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Prenatal and postnatal maternal depression and infant hospitalization and mortality in the first year of life: a systematic review and meta-analysis

Nadege Jacques

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Highlights:

- Children of mothers with postnatal depressive symptoms or depression had an increased risk of death in the first year of life.
- Children of mothers with prenatal and postnatal depressive symptoms or depression had a higher risk of hospitalization than those whose mothers did not have the disorder during prenatal and/or postnatal periods.
- As a limitation, different instrument and cut points were used to evaluate maternal depressive symptoms or depression.
- Other limitation one study do not clearly explain the dichotomization process of exposure since the authors used the ICD-9-CM codes.

Abstract

Background: Prenatal and postnatal depression have been well studied in recent decades, but few studies address their relationship with hospitalization and mortality in one-year-old children.

Objective: Review the literature about the effects of maternal depression on hospitalization and mortality of the child from birth to one year of age and conduct a meta-analysis.

Methods: A systematic search was performed in the PubMed and LILACS databases. We included original studies that evaluated the effect of prenatal and/or postnatal depressive symptoms on child hospitalization or mortality up to one year of age. Meta-analyses were conducted according to the outcome and stratified by prenatal and postnatal depression, using random effects models.

Results: Six studies were included in this review (170,371). Children of mothers with prenatal and postnatal depressive symptoms or depression had 1.44 (CI_{95%} 1.10 – 1.89) greater risk of hospitalization, and children of mothers with postnatal depressive symptoms or depression had 1.93 (CI_{95%} 1.02 – 3.64) greater risk of death before one year of age than those whose mothers did not have the disorder.

Limitations: Small number of studies (n <10), different instrument and cut points were used to evaluate maternal depressive symptoms or diagnose depression.

Conclusion: Maternal depressive symptoms or depression have an unfavorable effect on hospitalization and mortality in children up to one year of age. This finding is relevant to public health and should stimulate the systematic screening of prenatal

and postnatal depressive symptoms, so that adequate care can be provided for women and their children.

Keywords: systematic review, meta-analysis, prenatal depression, postnatal depression, prenatal and postnatal depressive symptoms, child hospitalization, child mortality

Introduction

Newborns and children are particularly vulnerable to a number of diseases, many of which can be effectively prevented or treated (Saúde 2011, SANTO 2017). In the world, about 7.6 million children under the age of five died in 2010, and more than 40% (3.3 million) of these deaths occurred in the first few months after birth (WHO 2011). Among the determinants that could affect child health, prenatal and postnatal maternal depression are important factors (McPeak, Sandrock et al. 2015).

The adverse effects of prenatal maternal depression are manifold in children: low birth weight (Accortt, Cheadle et al. 2015), preterm birth (Ding, Wu et al. 2014);(Szegda, Markenson et al. 2014) decreased Apgar score, decreased head circumference, gestational growth retardation, (Rahman, Bunn et al. 2007, Marcus 2009, Uguz, Gezginc et al. 2011, Smith, Huber et al. 2015); (Davalos, Yadon et al. 2012, Chang, Keyes et al. 2014), fetal anomalies, as well as fetal death and suffering (Bansil, Kuklina et al. 2010). Prenatal maternal depression is a predictor of internalization problems in children (Brand 2009, Betts, Williams et al.

2014);(Bergman, Sarkar et al. 2007), attachment difficulties between mothers and children (Lefkovic, Baji et al. 2014), problem of psychomotor development (Podesta, Alarcon et al. 2013), and emotional or behavioral problems in children. (O'Connor, Heron et al. 2002),(Davis E 2004,).

The placenta is the primary means of exchange between the mother and the fetus. Studies have shown that the biological mechanism of adverse outcomes in the fetus passes through the placenta, in most cases, cortisol disrupts ongoing fetal development processes and causes adverse effects on the fetus. The magnitude of the long-term effects of antenatal maternal anxiety/stress on the child is substantial (Van den Bergh, Mulder et al. 2005); (Claudia Bussa 2010);(Mennes, Stiers et al. 2006); (Elysia Poggi Davis 2010).

In fact, a curtailment of child care, such as conducting routine medical follow-up and providing adequate nutrition, has been observed in mothers with postnatal depression. Children of depressed mothers are breastfed for less time, get sick more often and are treated for disease more frequently in primary health care and emergency services (De Magistris, Coni et al. 2010); (Greene, Rossman et al. 2015); (Mew, Holditch-Davis et al. 2003, Lefkowitz, Baxt et al. 2010, Greene, Rossman et al. 2015); (Segre, Chuffo-Siewert et al. 2013); (Segre, McCabe et al. 2014) due to lack of care at home.

The comorbidity of anxiety and depression is common in the general population (Hirschfeld 2001). In the prenatal and postnatal periods, the coexistence of these morbidities is also common (Austin, Hadzi-Pavlovic et al. 2010, Field, Diego et al. 2010).The possible mechanisms explaining maternal depression are of two types: biological and psychosocial. The biological part can be explained by hormonal changes in the gestation and after the baby's birth. The strongest predictors of

postnatal depression risk among the biological processes designed by the literature are hypothalamic-pituitary-adrenal dysregulation, inflammatory processes and genetic vulnerabilities. From a psychosocial point of view, the strongest predictors are serious life events, some forms of chronic tension, quality of the relationship between the mother and her partner and support of the partner (Ilona S. Yim¹ 2015); (Leigh and Milgrom 2008).

In one hand, the great challenge in detecting prenatal maternal depressive symptoms is the similarity between its symptoms and the general symptoms of the first months of pregnancy, which makes it difficult to diagnose at this stage (Kaplan 1983, Alder, Fink et al. 2011, Apter, Devouche et al. 2013). On the other hand, postnatal maternal depressive symptoms often go unnoticed by caregivers, and therefore untreated in clinical practice. The lack of treatment is partly due to the fact that women do not report their symptoms to health professionals (Appleby, Gregoire et al. 1994). Silent after childbirth, maternal depression is often related to problems in the child's emotional development, behavior and social relationships, not only during childhood but throughout life (Agnafors, Sydsjo et al. 2013); (Betts, Williams et al. 2015).

In light of these factors, there is great difficulty in screening, diagnosing and treating these forms of depression, despite the numerous studies showing that this is possible. The literature is clear on the subject and provides countless studies showing that it is possible to screen and treat maternal depression prenatal or postnatal, using validated and available screening tools such as Edinburgh's prenatal (Murray 1990) and postnatal depression scale (EPDS)(J L Cox 1987), but because most primary and secondary maternal and child health services do not systematize screening of the disease symptoms, it often goes undiagnosed. Systematic

screening based on known and validated methods during prenatal and postnatal consultations is fundamental for identifying cases and reducing the likelihood of adverse birth outcomes, postpartum mental health problems, and adverse effects on offspring (Accortt and Wong 2017). Furthermore, the underdiagnosis of prenatal and postnatal depression due to lack of routine screening in maternal health services, but also lack of follow-up of women screened positive, makes it even more difficult to identify a possible relationship between maternal depression and child health problems. There are few studies about the influence of prenatal and postnatal maternal depression on the more severe aspects of child health, such as hospitalization and mortality. The purpose of this study is to review the literature about the effects of maternal depression on child hospitalization and mortality from birth to one year of age and conduct a meta-analysis.

Methodology

Research strategy

A systematic search was performed in the PubMed and LILACS databases on September 22, 2017. The search did not control for year of publication and limited the results to human studies in French, English, Spanish and Portuguese. The following search keys were used: (((((((((((((infant illness[MeSH Terms]) OR infant diarrhea[MeSH Terms]) OR infant pneumonia[MeSH Terms]) OR infant icterus/jaundice[MeSH Terms]) OR child pneumonia[MeSH Terms]) OR child wheezing[MeSH Terms]) OR child urinary infection[MeSH Terms]) OR infant morbidity[MeSH Terms]) OR infant mortality[MeSH Terms]) OR child hospitalizations[MeSH Terms]) AND Depression[MeSH Terms]) OR Maternal

Depression disorders[MeSH Terms]) OR Antenatal Depression[MeSH Terms]) OR Postnatal Depression[MeSH Terms]) OR Pregnancy/depression[MeSH Terms]. We included original studies evaluating the effect of prenatal and/or postnatal maternal depression on unfavorable child health outcomes (hospitalization and mortality) up to one year of age. We excluded studies that evaluated the effects of depression medications on fetuses or newborns, congenital malformation, literature reviews and studies that evaluated children at least 5 years of age. We also analyzed the studies' reference lists.

Defining exposure and outcome

Exposure was defined as women with symptoms of major depression and/or with depressive disorders who had been diagnosed using specific instruments and cut points used to assess the disorder, beginning with the first trimester of pregnancy and/or from four weeks to one year postpartum.

The outcomes evaluated were hospitalization and mortality in children up to one year of age. Hospitalization was considered admission for at least 24 hours to a healthcare institution in the first year of life. Mortality was defined as death reported by qualified professionals.

Study selection and data collection

Study eligibility was evaluated independently by two reviewers, both PhD students in Epidemiology. Disagreements between reviewers were resolved by consensus, however when reviewers were unable to achieve consensus the disagreements were solved by a professor acting as a third independent reviewer. Duplicate publications

were eliminated. Initial selection was carried out according to title and then according to abstract and full text.

Data extraction

The search yielded 8674 articles: 642 articles in LILACS and 8032 in PubMed. A total of 58 duplicates were eliminated. After reading the titles and abstracts, a further 8570 studies were excluded for not dealing with the topic of interest to this study. Thus, 46 studies were read in their entirety, in addition to 10 references found in the selected studies, although none of these were included since they did not evaluate the outcomes of interest. Of the 46 studies, six were included in the meta-analysis. The other forty were excluded because they either could not be located, were literature reviews, case reports, author responses, studies on children at least seven years of age, studies involving depression treatment, studies without clearly defined exposure or studies whose population base was duplicated in other studies. The following data were extracted from the selected articles (see Table 1): author, year of publication, country, study design, sample size, exposure, depression instrument, cutoff point, health outcomes, and adjustment factors for confounders and associations, Downs and Black quality index. The original estimates of two articles (Minkovitz, Strobino et al. 2005); (Sanderson, Cowden et al. 2002) were converted from odds ratio (OR) to relative risk (RR), as were their respective 95% confidence intervals, in order to compare them with the other included articles. The total sample is 170,371 mother-child pairs. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations (Shamseer L 2015).

Statistical analysis

After descriptions of the selected studies were made (Table 1), a meta-analysis was performed, stratified by prenatal and postnatal maternal depression, using random effects models to group the estimates. An independent meta-analysis was also conducted for each outcome (hospitalization and mortality). The heterogeneity between the studies was evaluated using the I^2 statistic (THOMPSON 2002). A funnel plot was used to assess the presence of publication bias (Egger, Davey Smith et al. 1997). All analyses were performed in Stata version 12.0 (StataCorp, 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

A total of 8,674 articles were identified (8,032 articles in PubMed and 642 in LILACS). After excluding 58 duplicates and another 8,570 articles after reading the titles and abstracts, 46 articles were read in full. At the end of the process, 6 studies were included in this review, representing a total population of 170,371 mother-child pairs. The third independent reviewer was needed once to resolve a consensus problem about including two studies, which were not included. The studies are all cohorts and have sufficient power to find associations. Respectively the sample size of each study: Chen, Y.H. et al. 90731 mother-child pairs; Chung, T.K. et al. 959 mother-child pairs; Farr et al. 24263 mother-child pairs; Minkovitz, C.S. et al. 4874 mother-child pairs; Sanderson, C.A. et al. 32984 mother-child pairs; Woebong, B. et al. 16560 mother-child pairs. The mean follow-up time of the children in the identified studies was 2.7 years.

Among the six selected articles, Chen, Y.H. et al. (Chen, Tsai et al. 2011) and Sanderson, C.A. et al. (Sanderson, Cowden et al. 2002) studied the relationship between postnatal maternal depression and infant mortality, Chung, T.K. et

al.(Chung, Lau et al. 2001) assessed the relationship between prenatal maternal depression and newborn hospitalization, Farr et al.(Farr, Dietz et al. 2013) assessed the relationship between prenatal and postnatal maternal depression and hospitalization in children, Minkovitz, C.S. et al.(Minkovitz, Strobino et al. 2005) studied postnatal maternal depression and hospitalization in children and Woebong, B. et al.(Woebong, ten Asbroek et al. 2015) assessed the relationship between postnatal maternal depression and child mortality.

Table 1 shows a summary of the studies included in this systematic review and meta-analysis. Two studies were conducted in the USA (Farr, Dietz et al. 2013),(Minkovitz, Strobino et al. 2005) one in Taiwan (Chen, Tsai et al. 2011), one in China (Chung, Lau et al. 2001), one in the UK (Sanderson, Cowden et al. 2002) and one in Ghana (Woebong, ten Asbroek et al. 2015). All studies were population-based with a prospective cohort design. The instruments used to measure depression included: the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (Chen, Tsai et al. 2011), the Beck Depression Inventory (BDI) (Chung, Lau et al. 2001), Center for Epidemiological Studies - Depression Scale (CES-D) (Minkovitz, Strobino et al. 2005), Edinburgh Postnatal Depression Scale (EPDS) (Sanderson, Cowden et al. 2002), the Patient Health Questionnaire (PHQ-9) (Woebong, ten Asbroek et al. 2015) and The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (Farr, Dietz et al. 2013). Minkovitz, C.S. et al. (Minkovitz, Strobino et al. 2005) and Chen, Y.H. et al. (Chen, Tsai et al. 2011) assessed the effect of maternal depression at various times in the child's life, up to 5 years of age. However, in this systematic review and meta-analysis, we evaluated only the effects of exposure in the first year.

Methodological Quality

All articles were ranked according to an adapted version of the Downs and Black quality index (Downs and Black 1998) that included 17 of the 27 original items. Specific questions for intervention studies were excluded (questions 4, 8, 12 to 15, 17, 19, 23 and 24). Each item contributed up to one point, except for item 4, which contributed up to two points (0 (no), 1 (partially) and 2 (yes)), such that the total score could vary from 0 to 18. The articles were classified as: high risk of bias (0 to 5 points), average risk of bias (6 to 11 points) or low risk of bias (12 to 18 points). All of the articles included in this review received between 14 and 16 points and are considered to be of low risk of bias.

Figure 2 presents the grouped effect of prenatal and postnatal maternal depressive symptoms or maternal depression on the child's physical health. A total of five studies (83,3%) reported postnatal depressive symptoms or depression totaling a sample size of 169,412 mother-child pairs and two studies (33,3%) reported prenatal depressive symptoms or depression totaling a sample size of 25,222 mother-child pairs. Five studies (83,3%) estimated a statistically significant effect for maternal depressive symptoms or depression on hospitalization and mortality in one-year-old children. The pooled relative risk of hospitalization or death for children whose mothers had prenatal and postnatal depressive symptoms or depression was 1.59 (CI_{95%} 1.17 - 2.16) times greater than those who did not. The pooled articles were very heterogeneous ($I^2 = 90.7\%$).

Effects of prenatal maternal depressive symptoms or depression on child health

Two studies (33, 3%) evaluated the effects of prenatal depressive symptoms or depression. Chung, T.K. et al. (Chung, Lau et al. 2001) suggested that children whose mothers have prenatal depressive symptoms or depression face twice the

risk of ICU admission than those who do not, while Farr et al. (Farr, Dietz et al. 2013) found no association between prenatal depression and hospitalization. The pooled relative risk estimate was 1.37 times higher for children whose mothers had prenatal depressive symptoms or depression (CI_{95%} 0.65 – 2.89) $I^2= 70.1%$ (Figure 2).

Effects of postnatal maternal depressive symptoms or depression on child health

Five articles (83,3%) assessed the effects of postnatal depressive symptoms or depression on child health. Of these three (50%), suggested a relatively low risk of death, Minkovitz, C.S. et al. (Minkovitz, Strobino et al. 2005), Farr et al. (Farr, Dietz et al. 2013) and Woebong, B. et al. (Woebong, ten Asbroek et al. 2015), while Sanderson, C.A. et al. (Sanderson, Cowden et al. 2002) suggested a threefold higher risk of death for children whose mothers had postnatal depressive symptoms than those who did not. These results were statistically significant. Chen et al. (Chen, Tsai et al. 2011) also found a positive association between postnatal depression and mortality, but the confidence interval of this risk includes the unit. The pooled relative risk estimate was 1.68 (CI_{95%} 1.18 - 2.38), $I^2 = 92.9%$) times greater in children whose mothers had postnatal depression (Figure 2).

Effects of prenatal and postnatal maternal depressive symptoms or depression and hospitalization and mortality in children

Figure 3 shows the results of the analysis stratified by outcome (mortality and hospitalization). A total of three studies (50%) reported mortality in children totaling a sample size of 140,275 mother-child pairs, while three studies (50%) reported hospitalization totaling 30,096 mother-child pairs. The pooled risk estimate for

hospitalization or death was 1.71 (CI_{95%} 1.24 – 2.37) times greater in children whose mothers had prenatal and postnatal depression; however, the studies had a high percentage of heterogeneity ($I^2 = 93.9\%$).

Effects of postnatal maternal depressive symptoms or depression on infant mortality

Three studies (50%) assessed the relationship between mortality in one-year-old children and postnatal depressive symptoms or depression. Two of them (33,3%), Sanderson, C.A. et al. (Sanderson, Cowden et al. 2002) and Woebong, B. et al. (Woebong, ten Asbroek et al. 2015), presented high and statistically significant relative risks. The pooled risk estimate of death in one-year-old children whose mothers had postnatal depressive symptoms or depression was 1.93 (CI_{95%} 1.02 – 3.64) times higher than those who did not ($I^2 = 92\%$) (Figure 3).

Effects of prenatal and postnatal maternal depressive symptoms or depression and hospitalization in children

Three studies (50%) evaluated the relationship between prenatal and/or postnatal depressive symptoms or depression and hospitalization in children. Chung, T.K. et al. (Chung, Lau et al. 2001) studied the relationship between prenatal depressive symptoms and hospitalization, finding a higher risk of hospitalization for children whose mothers had depressive symptoms than those who did not. Minkovitz, C.S. et al. (Minkovitz, Strobino et al. 2005) found a positive association between postnatal depressive symptoms and hospitalization, while Farr et al. (Farr, Dietz et al. 2013) found an association between prenatal and postnatal depression and hospitalization; these associations were statistically significant. The pooled risk estimate for hospitalization in children whose mothers had prenatal and postnatal depressive

symptoms or depression was 1.44 (CI_{95%} 1.10 – 1.89) times greater than those who did not ($I^2= 87.2%$) (Figure 3).

The funnel plot asymmetry (Figure 4) is probably due to the heterogeneity between studies, since the number of included studies did not allow publication bias assessment (T. 2014).

Discussion

An association was found between prenatal/postnatal depressive symptoms or depression and hospitalization and mortality in children up to one year of age. One plausible explanation for this result may be the fact that child health depends almost exclusively on the care that the mother provides. However, maternal depression negatively influences self-efficacy (Tuominen, Junttila et al. 2016), which has direct repercussions on certain factors related to child health, such as abandonment, a shortened period of exclusive breastfeeding (Machado, Assis et al. 2014, Rahman, Hafeez et al. 2016) and malnutrition in children under 5 years of age (Strobino, Ahmed et al. 2016, Wemakor and Mensah 2016, Motlhatlheddi, Setlhare et al. 2017). Anderson et al. (Anderson, Campbell et al. 2008) conducted a study in Canada about the effects of postnatal depression on emergency service usage in one-year-old children and found no association between them (Anderson, Campbell et al. 2008). The authors attributed this result to non-responder bias and memory bias, since the mothers who reported the number of times such services were utilized. Darcy, J.M. et al. (Darcy, Grzywacz et al. 2011) studied postnatal depression and quality of life related to child and maternal health in North Carolina, finding that mothers with significant postnatal depression symptoms reported that their children had more pain or discomfort and that their child's health-related quality of life was worse than

children whose mothers did not have such symptoms (Darcy, Grzywacz et al. 2011). Nevertheless, the authors cited reliance on parental report as a limitation, since by this method it could not be determined whether these infants actually had more pain and discomfort or whether these mothers were somatizing.

The lack of association we found between prenatal depressive symptoms or depression and child health (Figure 2) should be interpreted with caution for two reasons: (1) only two studies on prenatal depression and its effects on the health of children up to one year of age were included in this review and meta-analysis, too few to detect a possible association, (2) the included studies used different depression assessment tools and outcomes which, despite going in the same direction, differ in some way, for example, Chung, T.K. et al. (Chung, Lau et al. 2001) assessed the association between prenatal depression and intensive care unit (ICU) admissions (i.e. morbidity) in newborns, while Farr et al. (Farr, Dietz et al. 2013) studied service utilization or hospitalization in children up to one year of age.

Farr et al. (Farr, Dietz et al. 2013) evaluated maternal depression and hospitalization in children up to one year of age, finding an association with increased risk, however, when stratified according to prenatal or postnatal depression, the results differed, with only postnatal depression having an effect on hospitalization; the effect of prenatal depression disappeared. In addition, a reverse causality bias may have occurred in the association between postnatal depression and hospitalization, since about 70% of the mothers were diagnosed with depression after their child was hospitalized. Also the authors used the diagnosis of depression and anxiety with ICD-9-CM codes. They used maternal depression [ICD-9-CM codes 296.20–296.25 (major depressive episode, single episode), 296.30–296.35 (major depressive

episode, recurrent episode), 296.82 (atypical depressive disorder), 300.4 (dysthymic disorder), 309.0 (adjustment disorder with depressed mood), 309.1 (prolonged depressive reaction) and 309.28 (adjustment disorder with mixed anxiety and depressed mood)] and anxiety diagnoses [ICD-9-CM codes 300.00–300.02 and 300.09 (anxiety states), 300.20–300.29 (phobic disorders), 300.3 (obsessive compulsive disorders), 300.7 (hypochondriasis), 308.1–308.3 and 308.9 (acute reaction to stress), 309.21 (separation anxiety disorder), 309.24 (adjustment disorder with anxiety), 309.81 (posttraumatic stress disorder) and 313.0 (overanxious disorder)] diagnosed during pregnancy and/ or the first year after delivery. Based on their mother's diagnoses, the authors grouped infants into two categories of depression: maternal depression diagnosed during pregnancy and/or postpartum, and no depression diagnosed during pregnancy or postpartum, then, created a similar dichotomous anxiety variable. Mothers could have both depression and anxiety diagnoses. Once the diagnosis is made by a qualified professional as a psychologist or psychiatrist the diagnosis can be considered as the gold standard of any screening instrument for the disease. The problem is the authors did not specify who made the diagnoses and how they combined the codes to dichotomize the exposures.

We cannot assume that specific races or ethnicities are more affected or not by symptoms of depression or depression in this paper because four articles (66,7%) did not mention racial composition, assuming that the population of the studies was homogenous (Chen - Taiwan), (Chung – China), (Sanderson – UK), and (Woebong – Ghana). For those who related racial or ethnicity, Minkovitz's study has 59,4% and 24% of his population study respectively white and black in which 48,3% of white people and 33,3% of black people have symptoms of depression, while Farr's study

described its population as predominantly white 74% in which 84,3% have symptoms of depression. The total sample is not representative of all races or ethnicities.

The results show large variations due to the high heterogeneity between the studies ($I^2 = 93.9\%$) (Figure 2). Given the small number of studies included in this meta-analysis, it was not possible to perform a meta-regression to determine the causes of the high heterogeneity. Probable causes for it could include the variety of instruments used to screen for or diagnose depression and the different cut points involved, since the prevalence of depression varies according to both (Norhayati, Hazlina et al. 2015). Two studies used a clinical depression diagnosis (Chen, Tsai et al. 2011, Farr, Dietz et al. 2013), while four others used reliable and validated instruments to assess risk for depression. The way outcomes are measured can also be considered a source of heterogeneity between the studies. Minkovitz's study used a self-reported outcome (Minkovitz, Strobino et al. 2005), which can lead to memory bias, since some mothers may remember their child's health problems differently from others, which could change the effect estimate (Sedgwick 2014). Other characteristics of the study design, such as selection bias (Minkovitz, Strobino et al. 2005, Chen, Tsai et al. 2011) and non-respondent bias (Chung, Lau et al. 2001, Minkovitz, Strobino et al. 2005, Weobong, ten Asbroek et al. 2015), can decrease the power and accuracy of the results (Sedgwick 2011).

Strengths, Limitations and Future directions

We used the meta-analysis to determine the combined effects of the results of articles included in the study. Despite the limitations, the studies showed an effect of risk of hospitalization and mortality in children of depressive mothers or mothers with symptoms of depression.

As limitations of this study, different instruments and cut points were used to evaluate maternal depressive symptoms or maternal depression. On another side, one article did not report the cut points used to evaluate postnatal depression and another used the ICD-9-CM codes and did not clearly explain the dichotomization process of exposure. These flaws made it difficult to verify the validity of the instrument used to determine depression, even though the authors claim to have used secondary databases in which the patients were diagnosed with depression. An additional limitation is the non-standardized way in which hospitalization was defined, e.g. admission to the ICU or the use of health services. A further limitation is the small number of studies ($n < 10$), which allowed neither assessment for potential publication bias nor a meta-regression to determine the causes of the high heterogeneity between the studies.

Once again, this study highlights consequences of maternal depression on the medical health of children and the severity of the outcomes, future directions would be the implications of maternal and child health services in the early screening of symptoms of maternal depression.

Final considerations

The study showed the impact of prenatal and postnatal maternal depressive symptoms/depression on children, is a higher risk of hospitalization and mortality. It is an important public health problem that involves the health of both, the mother and the child supporting the need to systematize the screening of prenatal and postnatal maternal depression aiming for primary and secondary care treatment, which subsequently can improve the quality of care for pregnant women with depressive

symptoms/ Depression and their children. Few studies are focused on the effects of prenatal and postnatal maternal depression on the medical health of children, limiting the magnitude of possible results. In the future, more studies are needed to better explore the serious impact of the prenatal e postnatal maternal depression in the health of infants leading to an increase in children hospitalization and mortality.

This review has been registered with PROSPERO (number CRD42016051049)

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Figures

Figure 1: Study selection flowchart

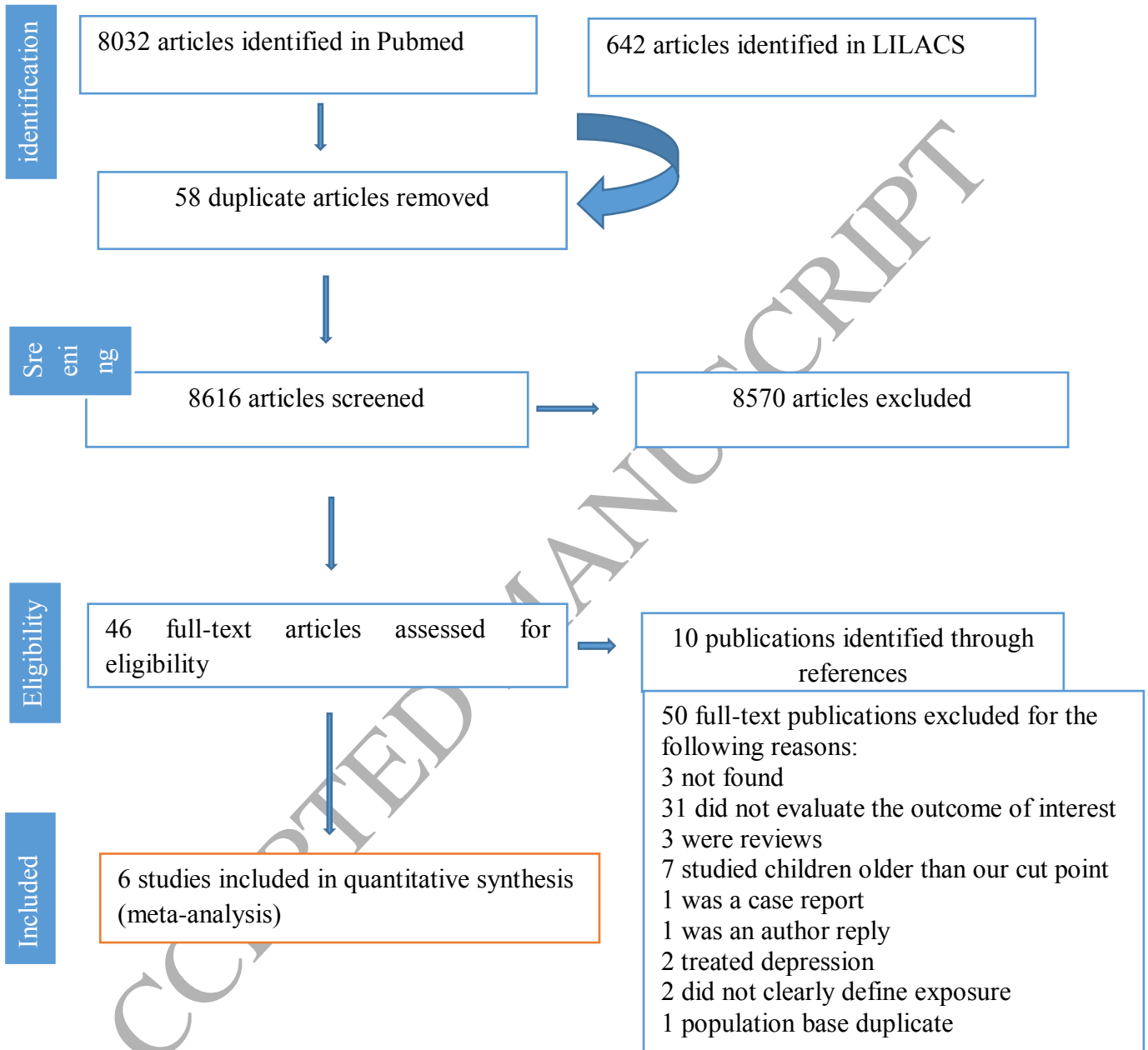


Figure 2: Meta-analysis of studies evaluating the effect of prenatal and postnatal depression on the physical health of children up to one year of age

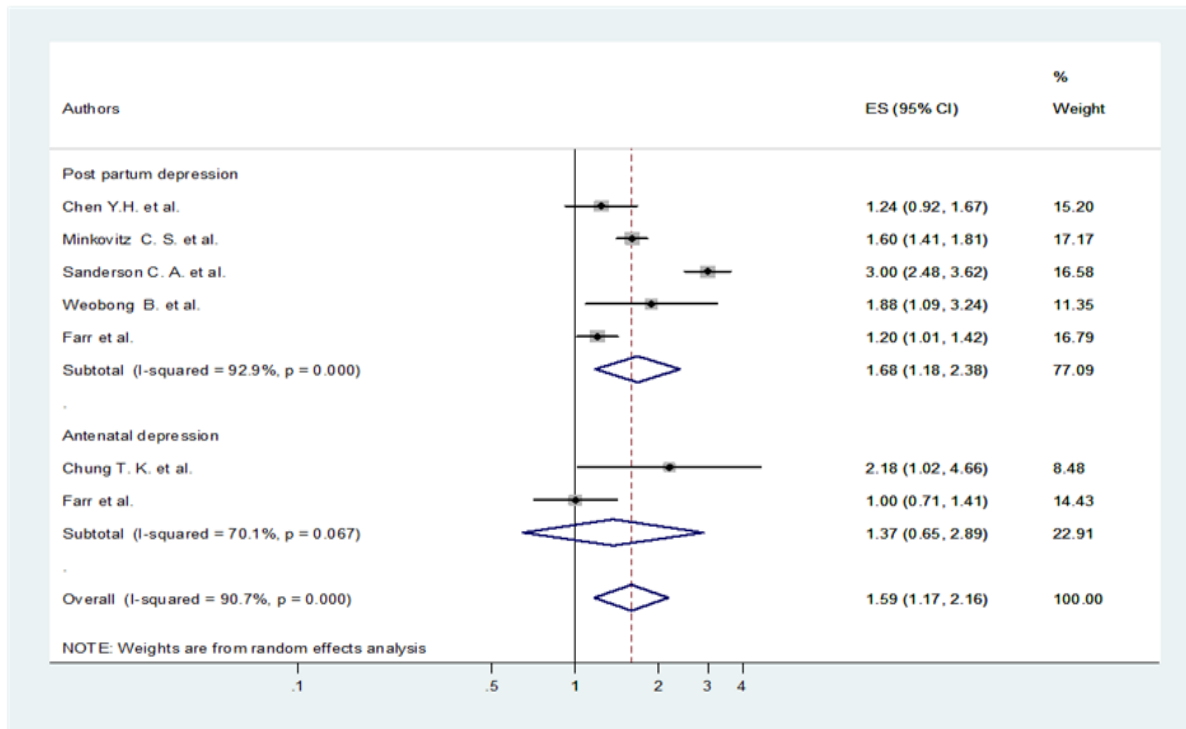


Figure 3: Randomized effect of studies evaluating hospitalization, mortality, and prenatal and postnatal depression in one-year-old children.

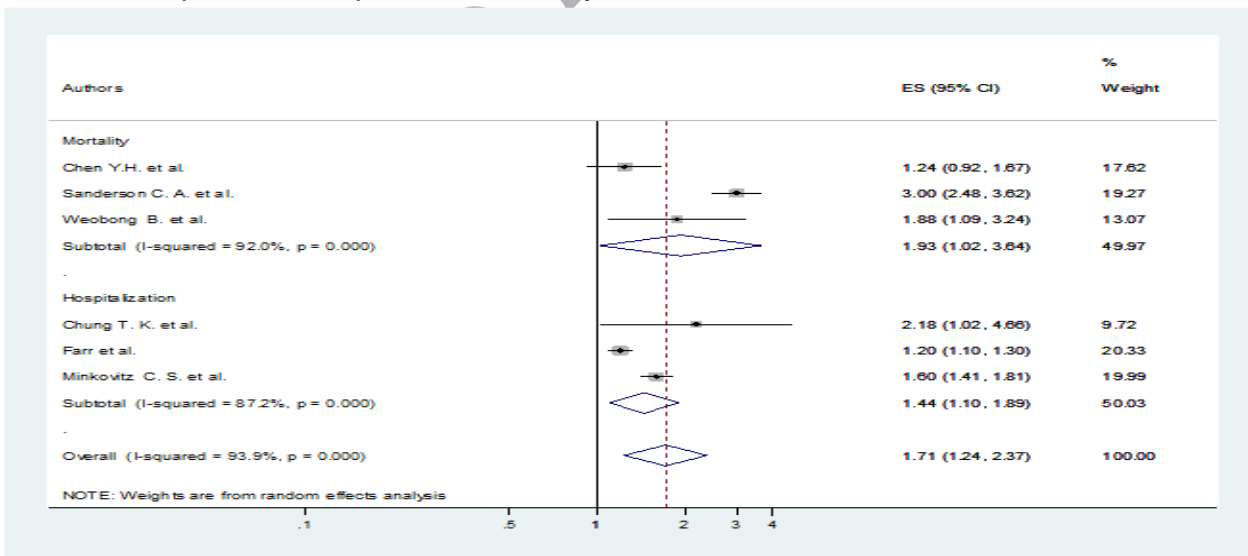
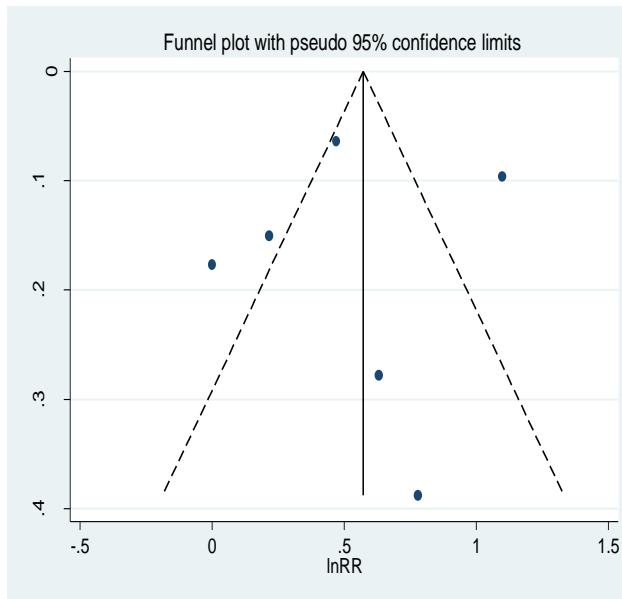


Figure 4: Funnel plot of study estimates



Table

Author /Year	Country	Study design	Sample size	Exposure	Instrument of measuring exposure	Outcome in child	Adjusted	Association	Down & Black quality scores
Chen Y.H. et al./2011	Taiwan	Cohort	90,731	Postnatal depression	DSM-IV	Mortality	Socioeconomic factors Gestational multimorbidity (including gestational diabetes and hypertension, coronary heart disease and a history of depressive disorder before delivery), Birth weight	No	15pts
Chung T.K. et al./2001	China	Cohort	959	Antenatal depression	BDI>14.5	Hospitalization	Demographic factors Parity Gestational multimorbidity (maternal diabetes, gestational hypertension, thyroid disorders, prenatal hemorrhage),	Yes	15pts
Farr et al./2013	USA	Cohort	24,263	Antenatal and postnatal depression	ICD-9-CM	Hospitalization	Socio-demographic factors Smoking Gestational age Gestational	Yes	15pts

							complication(hypertension/pre-eclampsia)		
Minkovitz C. S. et al./2005	USA	Cohort	4,874	Postnatal depression	CES-D>16	Hospitalization	Socioeconomic factors Demographic factors Birth weight Child health status	No	16pts
Sander son C.A. et al./2002	United Kingdom	Cohort	32,984	Postnatal depression	EPDS ≥9	Mortality	Social factors Demographic factors Parity Breast-feeding	Yes	14pts
Woebo ng B. et al./2015	Ghana	Cohort	16,560	Postnatal depression	PHQ-9>5	Mortality	Demographic factors Socioeconomic factors Parity Birth weight	Yes	16pts