, fatigue, irritability, and depressive symptoms associated with iron deficiency could contribute to the mother being less emotionally available to her baby and the infant being less responsive to its mother as a result. Importantly, these interactions improved following iron therapy, highlighting that knowledge of the specific mechanisms underlying an association can produce successful interventions.

Illness

Many low-income and middle-income countries face the additional threat of increased prevalence of infections such as HIV and other communicable diseases such as tuberculosis.[2] Prevalence of HIV varies greatly across these countries, and HIV remains a leading cause of death among pregnant women of reproductive age.[15,87] HIV is associated with depression[88] and increased risk for postnatal depression. A study of 83 South African women with HIV and their infants,[89] found that 42·2% of mothers met criteria for depression and 31·3% of babies were socially withdrawn at 10–12 months of age. Results did not support a direct link between maternal depression and infant social withdrawal, although the authors suggested that maternal depression might be associated with mothers' immunity and HIV disease progression, which could in turn negatively influence mother–child interactions and subsequent behaviour of the baby. A study from China[90] recruited 754 parent–child dyads in which a parent was diagnosed with HIV. Parenting stress mediated associations between caregiver distress (ie, depression) and child wellbeing (assessing loneliness, depression, and self-esteem). However, this study did not stipulate the number of mothers versus fathers who were included or record the identity of the parent completing

the questionnaire. Consistent with this work, a study from South Africa[91] has indicated that parents and caregivers with HIV or AIDS might have difficulty engaging in positive interactions with their child.

There is accumulating evidence of a consistent and strong association between maternal depression and an increased risk of a range of adverse child outcomes in low-income and middle-income countries. There are also plausible psychological, social, and biological pathways through which effects of maternal depression can affect various aspects of child development. However, two challenges still present themselves. The first is that the link between maternal depression and child outcome is not necessarily entirely causal. Other, sometimes unmeasured, confounders (eg, socioeconomic factors and family conflict),[92] are likely to account for at least some of the association. Most intervention studies to date have not established that an improvement in maternal perinatal depression leads to an improvement in child outcome,[33,93] raising questions as to the extent of confounding. Few sufficiently powered intervention trials have been done to date, so there is still much to establish. The second challenge is the disentangling of the complex interacting nature of depression and related risk factors such as nutritional deficiencies, serious infections like HIV, and other psychosocial adversities. The same factor might act as a moderator of the risk of depression, as a potential confounder, and could also lie on the causal pathway between maternal depression and child outcome. This complexity has to be considered when focusing on implications for treatment intervention—who might benefit from which intervention, and at what point in pregnancy or the postnatal period?

Strategies for interventions

A better understanding of the mechanisms underlying associations between maternal depression and child outcome can contribute valuable information to the development of more effective intervention programmes. There is still a substantial shortage of research on effective interventions for maternal depression and child development in low-income and middle-income countries.[18] A handful of randomised trials done in deprived areas have revealed benefits for mothers or children. The constructs targeted by interventions tested in these trials are varied, ranging from the mother–child interaction and maternal sensitivity, to specific symptoms of maternal depression targeted by use of principles of cognitive behavioural therapy. Although the direct comparison of these trials is difficult because of differences in the intervention, the age at which the child was assessed, the specific outcome assessed, and the measures used,[94] intervention-specific benefits are seen for the mother or child in relation to outcomes. For instance, a pilot study,[95] targeting 64 mother–child dyads found that among dyads in the intervention group, mothers revealed more positive affect and sensitivity during free play and feeding with infants aged 6 months, although symptoms of maternal depression were not specifically reduced. A randomised trial[96] in a deprived area of South Africa tested an intervention aimed at improving mother–child interaction. 441 women were recruited in their final trimester of pregnancy, mother–baby interactions were filmed and coded at 12 months, and attachment was assessed at 18 months. Mother–baby dyads that received the intervention, compared with those who did not, showed improved maternal sensitivity, lower coerciveness, and more secure attachment. However, the intervention did not reduce maternal depression symptoms. Similarly, a randomised trial[97] done in Bangladesh on 322 malnourished children aged 6–24 months assessed the effect of a psychosocial stimulation intervention in addition to food supplementation, and reported that although the intervention benefited the children in terms of growth and development, there was no significant benefit for the mothers' depression symptoms 6 months later.[98] A randomised trial[99] in rural Uganda tested the effects of a parenting intervention for 291 mother–infant dyads. Mothers were recruited when their child was aged 12–36 months. 12 group sessions and two home visits were done within a 10-month period. The intervention aimed to improve maternal psychological wellbeing and child development through targeting psychosocial stimulation, dietary diversity, hygiene, and mothers' relationships. This study included various measures of child development and examined mediators in the association between the intervention and outcomes, including the involvement of fathers in the study. Mothers in the intervention group reported fewer depression symptoms than reported in the control group, and after 3 months, children's cognitive and receptive language scores were higher in the intervention group than in the control group. The caregiving environment and stimulation partly mediated the association between the intervention and child outcome, perceived positive social support and active coping partly mediated the association between the intervention and maternal depressive symptoms. These results suggest that the intervention improved the stimulation provided to the child as well as the mothers' functioning, which partly explained the effect on child outcome and mothers' depression symptoms. A similar parenting intervention provided in Bangladesh[100] found that an intervention targeting parenting abilities (including dietary and hygiene in young children aged 6–12 months and 12–24 months, promotion of positive interactions, and reduced harsh discipline) was associated with benefits for child language and cognitive development. This study also tested whether the modality of intervention delivery (ie, at home or within a group based in the community) affected outcome. There was an advantage of the group-based delivery for reducing maternal depression symptoms.

The Healthy Thinking Programme in Pakistan,[101] has administered, through community health-care workers, sessions targeting cognitive behavioural principles such

as listening, questioning thought processes, and homework, and recruited women in their final trimester of pregnancy. Mothers and their babies in intervention and control groups were evaluated at 6 months and 12 months postnatally. The intervention did not specifically affect children's growth, although less stunting was seen at 12 months of age in the intervention group than in the control group.[101] Furthermore, children of mothers in the intervention group had fewer diarrhoeal episodes 2 weeks before the 12-month evaluation and were more likely to have been vaccinated. Mothers also had fewer symptoms of depression at follow-up. These results suggest that the intervention targeting maternal depression helped to reduce the mothers' depression while potentially aiding in their ability to care for the child. However, a follow-up study[33] of these participants when children were aged 7 years indicated that initial benefits did not continue long term; the intervention group showed no benefits in children's cognitive and behavioural difficulties, and even slightly worse (although not significant) scores on anxiety than did the control group. The authors noted that increased relapse rates of maternal depression could have accounted for the absence of a positive effect in the long term, but also questioned whether one targeted intervention is enough to have long-term effects on child development.

Qualitative work, including interviews with depressed women and their families, has pointed to the primary importance of having culturally sensitive interventions.[102] Investigations[102–104] have examined whether women's groups or interventions led by trained women from the community could be acceptable and effective. These studies generally point to the benefits of having community-based health-care workers: important characteristics included being local, trustworthy, and integrated within the health-care system. Other research[105] has highlighted that, in order not to overburden services, interventions should target specific issues. However, no one intervention is likely to affect child development and maternal depression long term,[33] and developmentally appropriate booster sessions might be necessary as the child develops. The Programme for Improving Mental Health Care, a WHO research consortium of five low-income and middle-income countries (Ethiopia, India, Nepal, South Africa, and Uganda), is a 6-year programme that aims to generate evidence-based knowledge on implementing mental health treatment programmes in resource-constrained areas.[106] Across these countries, the context of pregnancy, childbirth, and postnatal care varies widely, thus plans to integrate mental health into these primary care settings need to adapt the services to fit the context of care more closely.[15] Rahman and colleagues highlighted, in a meta-analysis of intervention studies,[94] the importance for psychological and educational components of the intervention to be well adapted to the living circumstances and cultural background of the participating women.

Challenges to studying mechanisms in low-income and middle-income countries

There remain large gaps in the knowledge of long-term effects and mechanisms underlying these associations despite valuable work done in the past 10–15 years (panel). Low-income and middle-income countries present additional challenges that make it difficult to study these kinds of mechanisms, including few resources for research, difficulties in following up people over time, and cultural influences on how mental health is viewed. Migration patterns, as seen in South Africa,[107,108] contribute to difficulties in following families longitudinally.[108,109] Furthermore, both the design and running of studies in areas facing severe deprivation (devastating effects of communicable diseases such as HIV and AIDS, food insecurity, war or political violence, and effects of climate change) raise logistical and ethical challenges.[107] Health-care workers are overburdened and face a crisis in which basic physical health issues might not be met, leaving little capacity or few resources for dealing with mental disorders,[102,105] including maternal depression. Delivery of treatment of maternal depression becomes an even greater challenge where resources are scarce and maternal depression could have wide-reaching effects for the mother and the child.[110] Hence, there is a need for integration of mental health care and shifting of tasks from professionals to trained health-care workers with fewer qualifications.[102,111]

Conclusions

Maternal depression is a global public health issue that must be addressed to break an inter-generational cycle of transmission. We have used a biopsychosocial model to explain the mechanisms underlying associations between maternal depression and child mental health outcome, and suggest that although the mechanisms are broadly similar in countries of all income levels, it is likely that the context within which the depression occurs is especially problematic in low-income and middle-income countries. Results of intervention studies

Panel: **Key challenges and research questions**

- Longitudinal studies in low-income and middle-income countries that incorporate both biological and psychosocial data are needed to understand the underlying mechanisms that link perinatal maternal depression and child outcome in these countries
- Better understanding of which factors (biological or psychosocial) are particularly important or specific to some low-income and middle-income countries is needed to inform policies to target those most at risk
- More detailed knowledge of the factors and mechanisms implicated will inform more effective intervention strategies
- Intervention studies should be done across different low-income and middle-income countries to develop feasible and effective interventions that can also take account of the sociocultural factors that are likely to be different in different contexts

Search strategy and selection criteria

We searched PubMed, Google-based search engines such as Google Scholar, Scopus, MEDLINE, and PsycINFO with the search terms "maternal depression", "child mental health", "child behaviour", "mechanisms", "prenatal depression", "postnatal depression", "antenatal depression", "postpartum depression", "intervention studies", and "low- and middle-income" or "developing country". We further consulted websites including the UN, WHO, and UNICEF websites for reports relevant to maternal and child health. We considered countries to be low and middle income according to the World Bank list. We searched for studies including cohort studies that were identified in relevant articles or reviews and searched for studies from particular low-income and middle-income countries (eg, Bangladesh, Brazil, India, Jamaica, Nepal, Pakistan, Uganda, Uruguay, and Vietnam). Searches were done between February and April, 2016, and repeated June 8–14, 2016, and there were no restrictions on studies included. Studies included were in English.

to date are consistent with some of the mechanisms that we present, although further research is necessary to better understand how risks to children of depressed mothers might be mitigated. As previously suggested, strategies to address the global burden of maternal depression are likely to need a multi-faceted social approach that can address child development, poverty, prevention of violence, education, and health. The integration of mental health into primary health-care settings is of central importance in this endeavour.

Contributors

CMH and VG contributed to the literature search for this report for this paper in the maternal depression Series. CMH drafted the following sections: introduction, postnatal mechanisms, strategies for intervention, and conclusion. VG drafted the section about prenatal maternal depression and mechanisms. PGR and MBR contributed feedback and discussions on various drafts of the manuscript. All authors contributed to the conceptualisation of the bio-psychosocial model presented in the figure.

Declaration of interests

We declare no competing interests.

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