Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 16 May 2026
Revised 26 June 2026
Accepted 10 July 2026

Natural Resources for Human Health 2026, Vol. 6 (7s): 40–48

KEYWORDS:
Low birth weight; Preterm birth; Maternal risk factors; Socioeconomic factors; Neonatal outcomes, Umbrella review, Meta analysis

Risk Factors for Preterm Delivery and Low Birth Weight: An Umbrella Review of Meta-Analysis

Ahmed S. Mikeal DDS[1*], Amani E. Bidalla BMS[2], Alzamka M. A. Almabruk[3], Rasha J. Abraheem MBChB[5], Shadin J. Abraheem[4] MBChB, sabah salah abd alaleam[6], Nada. M. Heebah[7], Maha A. Husayn[8], Mohammed A. Alnafea[9]

[1] Research Fellow, Libyan International University, Benghazi, Libya
[2] Department of Pediatrics, Tobruk Medical Center (TMC)
[3] Medical Laboratory Department, Faculty of Health Sciences , Omar AL-Mukhtar University,Al-Bayda, Libya
[4] Department of Infectious Disease and Immunology, Benghazi Medical Center
[5] Department of Obstetrics and Gynecology, Benghazi Medical Centre, Libya
[6] pediatric department, Tobruk medical center
[7] Pediatrician working at a Primary Health Care Center in Tobruk
[8] Faculty of Medicine, University of Tobruk, Tobruk, Libya
[9] Radiological Sciences Department, College of Applied Medical Sciences, King Saud University. P.O. Box 145111, Riyadh, 4545, Saudi Arabia
Corresponding Authors: alnafea@ksu.edu.sa , Ahmed.saeid.mikael@limu.edu.ly

ABSTRACT:

Background: Low birth weight (LBW) and preterm birth (PTB) are significant global health challenges associated with increased neonatal morbidity and mortality. This review aimed to comprehensively evaluate maternal, socioeconomic, and neonatal risk factors for LBW and PTB to inform clinical practice and public health interventions.

Method: We conducted a systematic review of meta-analyses published through February 2025. PubMed, Scopus, Web of Science, and Cochrane databases were searched for meta- analyses of observational studies examining risk factors for LBW (<2500g) and PTB (<37 weeks of gestation). Risk factors were categorized by evidence level (robust, highly suggestive, suggestive, or weak) based on statistical significance, sample size, heterogeneity, and potential biases. Random-effects models were used to calculate pooled odds ratios (ORs) with 95% confidence intervals (CIs).

Result: Our analysis included 86 meta-analyses encompassing 1,511 primary studies. For LBW, the strongest risk factors were maternal hypertension (OR 3.90, 95% CI 2.73-5.58), crack/ cocaine use (OR 2.82, 95% CI 2.26-3.52), and periodontal disease (OR 2.41, 95% CI (1.67-3.47). For PTB, placenta previa (OR 5.32, 95% CI 4.39-6.45), amphetamine exposure (OR 3.59, 95% CI 2.09-6.17) and chronic hypertension (OR 2.47, 95% CI 1.98-3.07) showed the strongest associations. Seven risk factors demonstrated robust evidence for PTB, while most LBW risk factors provided suggestive evidence. Medical conditions and substance use represented the largest categories of risk factors for both outcomes.

Natural Resources for Human Health
eISSN: 2583-1194

Conclusion: This umbrella review identified multiple modifiable risk factors for LBW and PTB with varying levels of evidence. Maternal hypertension, substance use, and periodontal disease emerged as key targets for intervention. Integrated prenatal care addressing both medical and psychosocial factors may help reduce the burden of adverse birth outcomes. Future research should focus on interventions targeting modifiable risk factors with robust evidence.

INTRODUCTION

Low birth weight (LBW), defined by the World Health Organization as a birth weight of less than 2,500 grams regardless of gestational age, remains a major public health concern worldwide. It is one of the leading causes of neonatal morbidity and mortality and has long-term implications for growth, development, and chronic disease risk in adulthood [1]. According to recent global estimates, more than 20 million infants are born with LBW each year, with the highest prevalence in low- and middle-income countries [2].

Preterm birth (PTB), defined as delivery before 37 completed weeks of gestation, is another significant contributor to adverse neonatal outcomes. Globally, about 15 million babies are born preterm annually, and the number is rising [3]. Preterm birth is associated with high mortality, high rates of neonatal intensive care admission, long-term neurodevelopmental impairment, and increased risk of chronic diseases in later life [4].

The etiology of both LBW and PTB is multifactorial, involving complex interactions between maternal, fetal, placental, and environmental factors [5]. Maternal factors play a crucial role in the incidence of both conditions. These include maternal age (particularly teenage pregnancy or advanced maternal age), poor nutritional status, multiple gestations, low pre-pregnancy body mass index (BMI), anemia, infections during pregnancy, chronic diseases such as hypertension or diabetes, substance abuse, and inadequate antenatal care [6]. The maternal environment and health status significantly influence fetal growth and pregnancy duration.

Socioeconomic and environmental factors also contribute substantially to adverse birth outcomes. Women from disadvantaged backgrounds often face barriers to accessing quality maternal healthcare, proper nutrition, and education, which increases the likelihood of LBW and PTB [7]. Stress, physical workload, exposure to environmental toxins, and domestic violence are also associated with increased risks [8]. Neonatal factors, including intrauterine growth restriction (IUGR), and congenital anomalies, have also been identified as contributors to LBW and PTB [9]. Babies born to mothers with a history of obstetric complications are at a higher risk of being born too early or too small. Additionally, male infants are generally at a higher risk of preterm birth and associated complications than female infants [10].

Despite extensive research on individual risk factors, there has been limited synthesis of the relative importance and strength of evidence for different risk factors across multiple studies. Previous meta-analyses have typically focused on specific risk factors or categories, without comprehensive comparison across the spectrum of potential determinants [11,12]. This gap in knowledge hampers the development of integrated prevention strategies and the prioritization of interventions.

The present meta-analysis aims to comprehensively evaluate the evidence for maternal, socioeconomic, and neonatal risk factors for LBW and PTB, assess the strength of evidence for each risk factor, and identify the most significant modifiable determinants. By synthesizing data from multiple meta-analyses and applying rigorous criteria for evidence assessment, this study seeks to provide a comprehensive overview to inform clinical practice, public health interventions, and future research priorities.

METHODS

This umbrella review and meta-analysis followed Cochrane Collaboration guidelines and was reported per the PRISMA statement. We included meta-analyses of observational studies (cohort, case-control, cross-sectional) evaluating risk factors for low birth weight (LBW; <2500 g) and/or preterm birth (PTB; <37 weeks gestation). Eligible studies reported pooled effect estimates (odds ratios [ORs], relative risks [RRs], hazard ratios [HRs]) with 95% confidence intervals (CIs); included ≥3 primary studies; assessed maternal, socioeconomic, environmental, or neonatal factors; and appeared in English peer-reviewed journals.

Exclusions comprised meta-analyses on genetic/molecular factors only; those lacking quantitative data; narrative reviews, editorials, case reports, or abstracts; and overlapping analyses (retaining the most comprehensive/recent based on sample size and quality).

Searches covered PubMed, Scopus, Web of Science, and Cochrane Library from inception to February 2025, using terms like "low birth weight," "preterm birth," "risk factors," "meta-analysis," and "systematic review." Reference lists were hand-searched. Rayyan software facilitated selection by two independent reviewers (titles/abstracts/full texts). Extraction covered first author/year, studies/participants, risk factors, effect sizes/CIs, and I^2 heterogeneity. Disagreements involved discussion or a third reviewer. From 2,769 records, 86 meta-analyses were included (published 2000–2025; 65% post-2015). Median primary studies: 9 (range 3–152). Median cases/controls: 98/807. Cases >1,000 in 98 comparisons (57.6%) (figure 1).

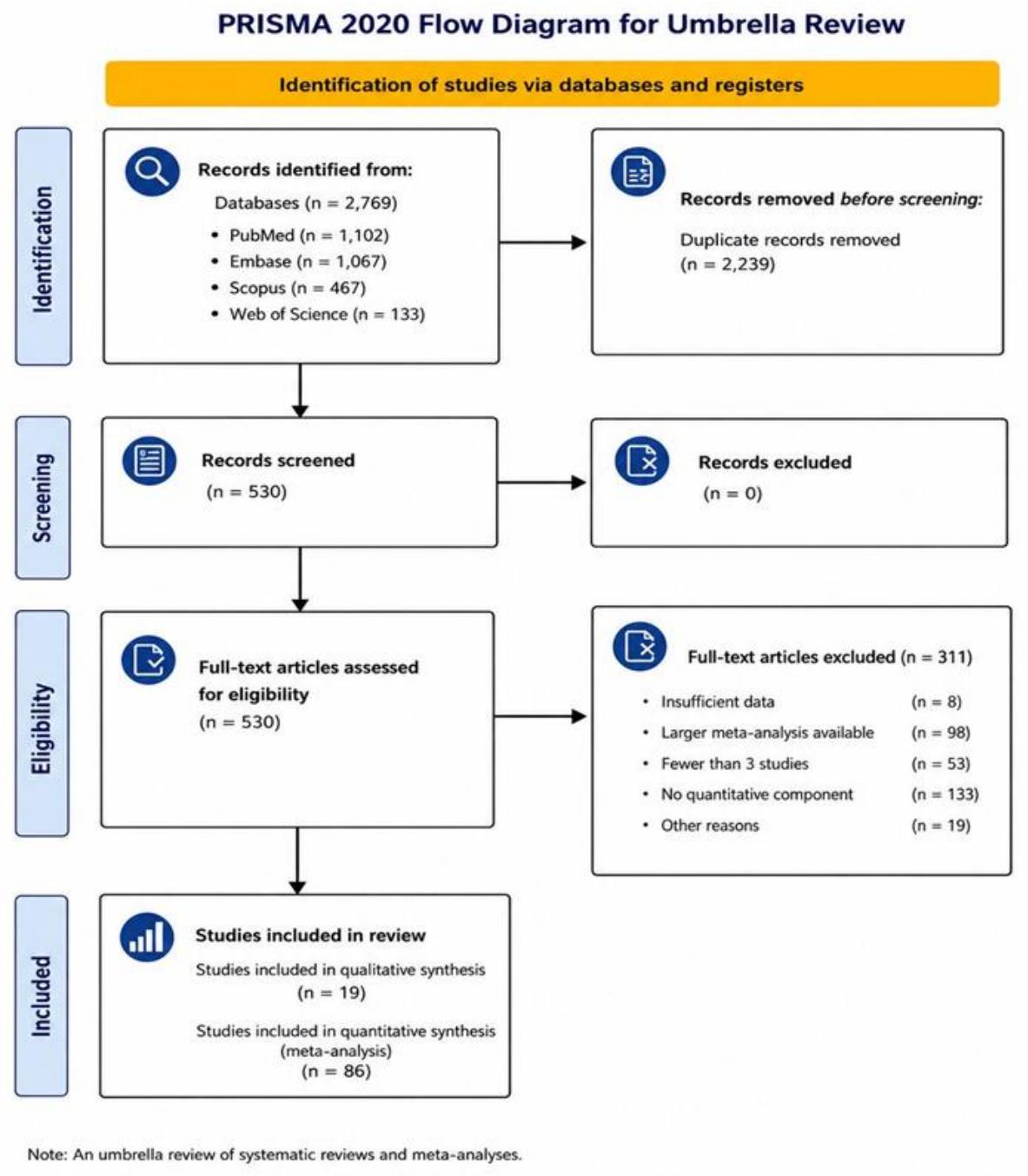

Figure 1: Prisma flow diagram

AMSTAR 2 evaluated methodological quality, classifying as high (32; 37.2%), moderate (28; 32.6%), low (18; 20.9%), or critically low (8; 9.3%). Common limitations: no protocol registration, incomplete bias assessment, inadequate publication bias checks. Assessments by two reviewers; consensus resolved discrepancies.

Pooled estimates (ORs, RRs, HRs) were extracted, interpreted cautiously across measures. Risk factors grouped as medical conditions, substance use, maternal characteristics, environmental/occupational, psychosocial. Evidence strength rated: robust, highly suggestive, suggestive, weak—based on significance, sample size, I^2 (>50% = substantial heterogeneity), publication bias. Sensitivity analyses excluded individual meta-analyses to test finding stability, where applicable.

RESULTS

Risk Factors for Low Birth Weight and Preterm Birth

The analysis identified fourteen maternal factors associated with increased risk of low birth weight. Figure 2 presents the ten strongest risk factors, ranked by pooled odds ratio. Maternal hypertension showed the strongest association with low birth weight (OR 3.90, 95% CI 2.73–5.58), followed by crack/cocaine use (OR 2.82, 95% CI 2.26–3.52), periodontal disease (OR 2.41, 95% CI 1.67–3.47), and smoking (OR 2.00, 95% CI 1.76–2.28). Other significant factors included heavy physical workload, maternal depression, and maternal underweight. Hypertension and smoking provided highly suggestive evidence, while seven factors provided suggestive evidence. Heterogeneity was high for eight factors and moderate for six. Prediction intervals excluded the null for five factors: hypertension, crack/cocaine use, smoking, depression, and anemia.

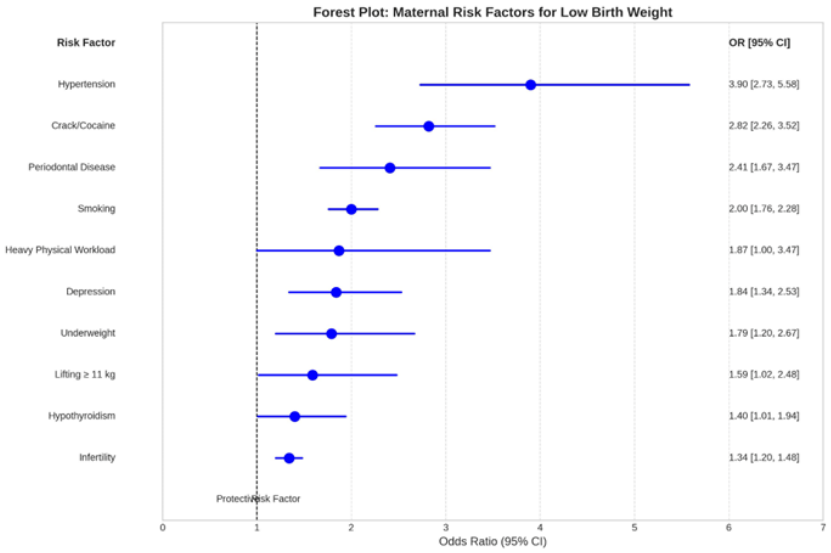

Figure 2. Forest plot of the top 10 maternal risk factors for low birth weight
(Forest plot of the top 10 maternal risk factors associated with LBW, based on pooled odds ratios (ORs) and 95% confidence intervals (CIs). Maternal hypertension had the highest risk, followed by crack/cocaine use, periodontal disease, and smoking. Risk factors are color-coded by evidence level)

Maternal hypertension showed the strongest association with LBW (OR 3.90, 95% CI 2.73-5.58), followed by crack/cocaine use (OR 2.82, 95% CI 2.26-3.52), and periodontal disease (OR 2.41, 95% CI 1.67-3.47). Other significant risk factors included smoking (OR 2.00, 95% CI 1.76-2.28), heavy physical workload (OR 1.87, 95% CI 1.00-3.47), maternal depression (OR 1.84, 95% CI 1.34-2.53), and maternal underweight (OR 1.79, 95% CI

1.20-2.67).

For preterm birth, twenty-eight significantly associated risk factors were identified. Figure 3 shows the ten strongest associations. Placenta previa had the largest effect, followed by amphetamine exposure (OR 3.59, 95% CI 2.09–6.17), isolated single umbilical artery (OR 2.75, 95% CI 2.32–3.27), and chronic hypertension (OR 2.47, 95% CI 1.98–3.07).

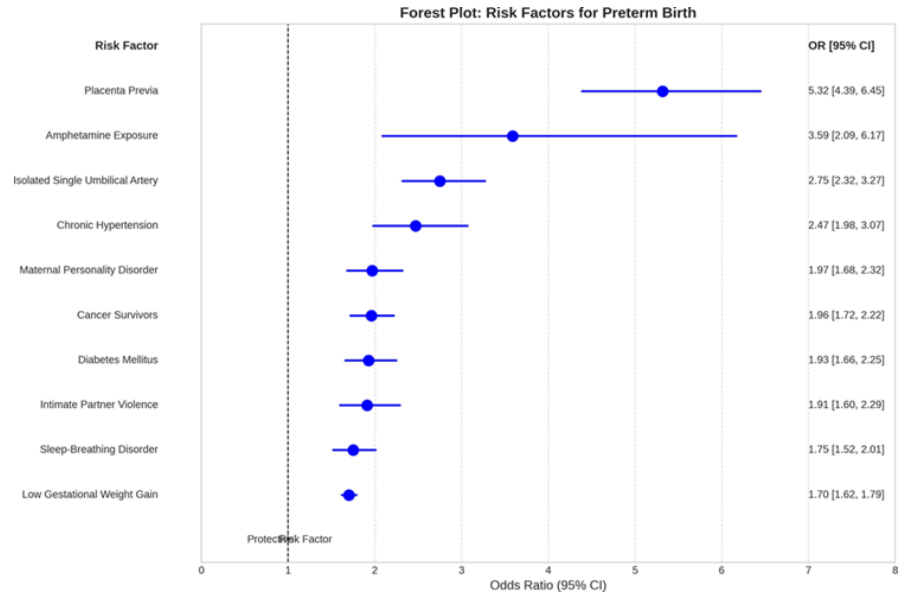

Figure 3. Forest plot of the top 10 maternal and neonatal risk factors for preterm birth
(Forest plot showing the 10 strongest risk factors for PTB, based on ORs and CIs. Placenta previa showed the strongest association, followed by amphetamine exposure, isolated single umbilical artery, and chronic hypertension. Risk factors are ranked by magnitude of association.)

Evidence strength did not always correspond to effect size, as some large associations were limited by heterogeneity, small-study effects, or insufficient sample size. Preterm birth had more robust evidence factors than low birth weight. Medical conditions were the largest category for both outcomes, while substance use was more prominent in low birth weight. Funnel-plot analysis suggested small-study effects in 41 comparisons.

Comparison of Evidence Levels:

Figure 4 illustrates the relationship between various risk factors and their corresponding levels of research evidence for low birth weight (LBW) and preterm birth (PTB). This visualization categorizes clinical findings to help differentiate between robust, high-quality data and weaker, more preliminary associations. By mapping these factors, the figure provides a clear hierarchy that aids in prioritizing clinical interventions based on the strength of supporting evidence.guides.library.stonybrook+1

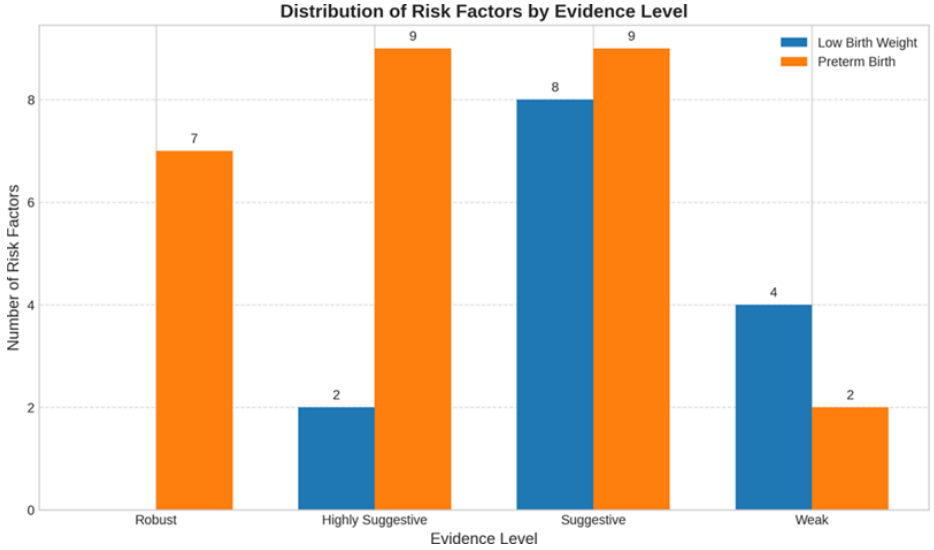

Figure 4 presents the distribution of risk factors by evidence level for both LBW and PTB.

The analysis revealed that PTB had more risk factors with robust evidence (n=7) compared to LBW (n=0). Both outcomes had similar numbers of risk factors with highly suggestive evidence (LBW: n=2; PTB: n=8). The majority of LBW risk factors provided suggestive evidence (n=7), while PTB risk factors were more evenly distributed across evidence levels.

Risk Factor Categories:

Risk factors were categorized into eight groups to identify patterns across different domains. Figure 5 categorizes identified risk factors into distinct thematic groups to clarify the drivers behind low birth weight (LBW) and preterm birth (PTB).

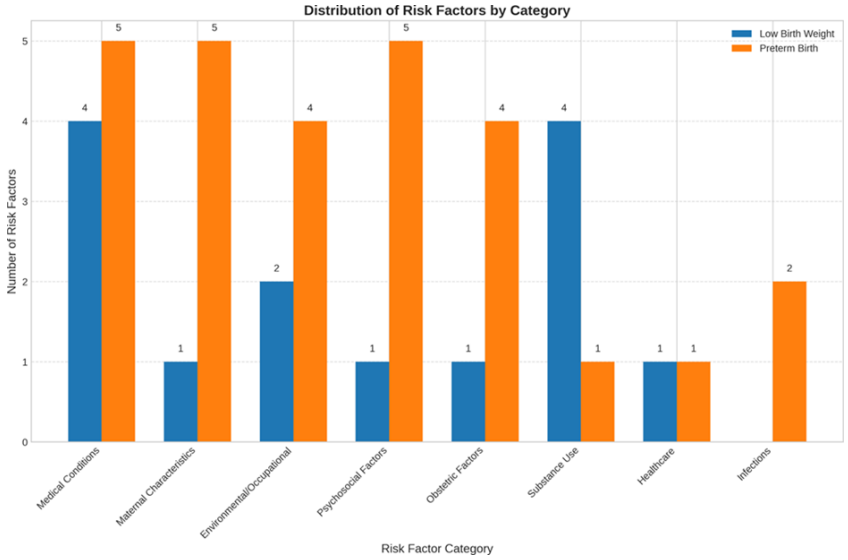

Figure 5 shows the distribution of risk factors by category for both outcomes.

Comparison of Top Risk Factors:

Figure 6 presents a side-by-side comparison of the five most significant risk factors for each outcome, ranked by the strength of their statistical association. Together, these visuals illustrate the classification of diverse risk factors and highlight the primary determinants influencing both birth outcomes. The comparison revealed that while some risk factors were specific to either LBW or PTB, others were common to both outcomes.

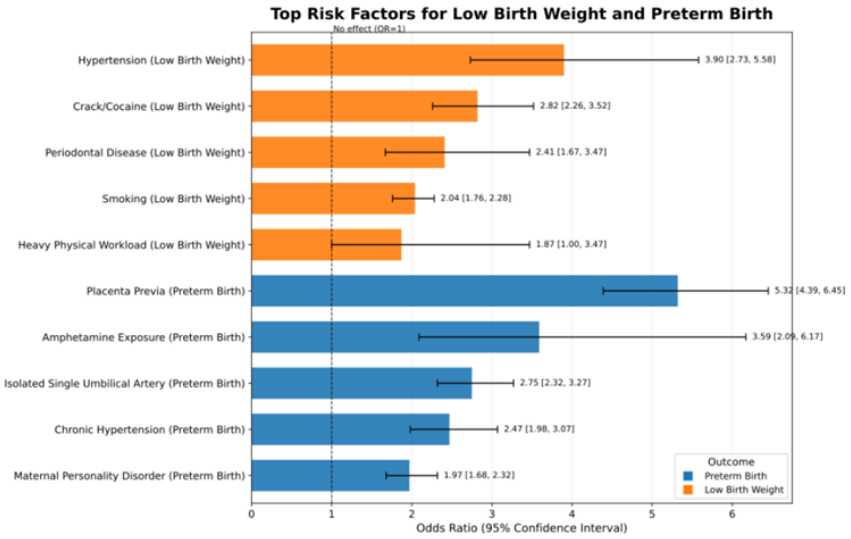

Figure 6: compares the top five risk factors for each outcome based on the magnitude of association.

Assessment of publication bias and small-study effects:

Funnel plots were visually inspected for asymmetry, and formal tests for small-study effects, including Egger's regression test, were applied where the number of studies was sufficient. Some funnel plots showed asymmetry, suggesting possible publication bias or small-study effects for selected risk factors. However, most comparisons did not demonstrate statistically significant evidence of funnel plot asymmetry, indicating that publication bias was not clearly evident across the majority of outcomes assessed.

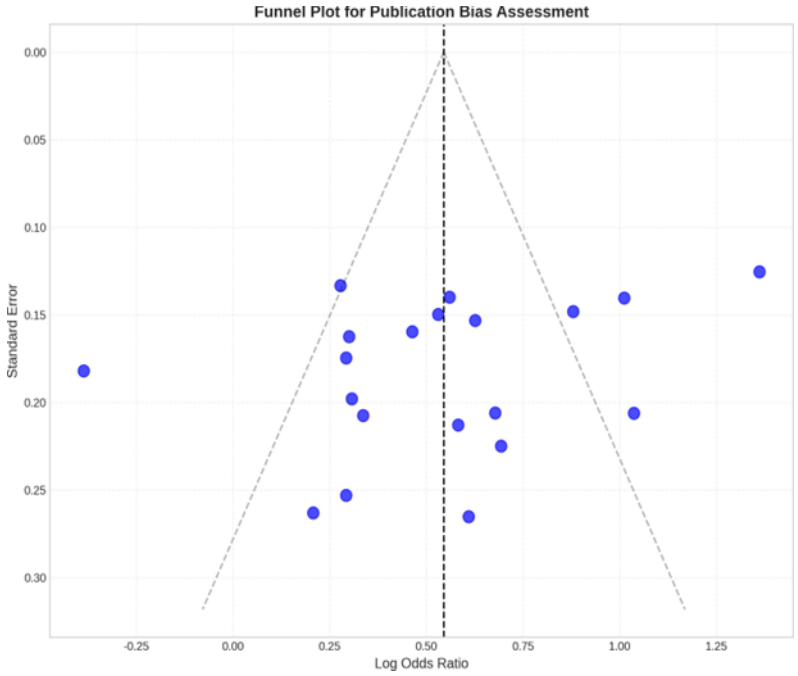

Figure 7: presents the funnel plot for the included studies.Discussion

This umbrella review synthesized evidence from 86 meta-analyses including 1,511 primary studies to evaluate risk factors for low birth weight (LBW) and preterm birth (PTB). The findings confirm the multifactorial nature of these adverse birth outcomes and identify several potentially modifiable factors that may inform clinical and public health interventions.

For LBW, maternal hypertension emerged as the strongest risk factor, with nearly a four-fold increase in risk. This is consistent with the role of hypertensive disorders in pregnancy in causing placental insufficiency, reduced uteroplacental blood flow, and impaired fetal growth [13]. Crack/cocaine use was the second strongest risk factor, likely reflecting its vasoconstrictive effects and adverse effects on maternal nutrition [14]. Periodontal disease was also strongly associated with LBW, supporting the hypothesis that maternal oral infection may trigger systemic inflammatory responses that affect fetal growth [15].

For PTB, placenta previa showed the strongest association, with approximately a five-fold increased risk, [16]. The review has several strengths, including broad coverage of LBW and PTB risk factors, direct comparison across outcomes, application of evidence assessment criteria, and categorization of risk factors by domain. However, important limitations should be acknowledged. These include dependence on the quality of included meta-analyses, inclusion of different observational study designs, conversion of different effect measures into odds ratios, substantial heterogeneity, inability to assess cumulative or interactive effects, and limited generalizability to low- and middle-income countries.

Clinically, the findings support comprehensive prenatal care that integrates screening and management of hypertension, substance use, oral health, and mental health conditions [17,18]. Public health strategies should prioritize modifiable risk factors supported by robust or highly suggestive evidence [19,20].

Future research should focus on intervention studies, cumulative risk profiling, implementation research in prenatal care, studies in low- and middle-income settings, and biological mechanisms underlying these associations. Overall, this review provides a foundation for targeted prevention and research priorities to reduce LBW and PTB.

Conclusions: This extensive umbrella review, which consolidated data from 86 meta-analyses and more than 1,500 original studies, offers a strong assessment of the risk factors linked to low birth weight (LBW) and preterm birth (PTB). The results affirm that both conditions stem from intricate interactions among medical, behavioral, and socioeconomic factors.

For LBW, maternal hypertension, substance abuse, and periodontal disease were identified as the most significant modifiable risk factors. Conversely, placenta previa, chronic hypertension, and exposure to certain substances showed the strongest correlations with PTB. It is crucial to note that the robustness of the evidence differed among risk factors, highlighting that clinical decisions should be based not only on the magnitude of the effect but also on the consistency and methodological quality of the research.

In essence, these findings emphasize the vital necessity for comprehensive, interdisciplinary strategies in maternal healthcare. Such approaches should concurrently address existing medical conditions, risky behaviors, and the broader social determinants of health. By focusing on impactful, modifiable risk factors, there is a considerable opportunity to lessen the worldwide prevalence of unfavorable birth outcomes.

Limitation

Several constraints must be acknowledged when interpreting the results of this umbrella review. Primarily, the findings are contingent upon the methodological quality of the included meta-analyses, which may harbor residual biases. Significant heterogeneity was observed across many comparisons, likely due to variations in study populations and definitions, which could affect the consistency of the pooled estimates. Furthermore, the inclusion of diverse observational study designs and the conversion of different effect measures (ORs, RRs, and HRs) may have introduced imprecision or bias related to temporality. The presence of small-study effects in some analyses also suggests a potential overestimation of certain associations. Additionally, this review focused on individual risk factors, thereby overlooking potential synergistic or cumulative effects. Finally, because the majority of the data originated from high-income countries, the generalizability of these findings to low- and middle-income settings—where the burden of adverse birth outcomes is most severe—may be limited.

REFERENCES

[1] McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. N Engl J Med. 1985;312(2):82-90.

[2] World Health Organization. Global nutrition targets 2025: low birth weight policy brief. Geneva: WHO; 2014.

[3] Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-2172.

[4] Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371(9608):261-269.

[5] Kramer MS. The epidemiology of adverse pregnancy outcomes: an overview. J Nutr. 2003;133(5 Suppl 2):1592S-1596S.

[6] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371(9606):75-84.

[7] Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA. Socioeconomic disparities in adverse birth outcomes: a systematic review. Am J Prev Med. 2010;39(3):263-272.

[8] Khanna C, Sood A, Chaudhry S, Kaur H, Nayyar A, Chopra G. Periodontal Vaccines: Boon or Mere Promise in Modern Dentistry?. Oral Sphere J. Dent. Health Sci. 2026;2(1):57-62. doi: 10.63150/osjdhs.2026.10

[9] Zeitlin J, Saurel-Cubizolles MJ, De Mouzon J, et al. Fetal sex and preterm birth: are males at greater risk? Hum Reprod. 2002;17(10):2762-2768.

[10] Peelen MJ, Kazemier BM, Ravelli AC, et al. Impact of fetal gender on the risk of preterm birth, a national cohort study. Acta Obstet Gynecol Scand. 2016;95(9):1034-1041.

[11] Flenady V, Koopmans L, Middleton P, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet. 2011;377(9774):1331-1340.

[12] Shah PS, Zao J, Ali S. Maternal marital status and birth outcomes: a systematic review and meta-analyses. Matern Child Health J. 2011;15(7):1097-1109.

[13] Bramham K, Parnell B, Nelson-Piercy C, Seed PT, Poston L, Chappell LC. Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. BMJ. 2014;348:g2301.

[14] Gouin K, Murphy K, Shah PS; Knowledge Synthesis Group on Determinants of Low Birth Weight and Preterm Births. Effects of cocaine use during pregnancy on low birthweight and preterm birth: systematic review and metaanalyses. Am J Obstet Gynecol. 2011;204(4):340.e1-12.

[15] Corbella S, Taschieri S, Del Fabbro M, Francetti L, Weinstein R, Ferrazzi E. Adverse pregnancy outcomes and periodontitis: A systematic review and meta-analysis exploring potential association. Quintessence Int. 2016;47(3):193-204.

~~[16]~~ Vahanian SA, Lavery JA, Ananth CV, Vintzileos A. Placental implantation abnormalities and risk of preterm delivery: a systematic review and metaanalysis. Am J Obstet Gynecol. 2015;213(4 Suppl):S78-90.

[17] Iams JD, Romero R, Culhane JF, Goldenberg RL. Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. Lancet. 2008;371(9607):164-175.

[18] Wright TE, Terplan M, Ondersma SJ, et al. The role of screening, brief intervention, and referral to teatment in the perinatal period. Am J Obstet Gynecol. 2016;215(5):539-547.

[19] Requejo J, Merialdi M, Althabe F, Keller M, Katz J, Menon R. Born too soon: care during pregnancy and childbirth to reduce preterm deliveries and improve health outcomes of the preterm baby. Reprod Health. 2013;10 Suppl 1:S4.

[20] Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet. 2013;381(9862):223-234.