

## Rassegna

# The mother-baby bond: a systematic review about perinatal depression and child developmental disorders

## *La relazione madre-figlio: rassegna sulla depressione perinatale e lo sviluppo del bambino*

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**SUMMARY. Background.** Perinatal depression is a common mental disorder, which has become a significant public health concern, especially in the western developed countries where it has a prevalence of 10-20%. As a mental illness, it does not only concern the affected mother but also the child and family. **Aim.** The aim of this review is to examine any developmental disorders in children of depressed mothers. **Methods.** Studies were identified from the following sources: PubMed (Database 2015-2021), Psycarticles (Database 2015-2021), and Psychinfo (Database 2015-2021). Of the 388 studies considered, 32 full-text articles have been analysed, and 22 have been included in the review. **Results.** Results suggest an increased risk of child emotional dysregulation and socio-emotional problems. Several studies reported an increased risk of cognitive, motor and language delay. Moreover, some studies suggest behaviour problems in preschool-age for the children of depressed mothers. **Conclusions.** These evidences lead to the importance of including maternal mental health into primary health care and adequately addressing the dyad to treat depressed mothers and prevent consequences for child development.

**KEY WORDS:** perinatal, depression, child development.

**RIASSUNTO. Introduzione.** La depressione perinatale è un disturbo mentale di elevato interesse nel contesto della sanità pubblica, soprattutto nei Paesi occidentali, ove si evidenzia una prevalenza del 10-20%. La depressione perinatale non riguarda solo la salute mentale della madre ma ha un impatto considerevole anche per il bambino e la famiglia. **Obiettivo.** A tal proposito, l'obiettivo di questa revisione sistematica della letteratura è stato quello di esaminare l'associazione tra depressione perinatale e difficoltà nello sviluppo del bambino. **Metodi.** Sono stati selezionati e revisionati gli articoli pubblicati dal 2015 al 2021 sui siti PubMed, Psycarticles e Psychinfo. Dei 388 titoli selezionati, 32 articoli sono stati analizzati e 22 sono stati inclusi nella sintesi qualitativa degli studi. **Risultati.** I risultati suggeriscono che i figli di madri depresse hanno un aumentato rischio di disregolazione emotiva e problemi nell'ambito socioemotivo. Le evidenze riportano difficoltà nell'acquisizione delle tappe dello sviluppo cognitivo, motorio e del linguaggio. Si evidenzia, inoltre, un rischio aumentato di insorgenza di disturbi esternalizzanti e internalizzanti in età evolutiva. **Conclusioni.** Queste evidenze suggeriscono l'importanza di individuare e trattare precocemente le madri depresse mediante un intervento terapeutico che includa la diade madre-bambino, utile a prevenire le conseguenze per lo sviluppo del bambino.

**PAROLE CHIAVE:** depressione, perinatale, sviluppo del bambino.

### BACKGROUND

Pregnancy, postpartum and puerperium are characterised by significant physical, relational, and psychological transformations in mother's life.

Women can experience feelings of fear, sadness and inadequacy but also anxious-depressive symptoms that should not be underestimated. Perinatal mental health is a topic of growing interest, with distinct clinical conditions that could affect mothers in such a period of high vulnerability. Baby or maternity blues occurs in about 40 to 80 percent of mothers during the first postpartum month, and it is usually mild, self-limiting condition without important consequences to the health of the mother and child<sup>1</sup>. Perinatal Depression (PD) is a frequent

and debilitating mental disorder, which has become of significant public health concern<sup>2</sup> especially in the western developed countries, where it has a prevalence of 10 to 20 percent<sup>3</sup>.

PD is a non-psychotic depressive episode that occurs in women either in pregnancy or from 4 weeks to 3 months after childbirth<sup>4,5</sup>.

The presence of depressive symptoms during the period of pregnancy and postpartum is evaluated using the Edinburgh Postnatal Depression Scale (EPDS)<sup>6</sup>.

Several studies report that children of depressed mothers have increased risk of socio-emotional development delay, neuropsychological, and cognitive deficit, externalising and internalising behaviour problems, in comparison with children of healthy mothers<sup>7</sup>.

Relevant findings of Schore's studies suggest some considerations regarding mother-child interaction and its role in child development<sup>8</sup>. These evidences underlines the importance of a tuning and responsive mother in childhood. Infact, through a series of non-verbal, tactile and gestural visual-facial modulations and a prosodic and auditory preverbal communication, the child and the caregiver can learn to have adequate interactions<sup>8</sup>.

The tuning is not continuous, but breaking moments are characterised by "interactive repair" or by a "break and repair" mechanism and the role of the caregiver, as an external regulator, should be in time to restore sufficiently and adequate regulation to prevent the negative arousal in the child<sup>8</sup>. The restoration of quiet corresponds to the production of neuropeptides (oxytocin), neuromodulators (catecholamines) and neurosteroids (cortisol)<sup>8</sup>. These neurotransmitters are fundamental in the development of the social and emotional brain with long-term effects on the hypothalamic-pituitary-adrenocortical axis<sup>8</sup>.

Depressed mothers, instead, present withdrawn and inhibited or intrusive and hyper-controlling behaviour; a show of poor physical and visual contact and difficulty in interpreting the child's needs<sup>9</sup>.

These events have an important correlation with the psychological and emotional development in the first eighteen months of life, because in this period myelination of the limbic system takes place and right hemisphere matures, with impact on the cortical areas<sup>10</sup>.

Hence, maternal depression can affect organ development (e.g., pre-frontal cortex) and the hypothalamic-pituitary-adrenal axis (HPA axis; the system responsible for regulating stress hormone production, e.g., cortisol) such that the fetus becomes overly sensitive to environmental stressors<sup>11,12</sup>. Indeed, studies have shown that chronically elevated levels of cortisol in depressed mothers during pregnancy can lead to slower fetal growth, premature birth, infant brain cell damage, and over-reactive infant biological stress responses, which can cause long-term cognitive and emotional deficits later in childhood<sup>12,13</sup>.

All those studies suggest the seriousness of maternal depression as a mental illness concerning not only the affected mother but also the fetus and child<sup>10-13</sup>.

Early diagnosis is important to prevent consequences on child development and to investigate the correlation between maternal depression and child outcomes.

This review is a part of a larger clinical project-intervention conducted by the Perinatal Psychiatry Unit in collaboration with the Child Neuropsychiatry Unit of the Human Neuroscience and Mental Health Department of Umberto I Hospital<sup>14-23</sup>. The goal of the project is to evaluate primary and secondary prevention and treat maternal depression to sustain a child-mother relationship in the first years after childbirth. The aim of this review is to examine perinatal depression influences on child development.

## METHODS

### Criteria for considering studies for this review

*Types of studies:* Prospective longitudinal studies, cohort and retrospective studies that analyse the consequences of perinatal depression on child development.

*Types of participants:* mothers with a diagnosis of perinatal depression and their children in infancy and preschool age.

*Type of intervention:* any type of intervention to evaluate the correlation between maternal depression and child outcomes (comparison between children of depressed and healthy mothers, longitudinal observation with periodic assessments of maternal depression and child development).

*Types of outcome:* measures of socio-emotional, cognitive and motor child development, effects of maternal depression on externalising and internalising behaviours of children.

## Selection of trials

The titles and abstracts were screened against the inclusion criteria by the second author to identify relevant articles. If it was unclear whether an article met the inclusion criteria, then the full-text version was obtained, and the article assessed more thoroughly. Once all potentially relevant studies had been obtained, each study was evaluated for inclusion independently by two reviewers. If there was a question about the inclusion of any study, the final decision was made by both authors. If the primary reviewers could not come to a consensus regarding the inclusion or exclusion of a study, the full article was submitted to the third reviewer. Reviewers were not blinded to the name(s) of the author(s), institution(s) or publication source.

The reviewers independently extracted the data from the articles using a form covering the following:

- *Methods:* any type of method to evaluate depressive symptoms and consequent child development outcomes (e.g. questionnaires and scales of child development).
- *Participants:* include women defined as depressed in the antenatal or postpartum period and their children in infancy and preschool age.
- Depression must be measured by a valid assessment tool (Edinburgh Postnatal Depression Scale)<sup>6</sup> or diagnosed by a physician and could range from mild to severe symptoms.
- *Outcomes:* child developmental outcomes are selected considering the main indicators of a typical developmental profile in infancy and preschool age (cognitive, language, motor and socioemotional development, emotive-behavioral skills). Hence, we have considered indicators of child developmental disorders: the emotional dysregulation and socioemotional problems, cognitive, language, motor, socioemotional developmental delay and early child behaviour problems.

Uncertainty and disagreement were resolved through discussion and consultation among the reviewers.

Studies were identified from the following sources: PubMed (Database: 2015-2021), Psycarticles (Database: 2015-2021), Psycinfo (Database: 2015-2021).

The following search terms were used to identify articles: "Perinatal", "Postnatal", "Maternal", "Depression" And "Child", "Children", "Developmental", "Disorders".

## RESULTS

We identified 388 articles and analysed 58 abstracts. We excluded 26 articles because 7 studies were systematic reviews, and 19 articles did not report measures about developmental disorders or perinatal depression (Figure 1).

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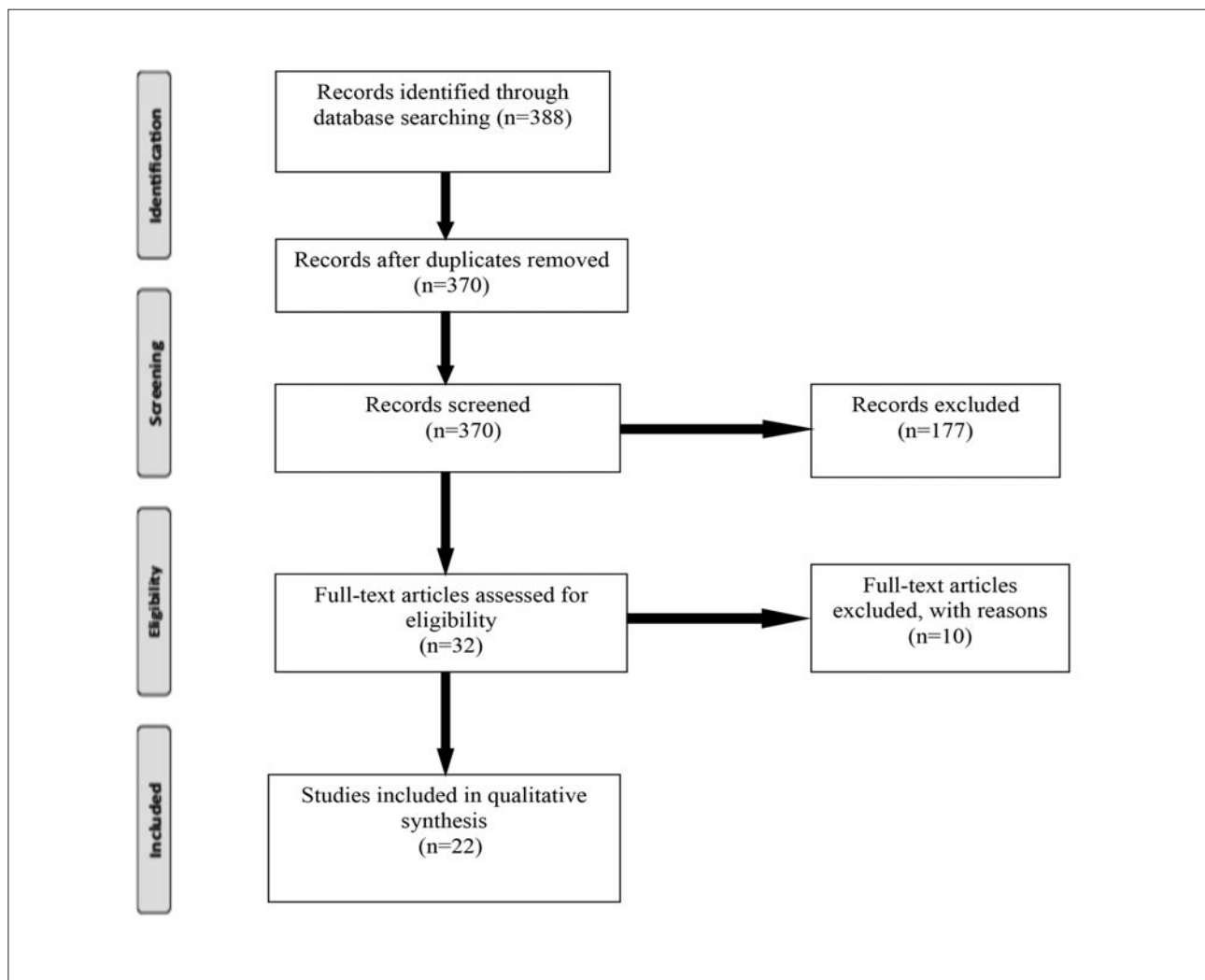


Figure 1. Overall flowchart of articles screened.

We analysed 32 full articles, included 22 articles, and we report the list of excluded full articles along with the reason for their exclusion (Table 1)<sup>24-33</sup>.

### Included articles

#### *Child emotional dysregulation and socioemotional problems (N=7)*

We have selected three different groups of studies that point out different child outcomes. The first group includes seven studies demonstrating that maternal depression is correlated with high levels of emotional reactivity, child emotional dysregulation and increased irritability in infancy and preschool age (Table 2).

We found that, in a multivariate analysis, prenatal depression symptoms [odds ratio(OR)=1.19, 95% confidence interval (CI) 1.15-1.25], postnatal depression symptoms (OR=1.17, 95% CI 1.12-1.23), unhealthy diet in pregnancy (OR=1.12, 95% CI 1.06-1.19) and at child age of 3 years (OR=1.34, 95% CI 1.26-1.42) and 4.5 years (OR=0.79, 95% CI 0.73-0.85), as well as child dysregulation at the age of 4 years (OR=1.17, 95% CI 1.10-1.24) are all significantly associated<sup>34</sup>. Hence, maternal depression symptoms and unhealthy diet show important developmental associations but they are also independent risk factors for atypical child development<sup>34</sup>.

Another study presents evidence regarding two distinct developmental pathways to adolescent depressive symptoms that involve specific early and mid-childhood features. The first links prenatal maternal depressive symptoms, toddler

Table 1. Excluded articles.

Excluded articles	Reason
Protocol for the Northern babies longitudinal study: predicting postpartum depression and improving parent-infant interaction with the Newborn Behavioral Observation <sup>24</sup>	Excluded because it is only a protocol without results
Maternal Prenatal Stress and Infant Emotional Reactivity Six Months Postpartum <sup>25</sup>	Excluded because it focuses on prenatal stress and not specifically on postpartum depression
Trajectories of Maternal Distress and Risk of Child Developmental Delays: Findings From the All Our Families (AOF) Pregnancy Cohort <sup>26</sup>	Excluded because it focuses on maternal distress, in general
Does Prenatal Stress Amplify Effects of Postnatal Maternal Depressive and Anxiety Symptoms on Child Problem Behavior? <sup>27</sup>	Excluded, it does not focus on maternal depression
Newborn Electroencephalographic Correlates of Maternal Prenatal Depressive Symptoms <sup>28</sup>	Excluded because we do not consider electroencephalographic correlates, but measures of child development
Hub Distribution of the Brain Functional Networks of Newborns Prenatally Exposed to Maternal Depression and SSRI Antidepressants <sup>29</sup>	Excluded because it does not focus on maternal depression and direct consequences on child development
Mercy Pregnancy and Emotional Well being Study (MPEWS): Understanding maternal mental health, fetal programming and child development. Study design and cohort profile <sup>30</sup>	Excluded because it is only a protocol
Maternal Depression and Anxiety, Social Synchrony, and Infant Regulation of Negative and Positive Emotions <sup>31</sup>	There are not clear results about child developmental outcomes
Longitudinal Contribution of Maternal and Paternal Depression to Toddler Behaviors: Interparental Conflict and Later Depression as Mediators <sup>32</sup>	It does not focus on maternal depression and child developmental disorders
The perinatal origins of childhood anxiety disorders and the role of early-life maternal predictors <sup>33</sup>	It does not focus on maternal depression as risk factor for child developmental disorders

temperament (high perceived intensity  $b=.11$  and low perceived adaptability  $b=.11$ ), childhood irritability symptoms, and adolescent depressive symptoms.

The second one links prenatal maternal depressive symptoms, toddler temperament (negative perceived mood  $b=.15$ ), childhood anxiety/depressive symptoms, and adoles-

cent depressive symptoms. This study suggests that distinct developmental pathways lead to adolescent depressive symptoms and are important targets and windows of opportunity for their prevention<sup>35</sup>.

Relevant findings suggest that the maternal depression is significantly related to the negative emotional tone and negative emotional reactivity of the child at 24 months postpartum, such that increase of the major depressive disorder trait invokes more negativity of the child during the interaction tasks and negative reactivity to the frustration<sup>36</sup>. Higher maternal prenatal mood entropy is predictive of increased child negative affectivity at 6 and 12 month, with increased child report of anxiety symptoms at age 10 ( $r=.24$ ;  $p<.01$ ;) and with adolescent reports of depressive symptoms at age 13 ( $r=.29$ ;  $p<.01$ ), suggesting the long-term consequences of perinatal depression on people mental health<sup>37</sup>. In this study, predictability of maternal mood is calculated by applying Shannon's entropy to the distribution of responses on mood questionnaires. This application involves a quantification of unpredictability of the item-by-item responses to assessments of mood states<sup>37</sup>. In this sense, mood entropy quantifies the degree of predictability of the item-specific response<sup>37</sup>.

Moreover, we included a study that focuses on the comparison between children of depressed mothers and healthy mothers.

From this study, it emerges that 37% of infants born from mothers with persistent preconception mental health problems are categorised as high in emotional reactivity as compared to 23% born from mothers without preconception history (adjusted OR: 2.1, 95% CI: 1.4-3.1)<sup>38</sup>. Ante and postnatal maternal depressive symptoms are similarly associated with infant emotional reactivity, but these perinatal associations reduce somewhat after adjustment for prior exposure.

These results suggest that maternal depression is related to a characteristic temperament in toddlerhood. In this regard, Wall-Wieler et al.<sup>39</sup>, report that children exposed to maternal depression before age 5 have a 17% higher risk of having at least 1 developmental vulnerability at school entry than children not exposed to maternal depression before age 5. Exposure to maternal depression is most strongly associated with difficulties in social competence (adjusted relative risk [aRR]=1.28; 95% confidence interval [CI]: 1.20-1.38, 1.36), and emotional maturity (aRR=1.27; 95% CI: 1.18-1.37)<sup>39</sup>. Another recent study suggests depressed mothers display lower regulatory caregiving at 9 months, 6 years, and 10 years, evaluated by mother-child interactions assessment (6 minutes of free play at 9 months and 10 min of play with age-appropriate toys that elicit creative-symbolic play at 6 years. At 10 years, mothers and children engaged in two well-validated discussion paradigms for 7 min each). Children of depressed mothers show significantly less social collaboration and lower emotion recognition, but there are no differences between the groups in children's executive function<sup>40</sup>.

#### Child Developmental Delay (N=8)

Eight studies suggest the difficulty of children of depressed mothers in acquiring different competences (motricity, cognitive development, problem-solving, communication) (Table 3).

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Table 2. Maternal depression, child emotional dysregulation and socioemotional problems.

Title	Authors	Objective	Study design	Population	Methods	Results
Maternal depression symptoms, unhealthy diet and child emotional-behavioural dysregulation	Camacho et al. <sup>34</sup>	To examine if prenatal maternal depression symptoms would be associated with child unhealthy dietary patterns, which, in turn, would increase emotional-behavioural dysregulation in childhood.	Prospective study	14,541 was the initial number of pregnancies. Of these initial pregnancies, there was a total of 14,676 fetuses, resulting in and 13,988 children who were alive at one year of age.	EPDS to measure depression symptoms, a food frequency questionnaire (FFQ) at 32 weeks' gestation. At child age of 2 years, four subscales of the Carey Infant Temperament Scale activity, adaptability, intensity and mood – were used.	Higher levels of child dysregulation (at the ages of 2, 4 and 7 years) were associated with higher levels of (prenatal and postnatal) maternal depressive symptoms and unhealthy diet.
Pathways from maternal depressive symptoms to adolescent depressive symptoms: the unique contribution of irritability symptoms	Whelan et. al. <sup>35</sup>	The authors tested three possible pathways linking prenatal maternal depressive symptoms to adolescent depressive symptoms. These pathways went through childhood Irritability Symptoms, Anxiety /Depressive Symptoms or Conduct Problems.	Observational longitudinal study	Data were collected from 3,963 mother-child pairs participating in the Avon Longitudinal Study of Parents and Children.	Measures include maternal depressive symptoms (pre- and postnatal) by using EPDS; toddler temperament at two years (Carey Infant Temperament subscales).	Maternal depressive symptoms were connected to specific early and mid-childhood features which lead to two distinct developmental pathways.
Maternal postnatal depression and anxiety and their association with child emotional negativity and behavior problems at two years	Prenoveau et al. <sup>36</sup>	To examine the role of postnatal major depressive disorder (MDD) and generalised anxiety disorder (GAD) symptom chronicity on children's emotional and behavioural functioning at 24 months.	Prospective longitudinal study	Following postnatal screening mothers (n=296) were identified as having MDD, GAD, MDD and GAD, or no disorder at three months postnatal; the average age was 32.3 (SD 5.0), 91.9% self-identified as Caucasian, and 62.2% were married.	Assessments at 3, 6, 10, 14, and 24 months postpartum, mothers completed the EPDS and GAD-Q. At 24 months postpartum, in addition to the maternal assessment, mothers also completed the Child Behavior Checklist for Ages 1.5-5.	A one standard deviation increase in standing on the MDD symptom severity trait factor was associated with a 0.38 standard deviation increase in child CBCL total problems at 24 months postpartum.
Prenatal maternal mood patterns predict child temperament and adolescent mental health	Glynn et al. <sup>37</sup>	To examine whether maternal prenatal mood entropy predicts child temperament and internalising symptoms.	Cohort study	Participants in both cohorts were recruited during the first trimester of pregnancy and participated in four to five prenatal study visits. Cohort 1 consisted of 227 mother-child pairs and Cohort 2 of 180 pairs.	Maternal mood : the nine-item form of the Center for Epidemiologic Studies Depression Scale, the 10-item state anxiety subscale of the State- Trait Personality Inventory were used. Child negative affectivity was assessed at 6 and 12 months with the Infant Behavior Questionnaire (IBQ), at 2 years with the Early Childhood Behavior Questionnaire (ECBQ).	Higher maternal prenatal mood Shannon's entropy was predictive of increased child negative affectivity at 6 (r=.23, p<.01), 12-months of age (r =.36, p<.01;) and 24 months (r=.31, p<.01).

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(Continued) - Table 2. Maternal depression, child emotional dysregulation and socioemotional problems.

Title	Authors	Objective	Study design	Population	Methods	Results
Maternal mental health and infant emotional reactivity: a 20-year two-cohort study of preconception and perinatal exposures	Spry et al. <sup>38</sup>	To examine the consequences of preconception maternal mental health for children's early emotional development.	Cohort study	756 women Repeatedly assessed for mental health problems before pregnancy, during pregnancy and at one year postpartum for 1231 subsequent pregnancies.	Postpartum infant offspring emotional reactivity was assessed at one year by using the Short Temperament Scale for Toddlers (STST). High scores indicate a tendency to react negatively to unpleasant experiences.	Thirty-seven percent of infants born to mothers with persistent preconception mental health problems were categorised as high in emotional reactivity, compared to 23% born to mothers without preconception history (adjusted OR 2.1, 95% CI 1.4-3.1).
Maternal depression in early childhood and developmental vulnerability at school entry	Wall-Wieler et al. <sup>39</sup>	To assess the relation between exposure to maternal depression before age 5 and 5 domains of developmental vulnerability at school entry.	Cohort study	This cohort study included all children born in Manitoba, Canada, who completed the Early Development Instrument between 2005 and 2016 (N=52,103)	Maternal depression was defined by using physician visits, and pharmaceutical data; developmental vulnerability was assessed by using the Early Development Instrument.	Children exposed to maternal depression before age 5 had a 17% higher risk of having at least 1 developmental vulnerability at school entry than did children not exposed to maternal depression.
Maternal depression impairs child emotion understanding and executive functions: the role of dysregulated maternal care across the first decade of life	Priel et al. <sup>40</sup>	To examine the impact of deficits in maternal regulatory caregiving across the first decade of life on children's emotional, social, and cognitive outcomes at 10 years.	Longitudinal study	Of the 192 families visited at 9 months, 156 were revisited at 6 years and 125 were visited at 10 years	Children were administered the Stockings of Cambridge test (Executive Function). Social collaboration (SC) was evaluated and Emotion Recognition (EC) Toolbox was used	Children of depressed mothers showed significantly less social collaboration and lower emotion recognition (p<0,05), but no differences were found between the group in children's EF.

Hence, in preschool age, children of mothers with depressive symptoms have reduced scores at cognitive assessment<sup>41</sup>. This result is in line with prior studies demonstrating experiences with insensitive maternal interactions and insecure mother-child attachment appear to be predictive of impaired cognitive functioning<sup>42</sup>. Moreover, chronic maternal depression could influence the child's cognitive development through maladaptive parenting behaviours; it is difficult for depressed mothers to propose stimulating activities, books or objects.

Relevant findings from another study suggest the women with current depression and those with both postpartum depression and current depression are significantly more likely to have a child with developmental disabilities in communication, gross motor and personal-social domains assessed four years after childbirth (OR=2.59, 95% CI=1.16-5.78; OR=4.34, 95% CI=2.10-8.96 and OR=5.66, 95% CI=1.94-16.54, respectively)<sup>43</sup>.

Tuovinen et al.<sup>44</sup> suggest similar results underlying that higher mean maternal depressive symptoms predict lower total developmental milestones, fine and gross motor, communication, problem-solving, and personal/social skills scores in children (p<0.001).

Wang et al.<sup>45</sup> demonstrated an increased risk of psychomotor developmental delay in preterm children of depressive mothers; these data were collected when the children were eight months old, according to the concept that early maternal depression and environmental risk factors directly affect the cognitive and social functioning of children.

Relevant findings from two studies demonstrate the poorer performance of babies exposed to antenatal or prenatal depression by in the first week after birth<sup>46,47</sup>.

The lack of effect of antenatal depression on developmental outcomes at 12 months demonstrated in the first study of these<sup>46</sup> is potentially surprising.

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Table 3. Maternal depression and child developmental delay.

Title	Authors	Objective	Study design	Population	Methods	Results
Persistent maternal depressive symptoms trajectories influence children's IQ: the EDEN Mother-Child Cohort	Van der Waerden, et al. <sup>41</sup>	The association between timing and course of maternal depression from pregnancy onwards and children's cognitive development at ages 5 to 6.	Longitudinal study	One thousand thirty-nine mother-child pairs from the French EDEN mother-childbirth cohort were followed from 24 to 28 weeks of pregnancy onwards.	EPDS scores assessed at six time points. Children's cognitive function was assessed at ages 5 to 6 with the (WPPSI-III), resulting in three composite scores: Verbal IQ (VIQ), Performance IQ (PIQ), and Full-Scale IQ (FSIQ).	Compared to children of mothers who were never depressed, children of mothers with persistently high levels of depressive symptoms had reduced VIQ (p=0,018), PIQ (p=0,043), and FSIQ (p=0,018) scores.
Post-partum depression effect on child health and development	Abdollahi et al. <sup>43</sup>	This study examined the relative significance of maternal PPD in children's developmental disabilities at age four.	Longitudinal study	204 women experiencing PPD were considered as cases, compared with 467 healthy mothers.	The association between maternal depression at different times and childhood developmental disabilities was calculated by using Ages and Stages Questionnaire (ASQ).	At age four, Childhood developmental disabilities in communication, gross motor and personal-social domains of ASQ were associated with the current and concurrent maternal depressive symptoms.
Association of maternal depression with dietary intake, growth, and development of preterm infants: a cohort study in Beijing, China	Wang et al. <sup>45</sup>	To examine the association of maternal depression with dietary intake, growth and development of preterm infants.	Cohort study	Based on the gestational age of an infant and status of the mother, the infants were divided into four groups: non-depression-full-term (64), non-depression-preterm (70), depression-full-term (36), and depression-preterm (31).	Developmental status of children at eight months (corrected ages) were collected using a quantitative questionnaire (Bayley Scales of Infant Development).	Z-scores for weight and the Bayley-III composite scores for the cognitive and motor scales of preterm infants in the depression group were lower than those in the non-depression group (p<0.05).
Antenatal depression program cortisol stress reactivity in offspring through increased maternal inflammation and cortisol in pregnancy: the Psychiatry Research and Motherhood – Depression (PRAM-D) Study	Osborne et al. <sup>47</sup>	To study the effect of maternal depression in pregnancy and associated early neurobehavior (Neonatal Behavioral Assessment Scale - NBAS, at day 6), and cognitive, Language and motor development (Bayley Scales Of Infant and Toddler Development at 12 months).	Prospective longitudinal study	The sample comprised 106 women recruited in the late second trimester of pregnancy (25 weeks gestation): 49 cases with MDD in pregnancy and 57 healthy controls, all at King's College Hospital.	Gestational age at birth and birth weight were recorded, and neonatal neurobehavioral function was assessed at 6 days postnatal. At 12 month, cognitive, language and motor development were assessed by using Bayley Scales.	The neuro-behavioral assessment (NBAS) of full-term babies conducted at 6 days postnatal showed that babies exposed to antenatal depression demonstrated poorer performance on all five clusters: autonomic stability (δ=0.85), regulation of state (δ=0.61), range of state (δ=0.53), orientation (δ=1.22) and motor (δ=0.45).

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(Continued) - Table 3. Maternal depression and child developmental delay.

Title	Authors	Objective	Study design	Population	Methods	Results
Maternal depressive symptoms during and after pregnancy and child developmental milestones	Touvinen et al. <sup>44</sup>	Maternal depressive symptoms during and after pregnancy predict poorer child neurodevelopment.	Prospective longitudinal study	A total of 2,231 Mothers completed the Center for Epidemiological Studies Depression Scale biweekly up to 14 times during pregnancy and twice up to 12 months after pregnancy.	At child's age 1.9-5.7 years, the mothers completed the Beck Depression Inventory-II on their concurrent depressive symptoms and Ages and Stages Questionnaire on child developmental milestones.	Higher mean maternal depressive symptoms predicted lower total developmental milestones, fine and gross motor, communication, problem-solving, and personal/social skills scores in children. $p < 0.001$ .
Negative impact of maternal antenatal depressive symptoms on neonate's behavioral characteristics	Gressier et al. <sup>46</sup>	This work aims to explore the Links between early neonatal Behaviour and maternal prenatal depressive symptoms.	Prospective longitudinal study	Five hundred and ninety-eight women and their new borns from the MATQUID cohort were prospectively evaluated during the 8th month of pregnancy (T1) and at day 3 postpartum (T2).	To analyse the independent associations between neonates' behaviour (Neonatal Behavioral Assessment Scale-NBAS) at T2 and the intensity of maternal prenatal depressive symptoms at T2 (CES-D).	The results show a significant negative correlation between prenatal CES-D scores and NBAS scores on "habituation" ( $p = 0.0001$ ), "orientation" ( $p = 0.015$ ), "motor system" ( $p < 0.0001$ ), "autonomic stability" ( $p < 0.0001$ ).
Maternal depressive symptoms and developmental delay at age 2: a diverse population based longitudinal study	Chorbadjian et al. <sup>48</sup>	The purpose of this study was to determine whether maternal depression from pre-pregnancy to postpartum influences child development in children by age 2.5.	Longitudinal study	2679 racially and ethnically diverse mothers and their children were recruited completed.	Mothers completed the 2014 Los Angeles Mommy and Baby (LAMB) and 2016 Follow-Up surveys. Child development was measured using the CDC's Learn the Signs. Act Early Milestones Checklist.	Mothers reporting depressive symptoms at all four time points were significantly more likely to report a social-emotional delay in their child (aOR=4.39, 95% CI - 1.72 to 11.18).
Maternal depression, anxiety, psychoticism and paranoid ideation have effects on developmental delay types of infants: a study with clinical infant-mother dyads	Gül et al. <sup>49</sup>	To examine the association between some of the maternal psychiatric symptoms and developmental delay types.	Cohort study	The sample consisted of 79 infant-mother (26 girls, 53 boys) dyads who had been admitted to the Department of Child and Adolescent Psychiatry at Gulhane Research and Training Hospital over a one year period.	Brief Symptom Inventory (BSI) to assess mother's psychiatric symptoms. The Ankara Developmental Screening Inventory (ADSI) for assessments of infants' level of functioning. Brief Infant-Toddler Social and Emotional Assessment (BITSEA) scale for assessing the infant's social-emotional problems and abilities.	Higher scores of maternal depression increase the risk of having total developmental delay for infants (cognitive, motor, language, socioemotional development delay).



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It can be explained considering that cognitive and language scores are numerically lower in infants of depressed mothers.

However, the differences do not reach statistical significance. Further follow-up studies are required for better clarification of the antenatal depression's effect on infant development<sup>46</sup>. In a recent study data about maternal depressive symptoms and child development was collected before pregnancy, during pregnancy, 4 months postpartum, and at 2.5 years postpartum. Results suggest that compared to mothers with no maternal depressive symptoms (MDS), the mothers reporting cumulative MDS at all four time points are 2.19 (95% CI 1.55-3.11), 2.67 (95% CI 1.71-4.16), 2.79 (95% CI 1.59-4.92) and 3.25 (95% CI 1.30-8.15) times significantly more likely to have children with social-emotional developmental delay. Mothers with MDS at one and two time points are 3.67 (95% CI 1.29-10.47) and 3.68 (95% CI 1.83-7.41) times more likely to report child motor and cognitive/adaptive delay. Mothers reporting MDS at all four time points are 1.82 (95% CI 1.34-2.48), 2.60 (95% CI 1.78-3.80), 2.53 (95% CI 1.54-4.17) and 2.42 (95% CI 1.02-5.77) times significantly more likely to report any child developmental delay<sup>48</sup>. Gül et al.<sup>49</sup> 2020 found that higher scores of "maternal depression" increase the risk of having total development delay for infants (OR=1.59, 95% CI: 1.24-2.04,  $p < .001$ ). These studies report a specific effect of prenatal depressive symptoms on newborn's outcomes, and they highlight the crucial necessity for antenatal screening and adjusted treatments of maternal depressive symptoms.

*Early child behaviour problems (N=5)*

We included five articles about the association of perinatal depression with early child behaviour problems (Table 4).

Narayanan et al.<sup>50</sup> compared the associations between maternal and paternal depressive symptoms and early child behaviour problems. Higher levels of maternal symptoms at six months predict emotionally reactive ( $p=0.01$ ), anxious/depressed ( $p < 0.001$ ), withdrawn ( $p=0.03$ ), attention problems ( $p=0.02$ ) and aggressive child behaviour ( $p=0.01$ ) at 48 months, while higher levels of paternal symptoms do not predict child behaviour. The results confirm that mothers' mental health status shortly following childbirth seems to need the most attention, as it is most often the case today.

In a study, in particular, negative child affectivity in toddlerhood is associated with internalising and externalising behaviours at the age of seven. More specifically, the high maternal depressive symptom trajectory is associated with 7-year maternal depressive symptoms ( $b=5.52$ , SE 1.65,  $p < 0.01$ ), child internalising problems ( $b=7.60$ , SE= 3.12,  $p=0.02$ ) and externalising problems ( $b=6.23$ , SE=3.22,  $p=0.05$ ). Caregiving engagement among high depressive symptom trajectory mothers is significantly associated with observed child affect ( $b=-0.21$ , SE=0.11,  $p=0.05$ ). Parental nurturance in toddlerhood mediates the association between high maternal depressive symptom trajectory and child internalising problems at seven years (indirect effect  $b=2.33$ , 95% CI: 0.32-5.88).

These findings demonstrate the continuity of behavioral problems from toddlerhood to early school age, suggesting

the long term effects of postpartum maternal depressive symptoms on child behaviour<sup>51</sup>.

Relevant findings report that all maternal depressive time-points (1.5, 3, 5 years postpartum) are significantly and positively associated with child internalising and externalising problems. Analyses are repeated using a sibling comparison design to adjust for familial confounding. After sibling comparison, however, only concurrent maternal depression is significantly associated with internalizing [estimate=2.82 (1.91-3.73, 95% CI)] and externalizing problems [estimate=2.40 (1.56-3.23, 95% CI)].

A potential explanation for these findings is that after toddlerhood, the child may need more behaviorally engaged mothers. Hence, it may also take a few years before the effects are expressed as children behaviour problems.

Instead, effects may be reflected in other developmental domains<sup>52</sup>. Moreover, two recent studies report that maternal depression during toddlerhood has a stronger effect on child internalizing (SE=0.21) and externalizing (SE=0.22) symptoms and social skills (SE=-0.08) at age 5, than either prenatal or postnatal depression<sup>53</sup>. Rotheram-Fuller et al.<sup>54</sup> recruited a clinical sample of Pregnant women and their children in 24 periurban township neighborhoods in Cape Town, South Africa (N=1,238 mothers). This study found that at 36 months the pattern of maternal depressed mood is significantly associated with Child Behavior Checklist Internalizing Problems Scale Score ( $F=7.8$ ,  $p=0.01$ ), Externalizing Problems Scale Score ( $F=7.8$ ,  $p < 0.01$ ), and Total Problems Score ( $F=8.4$ ,  $p < 0.01$ )<sup>54</sup>.

*No significant association between maternal depression and child development (N=2)*

Finally, two studies demonstrated no significant association between maternal depression and child development (Table 5).

The first study, conducted in South Africa, demonstrates that growth and developmental delays, motor, speech milestones through 24 months post-birth are similar for mothers with and without perinatal depressed mood<sup>55</sup>.

The second of such studies underlies a correlation between developmental delay in children at psychosocial risk and low quality of mother-child interaction. However, there is not a direct correlation with depressive symptoms<sup>56</sup>.

## DISCUSSION AND CONCLUSIONS

Maternal depression is a global public health issue that must be addressed early in order to protect the mother-child relationship and to prevent negative consequences on child development. The reviewed studies and our daily clinic observations suggest that maternal depression is a significant risk factor for child psycho-motor and socio-emotional development delay. Moreover, Laucht et al.<sup>57</sup> report that social-emotional outcomes of children of postnatally depressed mothers is significantly poorer than in the healthy mothers' group. We found seven studies that report an association between maternal mental health and early child emotional dysregulation as well as socioemotional troubles<sup>34-40</sup>.

These data suggest negative emotional reactivity and irri-

Table 4. Maternal Depression and early Child Behavior Problems.

Title	Authors	Objective	Study design	Population	Methods	Results
Associations between maternal and paternal depressive symptoms and early child behavior problems: testing a mutually adjusted prospective longitudinal model	Narayanan et al. <sup>50</sup>	The relationship between parental depressive symptoms and child behaviour problems in early childhood.	Prospective longitudinal study	1159 children and depressed mothers from five municipalities in south-east Norway.	Parental depressive symptoms were assessed using a 10-item version of the Hopkins Symptom Checklist (SCL-10) at 6,12,24,36 and 48 months following child birth. Child behaviour problems were assessed using mother and father reports on the Child Behavior Checklist (CBCL/1½-5), and teacher reports on the equivalent Teacher report form at 48 months (C-TRF).	Mothers' depressive symptoms at six months predicted behaviour problems at 48 months for all syndrome scales, while fathers' did not.
Maternal perinatal and concurrent depressive symptoms and child behavior problems: a sibling comparison study	Gjerde et al. <sup>52</sup>	To examine the association between maternal prenatal and postpartum depression and child behaviour problems (CBP) in a prospective longitudinal design.	Prospective longitudinal study	The sample comprised 11,599 families including 17,830 siblings from the Norwegian Mother and Child Cohort study. Included children had at least one participating, biological sibling.	Mothers reported depressive symptoms at gestational weeks 17 and 30, as well as 6 months, 1.5, 3, and 5 years postpartum (SCL). At the last three time-points, child internalising and externalising problems were concurrently assessed (CBCL).	After sibling comparison only concurrent maternal depression was significantly associated with internalizing [estimate= 2.82 (1.91-3.73, 95% CI)] and externalizing problems [estimate= 2.40 (1.56-3.23, 95% CI)].
Early maternal depressive symptom trajectories: associations with 7-year maternal depressive symptoms and child behavior	Buckingham-Howes et al. <sup>51</sup>	To examine potential mechanisms linking maternal depressive symptoms over 2 years postpartum with child behaviour problems.	Prospective longitudinal study.	One hundred eighteen low-income African American adolescent mothers were recruited at delivery and followed through child age 7 years.	Subsequent home evaluations were conducted when children were 6, 13, and 24 months, and 7 years of age. Mothers and children participated in a video-recorded play observation at 24 months. At the 7-year evaluation, mothers used the Parent Rating Scales of the Behaviour Assessment System for Children II.	The high depressive symptom trajectory was significantly associated with more negative child affect in toddler-hood, externalising and internalising problems at 7-years.

(Continued)

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(Continued) - Table 4. Maternal Depression and early Child Behavior Problems.

Title	Authors	Objective	Study design	Population	Methods	Results
The chronicity and timing of prenatal and antenatal maternal depression and anxiety on child outcomes at age 5	Hentges et al. <sup>53</sup>	Six assessments of maternal depression across pregnancy (<25 and 35 weeks gestation), infancy (4 and 12 months), and toddlerhood (24 and 36 months), to examine the role of chronicity and timing of maternal mental health on child social skills, mental health, and communication abilities at age 5.	Prospective cohort study	Participants were drawn from a larger, on going prospective pregnancy cohort in western Canada (1992 mother-child pairs).	Mothers completed the Edinburgh postnatal depression scale. At age 5, mothers completed the behavior assessment system for children second edition (BASC 2) and the children's communication checklist.	Maternal depression during toddlerhood had a stronger effect on child internalizing) and externalizing symptoms and social skills at age 5.
Maternal patterns of antenatal and postnatal depressed mood and the impact on child health at 3-years postpartum	Rotheram-Fuller et al. <sup>54</sup>	The consequences of maternal depressed mood on children's growth, health, and cognitive and language development are examined over the first 3 years of life.	Cohort study	Pregnant women in 24 periurban township neighborhoods in Cape Town, South Africa (N=1,238 mothers) and their children were recruited. Reassessments were conducted for 93%-85% of mothers at 2-weeks, 6-, 18-, and 36-months postbirth.	Depressed mood was reported using the EPDS. At 36 months, mothers completed Achenbach's Preschool Child Behavior Checklist and The Executive Function Battery.	At 36 months, the pattern of maternal depressed mood over time was significantly associated with children's compromised physical growth, both in weight and height, and more internalizing and externalizing symptoms of behavior problems.

tability could be predictive factors of increased risk in childhood and adolescent mental health, and longitudinal studies allow us to analyse this risk of serious consequences on people mental health.

Our systematic review suggests that maternal depression is associated to global developmental delay. Eight studies report that maternal depression increases the risk of cognitive, language, motor and socioemotional developmental delay assessed from childbirth to three years after childbirth. Our selected studies demonstrated lower scores at cognitive assessment, personal-social domains and problem solving skills of children exposed to maternal depression, in preschool age, compared with children of undepressed mothers<sup>41,43-49</sup>.

These data suggest the possibility to early recognize the risk of child developmental disorders and the importance to detect them in the first years after childbirth.

Most of the cases described can evolve differently<sup>58</sup>. The persistence of an insufficient stimulation can transform a reversible functional fact into an irreversible alteration, due to failure in activating and organising specific functional activities, with development delay involving multiple areas<sup>58</sup>.

Literature suggests that initial difficulties in the cognitive use

of the motor act and of the perceptive act can interfere with the development of praxic, symbolic and communicative skills<sup>58</sup>.

We included five studies that report maternal depression as a risk factor for early child behavior problems (internalizing and externalizing problems), assessed in preschool age and at school entry<sup>50-54</sup>.

Finally, two studies demonstrated no significant association between maternal depression and child development<sup>55,56</sup>.

The first study is conducted in South Africa and the results could be explained considering that deficits in caregiving may be mitigated by the social connections that rural living demands, and more intact social structures, as compared to peri-urban townships. The rural environment may offer social protective factors in managing depression and other difficulties faced by women so that we can reflect on socio-cultural differences in maternal mental health<sup>55</sup>.

The second of such studies underlies a correlation between developmental delay in children at psychosocial risk and low quality of mother-child interaction<sup>56</sup>, but there is not a correlation with depressive symptoms. It is important to consider that the factors of care and context are interrelated.

Table 5. No association between maternal depression and child development.

Title	Authors	Objective	Study design	Population	Methods	Results
Perinatal maternal depression in rural South Africa: child outcomes over the first two years	Christodoulou et al. <sup>55</sup>	To examine child outcomes over time among mothers with perinatally depressed mood in rural South Africa (SA).	Study case-control	A sample of consecutive births (470/493) in South Africa (SA) were recruited and compared with a sample of healthy women.	Maternal depression was reported on the (EPDS). Structural resources were identified as education, employment, income, living with a partner, etc. Developmental Milestones at 6, 9, 12 and 24 months were administered.	Growth and developmental delays and motor and speech milestones through 24 months post-birth are similar for mothers with and without perinatal depressed mood.
Low quality of mother-child interaction in infants at psychosocial risk is associated with risk of developmental delay	Binda et al. <sup>56</sup>	To evaluate the association between risk of psycho motor developmental delay (PDD) with mother-child interaction quality, postpartum depressive symptoms, and other factors related to care and environment in healthy infants at psychosocial risk.	Analytical cross-sectional study	An analytical cross-sectional study in 181 mothers at psychosocial risk and their children aged under one year seen in Primary Health Care.	The presence of risk of PDD was determined using the ASQ and its association with interaction quality (CARE Index), EPDS, and other factors related to environment and care.	There was an increased risk of PDD (20% of infants) in association with low-quality mother-child interaction (OR=2.46, p=0.03), exclusive breastfeeding (EBF) <6 months (OR=2.58, p=0.01), and partner does not help with childcare (OR=2.97, p=0.03).

A mother who has a supportive social context in child caring is exposed to less stress and as a consequence is less likely to depressive symptoms. In this way, the mother is more likely to have good quality interactions with her child that are stimulating for his or her development.

Therefore, an early intervention on mother-child relationship to encourage the creation of a facilitating environment for the child is essential in the first years after childbirth, when a tuned and responsive mother can facilitate the development of the potential and hereditary tendencies of the infant.

Hence, it emerges the importance of including maternal mental health into primary health care and adequately address the dyad to treat depressed mothers with psychotherapy and psychopharmacology. Moreover, it's important to sustain an intervention on the mother-child relationship through baby observation and psychotherapy for the dyad. Through these measures, it could be identified as the early situation of dysfunctional parenting styles.

Therefore, if the risk of a delay in socio-emotional and psychomotor development is recognized early, immediate planning of the most appropriate intervention becomes possible, while accounting for social context and general resources that influence maternity experience.

Maternal-child interaction guidance and psychotherapeutic group support produce significant effects on parenting (e.g. sense of competence) and child development<sup>59</sup>.

Interpersonal psychotherapy (IPT), cognitive behavioural therapy (CBT) and psychotherapeutic group support show promising results for improving specific parental styles and/or child development outcomes<sup>59</sup>. In a very well designed study of CBT interventions for antenatal depression, the treatment group showed improved infant outcomes, including developmental progress (specifically, problem-solving), child self-regulation, infant temperament and behaviour variables such as high-intensity pleasure, reactivity and negative affectivity<sup>60</sup>.

Literature and clinic experience suggest that it is essential to consider perinatal depression as a pathology of the relationship. Hence, it's important to focus therapy on the mother-child relationship as well as an essential project of primary prevention in mental health.

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