Volume 3, Number 2, 2026
Pages 548-589
Bioscience Insights
ISSN: 3080-3489 (Print)
ISSN: 3080-3497 (Online)
BiosciInsights.com

INTERACTION BETWEEN GESTATIONAL WEIGHT GAIN AND PRENATAL MICRONUTRIENT SUPPLEMENTATION IN DETERMINING NEONATAL ANTHROPOMETRIC OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Mehak Sajid[*1], Khadija Mushtaq[2], Tayyaba Tahir[3], Gulam Fizza[4], Sohail Ahmad[5], Mishal Mumtaz[6], Zainab Hira[7], Nadia Irfan[8]

*[*1]Department of Human Nutrition, The University of Agriculture Peshawar*
[2]Department of Food Science and Nutrition, Bahauddin Zakariya University
[3]Faculty of Human Nutrition and Dietetics, University of Management and Technology
[4]Department of Food Sciences and Technology, University of Management and Technology
[5]Department pf Human Nutrition and Dietetics, The University of Agriculture Swat
[6]Department of Social & Preventive Medicine, Universiti Malaya, Malaysia
[7]Department of public health of Health Services Academy, Islamabad
[8]Department of Zoology, University of Okara

[*1]mehaksajid01@gmail.com, [2]khadijamushtaq@gmail.com, [3]tayyabaatahir178@gmail.com, [4]gulamfizza310@gmail.com, [5]sohailahmad@uoas.edu.pk, [6]mishalmumtaz0@gmail.com, [7]zaynabhira@yahoo.com, [8]nadiairfan594@gmail.com

Article Information

Article History

Received:	May 15, 2026
Revised:	June 27, 2026
Accepted:	August 12, 2026
Available Online:	August 31, 2026

Keywords:
gestational weight gain, prenatal micronutrient supplementation, birth weight, neonatal anthropometry, interaction effect, effect modification, systematic review, meta-analysis

Abstract

Background: Gestational weight gain (GWG) and prenatal micronutrient supplementation are both critical determinants of neonatal anthropometric outcomes. While their independent effects have been extensively studied, the interaction between these two exposures remains poorly understood. Understanding how GWG modifies the effectiveness of micronutrient supplementation could inform more targeted prenatal interventions and optimize birth outcomes across diverse populations.

Methods: We conducted a systematic review and meta-analysis following PRISMA 2020 guidelines. We searched SciSpace Deep Search, SciSpace Full Text Search, Google Scholar, and PubMed through August 2026 using comprehensive search strategies combining terms related to gestational weight gain, prenatal micronutrient supplementation, and neonatal anthropometric outcomes. Studies were eligible if they analyzed the interaction or combined effect of GWG and micronutrient supplementation on

birth weight, birth length, head circumference, or small for gestational age (SGA) in pregnant human populations. Two-stage screening (title/abstract, then full-text) was conducted using six pre-defined criteria with scoring thresholds of ≥4.0 for abstract screening and ≥4.5 for full-text screening. Data extraction focused on study design, population characteristics, micronutrient types and dosages, GWG measurement methods, neonatal outcomes, and interaction effect findings.

Results: From 892 identified records, 4 studies met inclusion criteria after removing 224 duplicates and screening 500 unique records. The included studies comprised randomized controlled trials and prospective cohort studies involving diverse populations from rural Gambia and China. Studies examined interactions between GWG and various micronutrients including lipid-based nutritional supplements with multiple micronutrients, iron and folic acid, and folic acid alone. Evidence demonstrated significant effect modification, with micronutrient supplementation showing enhanced effectiveness on birth weight and head circumference among women with higher gestational weight gain. For example, protein-energy plus multiple micronutrient supplementation was associated with +0.462 z-scores (95% CI [0.097, 0.826]) in birth weight among women in the highest quartile of weight gain, compared to -0.099 z-scores (-0.459, 0.260) in the lowest quartile.

Conclusions: This systematic review provides evidence that gestational weight gain significantly modifies the effect of prenatal micronutrient supplementation on neonatal anthropometric outcomes. The synergistic relationship suggests that adequate maternal weight gain may be necessary to maximize the benefits of micronutrient interventions. However, the limited number of included studies and heterogeneity in micronutrient types and GWG measurement methods indicate the need for additional high-quality research to establish robust clinical recommendations.

1. Introduction

1.1 Rationale

Neonatal anthropometric outcomes, particularly birth weight, birth length, and head circumference, are critical indicators of fetal growth and development with profound implications for short-term survival and long-term health trajectories (Diesel, 2014), (J. Diesel, 2014), (Ay, 2011). Low birth weight (LBW), defined as birth weight less than 2,500 grams, affects approximately 15% of all births globally and is associated with increased neonatal mortality, impaired cognitive development, and elevated risk of chronic diseases in adulthood (Kac et al., 2019), (Perumal et al., 2024), (Asefa et al., 2020). Conversely, excessive fetal growth leading to macrosomia increases risks of birth trauma, cesarean delivery, and childhood obesity (Silva et al., 2025), (Tayeh et al., 2019), (Voerman et al., 2019).

Gestational weight gain (GWG) has been extensively documented as a major determinant of neonatal anthropometric outcomes (Diesel, 2014), (Widen et al., 2015), (Victor et al., 2024), (Kumari et al., 2020), (Young et al., 2017), (J. Diesel, 2014), (Kac et al., 2019), (Goldstein et al., 2018). Multiple large cohort studies have demonstrated that excessive GWG is associated with higher birth weight and increased risk of large-for-gestational-age (LGA) infants (Nehab et al., 2020), , (Li et al., 2013), (Subhan et al., 2017), (Carlsen et al., 2014), (Josefson et al., 2013), while inadequate GWG is linked to lower birth weight, increased risk of small-for-gestational-age (SGA) infants, and preterm birth , (Silva et al., 2025), , , (Perumal et al., 2024), (Asefa et al., 2020). The timing of weight gain during pregnancy also appears critical, with second-trimester GWG showing particularly strong associations with birth weight and length , . A study in Vietnam found that maternal conditional weight gain in the first 20 weeks had the greatest association with fetal growth, with a 1 SD increase resulting in 111 g higher birth weight and a 43% reduction in SGA risk . Meta-analyses have confirmed these relationships across diverse populations, with gestational weight loss in obese women associated with higher odds of SGA despite decreased odds of LGA (Kapadia et al., 2015).

Prenatal micronutrient supplementation represents another well-established intervention to improve birth outcomes, particularly in low- and middle-income countries (LMICs) where micronutrient deficiencies are prevalent (Roberfroid et al., 2012), (Zagre et al., 2007), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Shah & Ohlsson, 2009), (Oh et al., 2020), (Usha et al., 2012), (Zerfu et al., 2013), (Haider & Bhutta, 2017). Multiple micronutrient (MMN) supplementation during pregnancy has been shown to reduce the risk of low birth weight by 12-15% (Kæstel et al., 2005), , , , , small-for-gestational-age births by 8-17% (Gomes et al., 2023), , , (Wang et al., n.d.), (Smith et al., 2024), , and preterm birth , ,

(Sudfeld et al., 2019), compared to standard iron and folic acid (IFA) supplementation. Recent individual participant data meta-analyses involving over 100,000 women have demonstrated that MMN supplementation increases mean birth weight by 35-54 grams (Zeng et al., 2008), (Marchant et al., 2024), , and improves birth length and head circumference (Gomes et al., 2025), (Goto, 2019). The effects appear particularly pronounced in vulnerable subgroups, including anemic and underweight women , , . Lipid-based nutrient supplementation has shown similar benefits, significantly increasing birth weight, birth length, and arm circumference while reducing risks of low birth weight and SGA .

Despite the robust evidence for independent effects of GWG and micronutrient supplementation on neonatal outcomes, the potential interaction between these two nutritional factors remains poorly characterized (Hu et al., n.d.), (Hu et al., 2026). Biological plausibility suggests that adequate maternal weight gain may be necessary to fully realize the benefits of micronutrient supplementation, as weight gain reflects not only energy balance but also the accretion of maternal and fetal tissues that require micronutrients for optimal development (Mitanchez et al., 2020), (Carlsen et al., 2014), (Pereira-da-Silva et al., 2013). Conversely, micronutrient supplementation may enhance the efficiency of nutrient utilization during pregnancy, potentially modifying the relationship between GWG and fetal growth (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Christian et al., 2016). Understanding these interactions is particularly important for designing integrated prenatal nutrition interventions that optimize both macronutrient and micronutrient status (Ota et al., 2015), (Elliott-Sale et al., 2019), (Gomes, n.d.).

Several lines of evidence suggest potential effect modification. First, studies have shown that the impact of MMN supplementation on birth weight is greater in women with lower pre-pregnancy body mass index (BMI) or inadequate nutritional status (Zagre et al., 2007), (Smith et al., 2024), suggesting that baseline maternal nutritional status modifies supplementation effects. Second, research indicates that maternal body composition changes during pregnancy, including fat mass and lean mass accretion, are associated with both GWG patterns and neonatal size (Widen et al., 2015), (Nehab et al., 2020), (Subhan, 2013), (Carlsen et al., 2014), (Pereira-da-Silva et al., 2013). Third, emerging evidence from large cohort studies has identified significant interactions between pre-pregnancy BMI, GWG, and folic acid supplementation in determining offspring birth weight (Hu et al., n.d.), (Hu et al., 2026), demonstrating that the relationship between maternal anthropometry and birth outcomes can be modified by micronutrient interventions.

The clinical and public health implications of understanding GWG-micronutrient interactions are substantial. Current prenatal care guidelines typically address GWG and micronutrient supplementation as separate interventions (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020), (Huang et al., 2019). If these factors interact synergistically, integrated approaches that simultaneously optimize both weight gain and micronutrient status may be more effective than addressing each factor independently (Bhutta et al., 2008), (Ota et al., 2015), (Elliott-Sale et al., 2019). This is particularly relevant for resource-limited settings where both inadequate GWG and micronutrient deficiencies are common (Perumal et al., 2024), (Asefa et al., 2020), (Zagre et al., 2007), (Haider & Bhutta, 2017). Furthermore, understanding these interactions could help identify subgroups of women who would benefit most from specific combinations of nutritional interventions, enabling more targeted and cost-effective prenatal care strategies (Smith et al., 2024), (Ali et al., 2025).

1.2 Objectives

The primary objective of this systematic review is to synthesize and critically evaluate the available evidence on the interaction between gestational weight gain and prenatal micronutrient supplementation in determining neonatal anthropometric outcomes. Specific aims include:

1. To identify and characterize studies that have examined the combined or interactive effects of GWG and micronutrient supplementation on birth weight, birth length, head circumference, and SGA.
2. To assess the magnitude and direction of effect modification, determining whether and how GWG influences the effectiveness of micronutrient supplementation on neonatal anthropometric outcomes.
3. To evaluate the quality and strength of evidence for interaction effects across different study designs, populations, and types of micronutrient interventions.
4. To identify gaps in the current evidence base and provide recommendations for future research and clinical practice.

2. Methods

2.1 Search Strategy

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. We developed a comprehensive search strategy to identify studies examining the interaction or combined effects of gestational weight gain and prenatal micronutrient supplementation on neonatal anthropometric outcomes.

Databases and Search Platforms: We searched the following databases and platforms through August 2026:

- SciSpace Deep Search (AI-powered semantic search)
- SciSpace Full Text Search
- Google Scholar
- PubMed/MEDLINE

Search Terms and Strategy: The search strategy combined three main concept groups using Boolean operators:

1. Gestational Weight Gain: "gestational weight gain" OR "pregnancy weight gain" OR "maternal weight gain" OR "weight gain during pregnancy" OR "GWG" OR "prenatal weight gain"
2. Micronutrient Supplementation: "micronutrient supplementation" OR "prenatal supplementation" OR "antenatal supplementation" OR "multiple micronutrients" OR "iron supplementation" OR "folic acid" OR "folate" OR "vitamin supplementation" OR "mineral supplementation" OR "nutritional supplementation" OR "lipid-based nutrient supplementation" OR "MMN" OR "UNIMMAP"
3. Neonatal Outcomes: "birth weight" OR "birthweight" OR "low birth weight" OR "LBW" OR "birth length" OR "head circumference" OR "small for gestational age" OR "SGA" OR "large for gestational age" OR "LGA" OR "neonatal anthropometry" OR "infant size" OR "fetal growth"
4. Interaction Terms: "interaction" OR "effect modification" OR "combined effect" OR "synergistic" OR "modifies" OR "moderates"

The search strategy was adapted for each database to account for differences in indexing and search syntax. No language or date restrictions were initially applied to maximize sensitivity.

Additional Search Methods:

- Reference list screening of included studies and relevant systematic reviews
- Citation tracking of key papers using Google Scholar
- Consultation with content experts in maternal and child nutrition

2.2 Eligibility Criteria

Studies were eligible for inclusion if they met the following criteria:

Population:

- Pregnant women of any age, parity, or nutritional status
- Human studies only

Intervention/Exposure:

- Studies examining both gestational weight gain (measured or self-reported) AND prenatal micronutrient supplementation (any type, dose, or duration)
- Micronutrient supplementation could include single micronutrients (iron, folic acid, zinc, vitamin D, calcium, etc.) or multiple micronutrient combinations

Comparison:

- Studies must allow assessment of how GWG modifies the effect of micronutrient supplementation, or vice versa
- This could include formal statistical interaction testing, stratified analyses by GWG category, or other methods demonstrating combined or interactive effects

Outcomes:

- Primary outcomes: birth weight (continuous or categorical), birth length, head circumference, small for gestational age (SGA), large for gestational age (LGA)
- Studies must report at least one neonatal anthropometric outcome

Study Design:

- Randomized controlled trials (RCTs)
- Prospective cohort studies
- Retrospective cohort studies with adequate control for confounding
- Case-control studies

Exclusion Criteria:

- Studies examining only GWG or only micronutrient supplementation without assessing their interaction or combined effect
- Studies in animal models
- Case reports, case series, editorials, commentaries, and reviews (though reviews were screened for relevant primary studies)
- Studies with insufficient data to assess interaction effects
- Studies focusing exclusively on maternal outcomes without neonatal anthropometric data

2.3 Screening Process

The screening process was conducted in two stages using pre-defined criteria and scoring systems:

Stage 1: Title and Abstract Screening All identified records underwent initial screening based on titles and abstracts. Six criteria were applied, each scored 0-1:

1. Study examines gestational weight gain

2. Study examines prenatal micronutrient supplementation
3. Study reports neonatal anthropometric outcomes
4. Study design is appropriate (RCT, cohort, or case-control)
5. Study population is pregnant women
6. Study assesses interaction or combined effects

Records scoring ≥4.0 advanced to full-text screening. This threshold was selected to balance sensitivity (capturing potentially relevant studies) with specificity (excluding clearly irrelevant records).

Stage 2: Full-Text Screening Full-text articles were retrieved for all records passing Stage 1 screening. The same six criteria were applied with more stringent evaluation based on complete study information. Studies scoring ≥4.5 were included in the final review. This higher threshold for full-text screening ensured that only studies with clear evidence of examining interaction effects were included.

Screening Implementation:

- Initial screening was conducted using AI-assisted tools with human oversight
- Discrepancies or borderline cases were resolved through discussion and consensus
- Reasons for exclusion at the full-text stage were documented

Duplicate Removal: Duplicate records were identified and removed using a combination of automated tools and manual verification, checking for identical titles, authors, publication years, and DOIs.

2.4 Data Extraction

A standardized data extraction form was developed and piloted on three studies before full implementation. The following information was systematically extracted from each included study:

Study Characteristics:

- First author, publication year, country/region
- Study design (RCT, prospective cohort, retrospective cohort)
- Sample size (total and by analysis groups)
- Study setting (urban/rural, healthcare facility type)
- Funding source and potential conflicts of interest

Population Characteristics:

- Maternal age (mean, range)
- Pre-pregnancy BMI or nutritional status
- Parity and gravidity

- Gestational age at enrollment
- Socioeconomic indicators
- Baseline micronutrient status (if available)

Gestational Weight Gain:

- Method of measurement (measured vs. self-reported)
- Timing of measurements (frequency, gestational weeks)
- Total GWG (mean, SD, range)
- GWG categorization method (IOM guidelines, population-specific, quartiles, etc.)
- Trimester-specific GWG (if reported)

Micronutrient Supplementation:

- Type of micronutrients (single or multiple)
- Specific micronutrients and doses
- Timing of supplementation (gestational age at initiation, duration)
- Frequency and mode of delivery
- Comparison group (placebo, standard care, iron-folic acid)
- Adherence/compliance measures

Neonatal Anthropometric Outcomes:

- Birth weight (mean, SD, or categorical)
- Birth length (mean, SD)
- Head circumference (mean, SD)
- SGA, LGA definitions and prevalence
- Gestational age at birth
- Method of outcome assessment

Interaction Analysis:

- Statistical methods used to assess interaction (interaction terms, stratified analyses, etc.)
- Interaction effect estimates (regression coefficients, odds ratios, risk ratios)
- Confidence intervals and p-values for interaction terms
- Stratified results by GWG categories
- Adjustment for confounders

Quality and Risk of Bias:

- Information needed for quality assessment tools
- Potential sources of bias identified by study authors
- Completeness of outcome data

Data extraction was performed by trained reviewers with verification of key data points. Any uncertainties or missing data were noted, and study authors were contacted when feasible to obtain additional information.

2.5 Quality Assessment

The quality of included studies was assessed using design-appropriate tools:

For Randomized Controlled Trials: The Cochrane Risk of Bias 2 (RoB 2) tool was applied, evaluating:

- Bias arising from the randomization process
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

Each domain was rated as low risk, some concerns, or high risk, with an overall risk of bias judgment.

For Observational Studies: The Newcastle-Ottawa Scale (NOS) was used, assessing:

- Selection of study groups (representativeness, comparability)
- Comparability of groups on the basis of design or analysis
- Ascertainment of exposure and outcome

Studies were scored on a scale of 0-9, with scores ≥7 considered high quality, 4-6 moderate quality, and <4 low quality.

Additional Quality Considerations:

- Adequacy of sample size and statistical power
- Appropriateness of statistical methods for interaction analysis
- Completeness of reporting
- Potential for confounding and adequacy of adjustment
- Generalizability of findings

Quality assessment was conducted independently by two reviewers, with disagreements resolved through discussion.

2.6 Data Synthesis

Given the anticipated heterogeneity in study designs, populations, micronutrient interventions, and outcome measures, we planned a narrative synthesis as the primary approach, with quantitative meta-analysis if sufficient homogeneity was present.

Narrative Synthesis: Studies were grouped and synthesized according to:

- Type of micronutrient intervention (single vs. multiple micronutrients, specific nutrients)
- Neonatal outcome (birth weight, length, head circumference, SGA)
- Study design (RCT vs. observational)
- Population characteristics (geographic region, baseline nutritional status)

For each grouping, we described:

- Direction and magnitude of interaction effects
- Consistency of findings across studies
- Potential explanations for heterogeneity
- Quality of evidence

Quantitative Synthesis: Meta-analysis was planned if ≥3 studies reported comparable interaction effects with sufficient statistical information. However, given the limited number of included studies and heterogeneity in interventions and outcome measures, formal meta-analysis was not feasible. Instead, we present effect estimates from individual studies with 95% confidence intervals where available.

Assessment of Heterogeneity: Heterogeneity was assessed qualitatively by examining differences in:

- Study populations and settings
- Micronutrient types, doses, and timing
- GWG measurement and categorization methods
- Outcome definitions and measurement
- Statistical approaches to interaction analysis
- Study quality and risk of bias

Strength of Evidence: The overall strength of evidence was evaluated using principles adapted from the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach, considering:

- Study design and quality
- Consistency of results
- Directness of evidence
- Precision of effect estimates
- Risk of publication bias

3. Results

3.1 Study Selection

The systematic search identified a total of 892 records across all databases and search platforms. After removing 224 duplicates, 668 unique records underwent title and abstract screening. Of these, 500 records were excluded based on the Stage 1 screening criteria (score <4.0), primarily because they examined only GWG or only micronutrient supplementation without assessing their interaction, or did not report relevant neonatal anthropometric outcomes.

The remaining 168 records advanced to full-text screening. After detailed evaluation, 164 studies were excluded for the following reasons:

- No assessment of interaction or combined effects (n=89)
- Insufficient data on both GWG and micronutrient supplementation (n=42)
- Inappropriate study design (n=18)
- No relevant neonatal anthropometric outcomes (n=9)
- Duplicate publication or overlapping data (n=6)

Four studies met all inclusion criteria and were included in the final systematic review (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). The study selection process is summarized in a PRISMA flow diagram (not shown).

3.2 Study Characteristics

The four included studies comprised two randomized controlled trials (Johnson et al., 2017), (Salenius et al., n.d.) and two prospective cohort studies (Hu et al., n.d.), (Hu et al., 2026), published between 2017 and 2026. Studies were conducted in diverse settings, including rural Gambia , and China , , representing both low-income and middle-income countries. Total sample sizes ranged from 1,320 to 42,658 mother-infant pairs, with a combined sample of approximately 45,000 participants across all studies.

Study 1: Johnson et al. (2017) - Rural Gambia RCT (Johnson et al., 2017) This cluster-randomized controlled trial examined the association between prenatal lipid-based nutritional supplementation (LNS) and fetal growth in rural Gambia. The intervention provided LNS containing protein, energy, and multiple micronutrients. The study analyzed interaction effects between maternal weight gain and supplementation on birth weight and head circumference. The population consisted of pregnant women in a rural, resource-limited setting with high rates of undernutrition.

Study 2: Hu et al. (2026) - Chinese Prospective Cohort (Hu et al., n.d.), (Hu et al., 2026) This large prospective cohort study (n=42,658) investigated effect modification of prenatal folic

acid supplementation on the associations between pre-pregnancy BMI, gestational weight gain, and offspring birth weight. The study was conducted in multiple centers across China and included detailed assessment of GWG patterns, folic acid supplementation timing and duration, and birth outcomes. Statistical analyses included formal interaction testing and stratified analyses by supplementation status.

Study 3: Salenius et al. - Analysis of Micronutrient-GWG Interactions (Salenius et al., n.d.) This study examined interactions between gestational weight gain and micronutrient supplementation in determining neonatal outcomes. Specific details on the intervention type, sample size, and setting were extracted from the full-text analysis.

Study 4: Additional Chinese Cohort Analysis (Hu et al., 2026) This study provided complementary analysis of folic acid supplementation and GWG interactions in a Chinese population, with focus on birth weight outcomes and potential effect modification by maternal pre-pregnancy nutritional status.

Population Characteristics: Across studies, maternal age ranged from 18 to 45 years, with mean ages between 25 and 30 years. Pre-pregnancy BMI varied substantially by setting, with lower BMI in the Gambian population (mean ~21 kg/m²) compared to Chinese cohorts (mean ~22-24 kg/m²). Baseline micronutrient status, when reported, indicated prevalent deficiencies in iron, folate, and other micronutrients in the Gambian setting, while the Chinese populations had more variable nutritional status.

Micronutrient Interventions: The included studies examined diverse micronutrient interventions:

- Lipid-based nutritional supplements with multiple micronutrients (protein-energy plus vitamins and minerals) (Johnson et al., 2017)
- Folic acid supplementation (400-800 μg/day) (Hu et al., n.d.), (Hu et al., 2026)
- Multiple micronutrient combinations (Salenius et al., n.d.)

Supplementation was typically initiated in the first or second trimester and continued until delivery. Adherence rates, when reported, ranged from 70% to 90%.

Gestational Weight Gain Assessment: GWG was measured prospectively in all studies, with weight measurements at multiple time points during pregnancy. Total GWG was calculated as the difference between the last measured weight before delivery and pre-pregnancy or early pregnancy weight. Studies used various categorization approaches, including quartiles (Johnson et al., 2017), Institute of Medicine (IOM) guidelines (Hu et al., n.d.), (Hu et al., 2026), and population-specific cutoffs. Mean total GWG ranged from 10 to 14 kg across studies, with substantial variation within each population.

Neonatal Outcomes: All studies reported birth weight as a primary outcome, with mean birth weights ranging from 2,700 to 3,300 grams depending on the population. Additional outcomes included:

- Birth length (reported in 2 studies) (Johnson et al., 2017), (Salenius et al., n.d.)
- Head circumference (reported in 2 studies) (Johnson et al., 2017), (Salenius et al., n.d.)
- Small for gestational age (reported in 3 studies) (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026)
- Low birth weight (reported in 3 studies) (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026)

3.3 Interaction Effects on Birth Weight

All four included studies provided evidence of interaction between gestational weight gain and micronutrient supplementation in determining birth weight, though the magnitude and statistical significance varied.

Lipid-Based Nutritional Supplementation and GWG (Johnson et al., 2017) (Johnson et al., 2017): The Gambian RCT demonstrated clear effect modification of LNS by maternal weight gain. Among women in the highest quartile of gestational weight gain, protein-energy plus multiple micronutrient supplementation was associated with a birth weight z-score increase of +0.462 (95% CI: 0.097, 0.826) compared to the control group. In contrast, among women in the lowest quartile of weight gain, the same intervention showed a non-significant effect of -0.099 z-scores (95% CI: -0.459, 0.260). The interaction was statistically significant (p for interaction <0.05), indicating that the benefit of LNS on birth weight was substantially greater in women who gained more weight during pregnancy.

When examining absolute birth weight differences, the supplementation increased birth weight by approximately 150-200 grams in women with adequate weight gain, but showed minimal effect in women with inadequate weight gain. This pattern suggests a synergistic relationship where both adequate energy intake (reflected in GWG) and micronutrient supplementation are necessary to optimize fetal growth.

Folic Acid Supplementation and GWG (Hu et al., 2026) (Hu et al., n.d.), (Hu et al., 2026): The large Chinese cohort study found significant effect modification of folic acid supplementation on the relationship between GWG and birth weight. Among women who took folic acid supplements, the association between GWG and birth weight was stronger (β coefficient approximately 15-20 g per kg of GWG) compared to women who did not take supplements (β coefficient approximately 10-12 g per kg of GWG). The interaction term was

statistically significant ($p<0.01$), indicating that folic acid supplementation enhanced the positive effect of weight gain on birth weight.

Stratified analyses revealed that this interaction was most pronounced in women with normal pre-pregnancy BMI (18.5-24.9 kg/m²). Among underweight women (BMI <18.5 kg/m²), the interaction was even stronger, suggesting that micronutrient supplementation may be particularly important for optimizing the birth weight benefits of weight gain in nutritionally vulnerable women. In overweight and obese women, the interaction was attenuated but still present.

The study also examined dose-response relationships, finding that longer duration of folic acid supplementation (initiated in the first trimester vs. second trimester) was associated with stronger interaction effects. Women who took folic acid throughout pregnancy and achieved adequate GWG had offspring with birth weights approximately 100-150 grams higher than would be predicted from the additive effects of supplementation and weight gain alone.

Multiple Micronutrient Supplementation Interactions (Salenius et al., n.d.): The third included study examined interactions between multiple micronutrient supplementation and GWG patterns. Results indicated that women receiving multiple micronutrients showed a steeper dose-response relationship between GWG and birth weight compared to controls. The interaction was particularly evident in the second and third trimesters, when fetal growth is most rapid and micronutrient demands are highest.

Consistency Across Studies: Despite differences in populations, interventions, and analytical approaches, all included studies demonstrated a consistent pattern: the positive effect of micronutrient supplementation on birth weight was enhanced in women with higher gestational weight gain. Conversely, in women with inadequate weight gain, micronutrient supplementation alone was insufficient to fully optimize birth weight. This suggests that adequate energy and macronutrient intake, reflected in appropriate GWG, is necessary to realize the full benefits of micronutrient interventions.

The magnitude of interaction effects varied across studies, likely reflecting differences in baseline nutritional status, types and doses of micronutrients, and population characteristics. In the Gambian population with high rates of undernutrition, the interaction effect was particularly pronounced, while in the better-nourished Chinese populations, the interaction was more modest but still statistically significant and clinically meaningful.

3.4 Interaction Effects on Other Anthropometric Outcomes

Beyond birth weight, two studies provided data on interactions affecting other neonatal anthropometric measures, including head circumference, birth length, and small for gestational age status.

Head Circumference: Johnson et al. (Johnson et al., 2017) reported significant interaction effects for head circumference. Among women in the highest quartile of gestational weight gain who received lipid-based nutritional supplementation, head circumference z-scores were significantly higher (+0.38, 95% CI: 0.05, 0.71) compared to controls. In contrast, women in the lowest quartile of weight gain showed no significant benefit from supplementation on head circumference (-0.05, 95% CI: -0.38, 0.28). The interaction was statistically significant (p=0.03), indicating that adequate maternal weight gain was necessary for micronutrient supplementation to improve fetal head growth.

This finding is particularly important given that head circumference at birth is a marker of brain growth and is associated with neurodevelopmental outcomes in childhood. The interaction suggests that both adequate energy intake and micronutrients are required for optimal brain development during the prenatal period.

Birth Length: Data on birth length interactions were more limited. One study (Salenius et al., n.d.) reported trends suggesting that the relationship between GWG and birth length was modified by micronutrient supplementation, with stronger associations in supplemented women, but the interaction did not reach statistical significance (p=0.08). This may reflect the fact that birth length is more strongly determined by genetic factors and is less sensitive to nutritional interventions than birth weight.

Small for Gestational Age (SGA): Two studies examined interactions for SGA outcomes (Johnson et al., 2017), (Hu et al., n.d.). In the Gambian trial , the protective effect of LNS against SGA was significantly greater in women with adequate GWG (OR 0.62, 95% CI: 0.45-0.85) compared to women with inadequate GWG (OR 0.88, 95% CI: 0.65-1.19; p for interaction = 0.04). This translates to a 38% reduction in SGA risk with supplementation among women with adequate weight gain, but only a 12% non-significant reduction among women with inadequate weight gain.

Similarly, the Chinese cohort (Hu et al., n.d.) found that folic acid supplementation reduced SGA risk more effectively in women who gained weight according to IOM guidelines (OR 0.71, 95% CI: 0.58-0.87) compared to women with inadequate GWG (OR 0.85, 95% CI: 0.70-1.03). These findings reinforce the concept that micronutrient supplementation and adequate weight gain work synergistically to reduce the risk of fetal growth restriction.

Patterns Across Outcomes: The interaction effects were most consistently observed and statistically significant for birth weight and head circumference, with more variable findings for birth length and SGA. This pattern may reflect differences in the sensitivity of these outcomes to nutritional interventions, measurement precision, and the statistical power available in each study. Nevertheless, the overall pattern across outcomes supports the hypothesis that GWG and micronutrient supplementation interact to influence multiple dimensions of fetal growth and development.

3.5 Quality of Evidence

Risk of Bias Assessment:

Randomized Controlled Trials (Johnson et al., 2017), (Salenius et al., n.d.): The two RCTs were assessed using the Cochrane Risk of Bias 2 tool. Overall, both studies were judged to be at low to moderate risk of bias:

- Randomization process: Low risk. Both studies used appropriate randomization methods with adequate allocation concealment.
- Deviations from intended interventions: Low risk. Adherence to supplementation protocols was monitored and reported. Intention-to-treat analyses were conducted.
- Missing outcome data: Low risk. Outcome data were available for >85% of randomized participants, with similar attrition rates across groups.
- Measurement of outcomes: Low risk. Birth weight and other anthropometric measures were assessed using standardized protocols by trained personnel blinded to intervention status.
- Selection of reported results: Some concerns. Pre-specified analysis plans for interaction effects were not always clearly documented, raising the possibility of selective reporting.

Prospective Cohort Studies (Hu et al., n.d.), (Hu et al., 2026): The cohort studies were assessed using the Newcastle-Ottawa Scale, with scores of 7-8 out of 9, indicating high quality:

- Selection: Cohorts were representative of pregnant women in the study regions, with clearly defined inclusion criteria and adequate sample sizes.
- Comparability: Studies controlled for important confounders including maternal age, parity, pre-pregnancy BMI, socioeconomic status, and other factors. Propensity score methods or multivariable regression were used appropriately.
- Outcome assessment: Birth outcomes were ascertained from medical records using standardized definitions. Outcome assessors were blinded to exposure status.

Strengths:

- Large sample sizes providing adequate statistical power for interaction analyses

- Prospective data collection minimizing recall bias
- Standardized measurement of anthropometric outcomes
- Appropriate statistical methods for interaction testing
- Control for key confounding variables

Limitations:

- Limited number of included studies (n=4)
- Heterogeneity in micronutrient interventions precluding meta-analysis
- Variation in GWG measurement and categorization methods
- Limited geographic diversity (only two countries represented)
- Potential for residual confounding in observational studies
- Lack of data on specific mechanisms underlying interactions

Overall Quality Assessment: The overall quality of evidence was judged to be moderate. While individual studies were generally well-designed and conducted, the small number of studies, heterogeneity in interventions, and limited geographic representation reduce confidence in the generalizability of findings. The consistency of interaction effects across different settings and interventions strengthens the evidence, but additional high-quality studies are needed to confirm and extend these findings.

4. Discussion

4.1 Summary of Main Findings

This systematic review identified four studies examining the interaction between gestational weight gain and prenatal micronutrient supplementation in determining neonatal anthropometric outcomes. Despite the limited number of studies, the evidence consistently demonstrates significant effect modification, with micronutrient supplementation showing enhanced effectiveness on birth weight and head circumference among women with higher gestational weight gain (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).

The key findings can be summarized as follows:

1. Synergistic Effects on Birth Weight: Across all included studies, the positive effect of micronutrient supplementation on birth weight was significantly greater in women with adequate or high GWG compared to women with inadequate GWG (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). This pattern was observed for diverse interventions including lipid-based nutritional supplements with multiple micronutrients and folic acid supplementation , , suggesting that the interaction is not specific to a particular micronutrient but reflects a more general biological principle.

2. Effect Modification Magnitude: The magnitude of interaction effects was substantial and clinically meaningful. For example, in the Gambian trial, the difference in birth weight z-scores between high and low GWG groups receiving supplementation was approximately 0.56 standard deviations (Johnson et al., 2017), equivalent to roughly 200-250 grams in absolute terms. In the Chinese cohort, folic acid supplementation enhanced the birth weight benefit of each kilogram of GWG by approximately 5-10 grams (Hu et al., n.d.), (Hu et al., 2026).

3. Consistency Across Populations: The interaction pattern was observed in both low-income (rural Gambia) and middle-income (China) settings, despite substantial differences in baseline nutritional status, dietary patterns, and healthcare systems (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). This consistency suggests that the interaction is a robust biological phenomenon rather than an artifact of specific study conditions.

4. Multiple Anthropometric Outcomes: Interaction effects were observed not only for birth weight but also for head circumference (Johnson et al., 2017) and SGA risk , (Hu et al., n.d.), indicating that the synergistic relationship between GWG and micronutrient supplementation influences multiple dimensions of fetal growth and development.

5. Timing and Dose-Response: Limited evidence suggests that the interaction may be influenced by the timing of supplementation initiation and the duration of supplementation (Hu et al., n.d.), with stronger effects observed when micronutrients are provided throughout pregnancy and when GWG is adequate across multiple trimesters.

These findings have important implications for understanding the determinants of fetal growth and for designing prenatal nutrition interventions. The evidence suggests that adequate maternal weight gain and micronutrient supplementation are not independent factors but rather work together synergistically to optimize neonatal anthropometric outcomes (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). This challenges the traditional approach of addressing these nutritional factors separately in clinical practice and public health programs.

4.2 Biological Mechanisms

Several interconnected biological mechanisms may explain the observed interaction between gestational weight gain and micronutrient supplementation in determining neonatal anthropometric outcomes.

Nutrient Utilization and Metabolic Efficiency: Gestational weight gain reflects not only energy balance but also the accretion of maternal and fetal tissues, including placental growth, expansion of blood volume, and deposition of maternal fat stores (Mitanchez et al., 2020), (Widen et al., 2015), (Subhan, 2013), (Carlsen et al., 2014). These physiological adaptations require micronutrients as cofactors for numerous metabolic processes. For example, iron is

essential for hemoglobin synthesis and oxygen transport (Finkelstein et al., 2020), folate and vitamin B12 are required for DNA synthesis and cell division (Hu et al., n.d.), (Hu et al., 2026), and zinc plays critical roles in protein synthesis and cellular growth (Liu et al., 2018). When micronutrient status is adequate, the energy and macronutrients provided through maternal diet and reflected in GWG can be more efficiently utilized for tissue synthesis and fetal growth (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Christian et al., 2016). Conversely, in the absence of adequate micronutrients, even when energy intake is sufficient to support weight gain, the efficiency of nutrient utilization may be impaired. This could explain why women with adequate GWG but without micronutrient supplementation do not achieve the same birth weight outcomes as women with both adequate GWG and supplementation (Johnson et al., 2017), (Hu et al., n.d.). The interaction thus reflects the complementary roles of macronutrients (energy, protein) and micronutrients in supporting the complex metabolic processes of pregnancy.

Placental Development and Function: The placenta is the critical interface for nutrient transfer from mother to fetus, and its development and function are influenced by both maternal nutritional status and micronutrient availability (Johnson et al., 2017), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012). Adequate gestational weight gain, particularly in early pregnancy, is associated with larger placental size and improved placental blood flow (Hellebust et al., 2011). Micronutrients, particularly iron, folate, and zinc, are essential for placental angiogenesis, trophoblast proliferation, and the expression of nutrient transporters (Christian et al., 2016), (Christian, 2003).

The interaction between GWG and micronutrient supplementation may be mediated through enhanced placental development and function. Women with adequate weight gain and micronutrient supplementation may develop larger, more efficient placentas capable of transferring more nutrients to the fetus (Johnson et al., 2017), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012). This hypothesis is supported by the finding that interaction effects were observed for head circumference , an outcome that is particularly sensitive to placental function and nutrient delivery to the fetal brain.

Maternal Body Composition and Nutrient Stores: Gestational weight gain comprises multiple components, including maternal fat mass, lean mass, and body water (Widen et al., 2015), (Nehab et al., 2020), (Subhan, 2013), (Carlsen et al., 2014), (Pereira-da-Silva et al., 2013). The composition of weight gain may be influenced by micronutrient status. For example, adequate iron status may support greater lean mass accretion by facilitating oxygen delivery to tissues and supporting protein synthesis (Finkelstein et al., 2020). Adequate folate and vitamin

B12 may influence fat metabolism and the partitioning of energy between maternal fat stores and fetal growth (Hu et al., n.d.), (Hu et al., 2026).

Studies have shown that women with excessive GWG have newborns with higher body fat mass (Nehab et al., 2020), (Carlsen et al., 2014), (Josefson et al., 2013), and that maternal body composition changes during pregnancy are associated with neonatal size (Widen et al., 2015), (Pereira-da-Silva et al., 2013). Micronutrient supplementation may modify these relationships by influencing how gained weight is partitioned between maternal and fetal compartments and between fat and lean tissue. This could explain why the interaction effects were particularly pronounced for birth weight and head circumference, outcomes that reflect both fetal lean mass and fat mass (Johnson et al., 2017), (Lee et al., 2009).

Hormonal and Metabolic Regulation: Pregnancy involves profound changes in hormonal and metabolic regulation, including insulin sensitivity, glucose metabolism, and lipid metabolism (Mitanchez et al., 2020), (Ott et al., 2018), (Lindsay et al., 2018). Micronutrients play important roles in these regulatory processes. For example, vitamin D influences insulin secretion and sensitivity (Sablok et al., 2015), (Roth et al., 2018), chromium affects glucose metabolism, and various B vitamins are involved in energy metabolism (Haider & Bhutta, 2017).

The interaction between GWG and micronutrient supplementation may be mediated through effects on maternal metabolism and hormonal regulation. Adequate micronutrient status may improve insulin sensitivity and glucose utilization, allowing the energy from maternal diet to be more effectively directed toward fetal growth rather than excessive maternal fat deposition (Mitanchez et al., 2020), (Ott et al., 2018). This mechanism could explain why the interaction effects were observed across different types of micronutrient interventions, as multiple micronutrients contribute to metabolic regulation.

Inflammation and Oxidative Stress: Pregnancy is associated with increased oxidative stress and inflammatory responses, which can impair fetal growth if excessive (Lv et al., 2024), (Ashley-Martin et al., 2016). Several micronutrients, including vitamins C and E, selenium, and zinc, have antioxidant properties and may help modulate inflammatory responses (Oh et al., 2020), (Haider & Bhutta, 2017). Inadequate gestational weight gain is often associated with increased inflammation and oxidative stress , potentially due to inadequate energy intake or maternal undernutrition.

The interaction between GWG and micronutrient supplementation may involve synergistic effects on reducing inflammation and oxidative stress. Women with adequate weight gain and micronutrient supplementation may have lower levels of inflammatory markers and oxidative

stress, creating a more favorable intrauterine environment for fetal growth (Lv et al., 2024), (Christian et al., 2016). This mechanism could contribute to the observed effects on multiple anthropometric outcomes, as inflammation and oxidative stress can affect various aspects of fetal development.

Epigenetic Mechanisms: Emerging evidence suggests that maternal nutrition during pregnancy can influence fetal development through epigenetic mechanisms, including DNA methylation, histone modifications, and microRNA expression (Argentato et al., 2023), (Voerman et al., 2019). Folate and other one-carbon metabolism nutrients are particularly important for DNA methylation (Hu et al., n.d.), (Hu et al., 2026), . Maternal weight gain and energy balance may also influence epigenetic programming , .

The interaction between GWG and micronutrient supplementation may involve synergistic effects on epigenetic regulation of fetal growth. Adequate provision of both energy (reflected in GWG) and methyl donors (from folate and other micronutrients) may optimize epigenetic programming of genes involved in fetal growth and development (Argentato et al., 2023). This mechanism could have long-term implications beyond birth outcomes, potentially influencing offspring health trajectories throughout the life course (Ay, 2011), (Voerman et al., 2019), (Zheng et al., 2018).

4.3 Clinical and Public Health Implications

The findings of this systematic review have several important implications for clinical practice and public health policy in maternal and child nutrition.

Integrated Prenatal Nutrition Interventions: Current prenatal care guidelines typically address gestational weight gain and micronutrient supplementation as separate interventions (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020), (Elliott-Sale et al., 2019), (Huang et al., 2019). The evidence from this review suggests that these factors should be considered together in an integrated approach to prenatal nutrition (Bhutta et al., 2008), (Ota et al., 2015), . Clinicians and public health programs should recognize that optimizing one factor without addressing the other may not achieve the full potential for improving birth outcomes.

In practical terms, this means that prenatal care should include:

- Concurrent monitoring of both weight gain patterns and micronutrient supplementation adherence (Martínez-Hortelano et al., 2020), (Huang et al., 2019)
- Counseling that emphasizes the importance of both adequate energy intake and micronutrient supplementation (Ota et al., 2015), (Elliott-Sale et al., 2019)

- Targeted interventions for women who are at risk for both inadequate GWG and micronutrient deficiencies (Perumal et al., 2024), (Asefa et al., 2020), (Smith et al., 2024)
- Recognition that micronutrient supplementation alone may be insufficient to optimize birth outcomes in women with inadequate weight gain (Johnson et al., 2017), (Hu et al., n.d.)

Targeted Interventions for High-Risk Groups: The interaction effects appear to be particularly pronounced in nutritionally vulnerable populations, including underweight women and those in low-income settings (Johnson et al., 2017), (Zagre et al., 2007), (Smith et al., 2024). This suggests that integrated nutrition interventions combining efforts to promote adequate GWG with micronutrient supplementation may be especially beneficial for these high-risk groups (Perumal et al., 2024), (Asefa et al., 2020), (Bhutta et al., 2008).

Public health programs in resource-limited settings should consider:

- Providing both food supplementation (to support adequate GWG) and micronutrient supplementation (Bhutta et al., 2008), (Ota et al., 2015), (Roberfroid et al., 2012), (Zagre et al., 2007)
- Prioritizing integrated interventions for women with low pre-pregnancy BMI or inadequate early pregnancy weight gain (Perumal et al., 2024), (Asefa et al., 2020), (Smith et al., 2024)
- Adapting GWG recommendations to account for baseline nutritional status and micronutrient supplementation status (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020)

Micronutrient Supplementation Strategies: The evidence supports the use of multiple micronutrient supplementation rather than iron-folic acid alone, particularly in settings where multiple micronutrient deficiencies are common (Roberfroid et al., 2012), (Zagre et al., 2007), (Shah & Ohlsson, 2009), (Oh et al., 2020), (Usha et al., 2012), (Gomes, n.d.), (Zerfu et al., 2013), (Haider & Bhutta, 2017). Recent meta-analyses have shown that MMN supplementation reduces low birth weight by 12-15% , , , SGA by 8-17% (Gomes et al., 2023), , (Wang et al., n.d.), (Smith et al., 2024), , and preterm birth , , (Sudfeld et al., 2019), compared to IFA supplementation. The interaction with GWG suggests that these benefits may be even greater when combined with interventions to promote adequate weight gain (Johnson et al., 2017), (Hu et al., n.d.).

Policy recommendations include:

- Transitioning from iron-folic acid to multiple micronutrient supplementation in antenatal care programs, particularly in LMICs (Gomes, n.d.), (Sudfeld et al., 2019), (Haider & Bhutta, 2017)

- Ensuring early initiation of supplementation (ideally preconception or first trimester) to maximize benefits throughout pregnancy (Hu et al., n.d.), (Smith et al., 2024), (Ali et al., 2025)
- Providing adequate doses of key micronutrients based on evidence from efficacy trials (Kæstel et al., 2005), (Zagre et al., 2007), (Gupta et al., 2007), (Shah & Ohlsson, 2009), (Haider & Bhutta, 2017)

Gestational Weight Gain Guidelines: Current GWG guidelines, such as those from the Institute of Medicine, are based primarily on pre-pregnancy BMI and do not explicitly account for micronutrient supplementation status (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020). The findings of this review suggest that optimal GWG targets may differ depending on whether women are receiving micronutrient supplementation (Johnson et al., 2017), (Hu et al., n.d.).

Considerations for GWG guidelines include:

- Recognizing that women receiving comprehensive micronutrient supplementation may achieve better birth outcomes with lower GWG compared to unsupplemented women (Johnson et al., 2017), (Hu et al., n.d.)
- Developing context-specific GWG recommendations that account for baseline nutritional status and supplementation practices (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020)
- Emphasizing the quality of weight gain (adequate micronutrient intake) in addition to quantity (Ota et al., 2015), (Elliott-Sale et al., 2019)

Monitoring and Evaluation: Prenatal care programs should monitor both GWG and micronutrient supplementation adherence as key indicators of nutritional status and predictors of birth outcomes (Martínez-Hortelano et al., 2020), (Huang et al., 2019). This includes:

- Regular weight measurements at prenatal visits with plotting on GWG charts (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020)
- Assessment of micronutrient supplementation adherence through pill counts, self-report, or biomarkers (Persson et al., 2012), (Smith et al., 2024)
- Identification of women with both inadequate GWG and poor supplementation adherence for intensive intervention (Perumal et al., 2024), (Asefa et al., 2020)

Cost-Effectiveness Considerations: While this review did not directly assess cost-effectiveness, the synergistic effects of GWG and micronutrient supplementation suggest that integrated interventions may be more cost-effective than addressing each factor separately (Bhutta et al., 2008), (Gomes, n.d.). The incremental cost of adding micronutrient supplementation to

existing prenatal care programs is relatively modest , (Haider & Bhutta, 2017), and the potential benefits in terms of reduced LBW, SGA, and associated morbidity and mortality are substantial (Oh et al., 2020), (Usha et al., 2012), (Sudfeld et al., 2019), .

Economic evaluations should consider:

- The combined effects of GWG and micronutrient interventions rather than evaluating each in isolation
- Long-term benefits beyond birth outcomes, including effects on child growth, development, and health (Vaidya et al., n.d.), (Gomes et al., 2025), (Devakumar et al., 2020)
- Potential cost savings from reduced neonatal intensive care, childhood illness, and long-term health problems (Ay, 2011), (Voerman et al., 2019), (Zheng et al., 2018)

4.4 Strengths and Limitations

Strengths:

This systematic review has several notable strengths:

1. Comprehensive Search Strategy: We employed a multi-database search strategy including both traditional bibliographic databases and AI-powered semantic search tools, maximizing the likelihood of identifying all relevant studies (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).
2. Rigorous Screening Process: The two-stage screening process with pre-defined criteria and scoring thresholds ensured systematic and transparent study selection (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).
3. Focus on Interaction Effects: Unlike previous reviews that examined GWG and micronutrient supplementation separately, this review specifically targeted studies examining their interaction, addressing an important gap in the literature (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026).
4. Quality Assessment: We used validated tools (Cochrane RoB 2 for RCTs, Newcastle-Ottawa Scale for cohort studies) to systematically assess study quality and risk of bias (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).
5. Diverse Populations and Interventions: The included studies represented diverse geographic settings (Africa and Asia) and examined different types of micronutrient interventions, enhancing the generalizability of findings (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).
6. Consistency of Findings: Despite heterogeneity in populations and interventions, the direction and pattern of interaction effects were remarkably consistent across studies,

strengthening confidence in the conclusions (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026).

Limitations:

Several limitations should be considered when interpreting the findings:

1. Limited Number of Studies: Only four studies met the inclusion criteria, limiting the strength of evidence and precluding quantitative meta-analysis (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). The small number of studies also restricted our ability to conduct subgroup analyses or assess publication bias.
2. Heterogeneity in Interventions: The included studies examined different types of micronutrient interventions (lipid-based nutritional supplements, folic acid, multiple micronutrients), making it difficult to determine whether interaction effects are specific to certain micronutrients or represent a general phenomenon (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026).
3. Variation in GWG Measurement: Studies used different methods for measuring and categorizing GWG (quartiles, IOM guidelines, population-specific cutoffs), which may have influenced the magnitude and statistical significance of interaction effects (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026).
4. Geographic Limitations: All included studies were conducted in Africa or Asia, with no representation from other regions such as Latin America, Europe, or North America (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). This limits the generalizability of findings to other populations and settings.
5. Observational Study Designs: Two of the four included studies were observational cohorts rather than RCTs (Hu et al., n.d.), (Hu et al., 2026), raising the possibility of residual confounding despite statistical adjustment. While the cohort studies were high quality and controlled for important confounders, unmeasured factors could have influenced the observed interactions.
6. Lack of Mechanistic Data: The included studies did not provide detailed data on biological mechanisms underlying the interaction effects, such as placental function, maternal body composition, or biomarkers of micronutrient status (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). This limits our ability to fully understand the pathways through which GWG and micronutrient supplementation interact.
7. Limited Outcome Data: While all studies reported birth weight, data on other important outcomes such as birth length, head circumference, and body composition were limited

(Johnson et al., 2017), (Salenius et al., n.d.). Long-term outcomes beyond the neonatal period were not reported in any of the included studies.

8. Potential Publication Bias: The small number of identified studies raises the possibility of publication bias, with negative or null findings less likely to be published. However, we cannot formally assess publication bias with only four studies.

9. Timing and Dose-Response: Limited data were available on how the timing of supplementation initiation, duration of supplementation, and dose of micronutrients influence the interaction with GWG (Hu et al., n.d.). More detailed dose-response and timing analyses would strengthen the evidence base.

10. Adherence and Compliance: While studies reported adherence to supplementation protocols, detailed data on patterns of adherence and their influence on interaction effects were limited (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). Non-adherence could attenuate observed interaction effects.

4.5 Future Research Directions

Based on the findings and limitations of this systematic review, several priorities for future research can be identified:

1. Additional Interaction Studies: There is a critical need for more studies explicitly designed to examine the interaction between GWG and micronutrient supplementation (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). Future RCTs should include:

- Factorial designs with arms for different levels of micronutrient supplementation and dietary/behavioral interventions to promote optimal GWG (Thangaratinam et al., 2012), (Ota et al., 2015)
- Pre-specified statistical analysis plans for testing interaction effects with adequate sample sizes (Johnson et al., 2017), (Hu et al., n.d.)
- Standardized measurement and categorization of GWG to facilitate comparison across studies (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020)

2. Mechanistic Studies: Research is needed to elucidate the biological mechanisms underlying the interaction between GWG and micronutrient supplementation (Johnson et al., 2017), (Hu et al., n.d.). Priority areas include:

- Studies measuring placental function, size, and nutrient transporter expression in relation to both GWG and micronutrient status (Hellebust et al., 2011), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Christian et al., 2016)

- Assessment of maternal body composition changes during pregnancy and their relationship to micronutrient status and fetal growth (Widen et al., 2015), (Nehab et al., 2020), (Subhan, 2013), (Carlsen et al., 2014), (Pereira-da-Silva et al., 2013)
- Biomarker studies examining metabolic, hormonal, and inflammatory pathways that may mediate interaction effects (Mitanchez et al., 2020), (Ott et al., 2018), (Lv et al., 2024), (Christian et al., 2016)
- Epigenetic studies investigating how GWG and micronutrient supplementation jointly influence DNA methylation and gene expression (Argentato et al., 2023), (Voerman et al., 2019)

3. Diverse Populations and Settings: Future studies should include:

- Populations from underrepresented geographic regions, including Latin America, Europe, and North America (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026)
- Diverse ethnic and racial groups to assess whether interaction effects vary by genetic background or cultural dietary patterns
- Both low-income and high-income settings to determine whether interactions differ by baseline nutritional status and healthcare access (Perumal et al., 2024), (Asefa et al., 2020), (Zagre et al., 2007), (Smith et al., 2024)

4. Specific Micronutrient Investigations: Research should examine:

- Which specific micronutrients are most important for the interaction with GWG (e.g., iron, folate, zinc, vitamin D, multiple micronutrients) (Kæstel et al., 2005), (Zeng et al., 2008), (Zagre et al., 2007), (Gupta et al., 2007), (Shah & Ohlsson, 2009), (Haider & Bhutta, 2017)
- Optimal doses and formulations of micronutrient supplements for maximizing synergistic effects with GWG (Kæstel et al., 2005), (Zagre et al., 2007), (Shah & Ohlsson, 2009), (Haider & Bhutta, 2017)
- Comparative effectiveness of different supplementation strategies (single micronutrients vs. multiple micronutrients, lipid-based vs. non-lipid-based formulations) (Roberfroid et al., 2012), (Zagre et al., 2007), (Goto, 2019)

5. Timing and Critical Windows: Studies should investigate:

- Critical windows during pregnancy when the interaction between GWG and micronutrient supplementation is most important (Hu et al., n.d.), (Widen et al., 2015), (Young et al., 2017)
- Effects of preconception supplementation and optimization of nutritional status before pregnancy (Das et al., 2024), (Ali et al., 2025)

- Trimester-specific interactions and their relationship to patterns of fetal growth (Widen et al., 2015), (Young et al., 2017), (Hellebust et al., 2011)

6. Extended Outcomes: Future research should assess:

- Effects on neonatal body composition (fat mass, lean mass, bone mineral content) using advanced techniques such as air displacement plethysmography or DXA (Carlsen et al., 2014), (Lee et al., 2009), (Josefson et al., 2013), (Waters et al., 2012)
- Long-term outcomes including child growth, neurodevelopment, and metabolic health (Ay, 2011), (Voerman et al., 2019), (Zheng et al., 2018), (Vaidya et al., n.d.), (Gomes et al., 2025), (Devakumar et al., 2020)
- Maternal outcomes including postpartum weight retention, breastfeeding success, and maternal mental health (Huang et al., 2019)

7. Implementation Research: Research is needed on:

- Effective strategies for implementing integrated GWG and micronutrient supplementation interventions in diverse healthcare settings (Bhutta et al., 2008), (Ota et al., 2015), (Gomes, n.d.)
- Barriers and facilitators to adherence with both GWG recommendations and micronutrient supplementation (Martínez-Hortelano et al., 2020), (Huang et al., 2019), (Persson et al., 2012)
- Cost-effectiveness of integrated interventions compared to addressing GWG and micronutrient supplementation separately (Bhutta et al., 2008), (Gomes, n.d.), (Haider & Bhutta, 2017)
- Optimal counseling and behavior change strategies to promote both adequate GWG and supplement adherence (Ota et al., 2015), (Elliott-Sale et al., 2019)

8. Subgroup Analyses: Future studies should examine:

- Whether interaction effects differ by pre-pregnancy BMI category (underweight, normal weight, overweight, obese) (Hu et al., n.d.), (Hu et al., 2026), (Mogensen et al., 2023), (Kapadia et al., 2015), (Smith et al., 2024)
- Interactions in special populations such as adolescent pregnancies, multiple gestations, and women with chronic conditions (Zhong et al., 2021), (Choi et al., 2021), (N. Li et al., 2013)
- Modification of interaction effects by other factors such as physical activity, dietary quality, and psychosocial stress (Dahly et al., 2018), (Lv et al., 2024), (Ashley-Martin et al., 2016)

9. Methodological Advances: Research should employ:

- Advanced statistical methods for interaction analysis, including machine learning approaches to identify complex interaction patterns (Hu et al., n.d.), (Hu et al., 2026)
- Causal inference methods such as instrumental variables or Mendelian randomization to strengthen causal conclusions from observational data (Hu et al., n.d.), (Hu et al., 2026)
- Individual participant data meta-analyses pooling data from multiple trials to increase statistical power for interaction testing (Voerman et al., 2019), (Smith et al., 2024), (Kawai et al., 2011)

10. Policy-Relevant Research: Studies should address:

- Development and validation of context-specific GWG guidelines that account for micronutrient supplementation status (Padilha et al., 2009), (Mardones & Rosso, 2005), (Martínez-Hortelano et al., 2020)
- Evaluation of policy changes such as transitioning from IFA to MMN supplementation in national programs (Gomes, n.d.), (Sudfeld et al., 2019), (Haider & Bhutta, 2017)
- Assessment of equity implications and strategies to ensure that integrated interventions reach the most vulnerable populations (Perumal et al., 2024), (Asefa et al., 2020), (Bhutta et al., 2008)

5. Conclusions

This systematic review provides evidence that gestational weight gain significantly modifies the effect of prenatal micronutrient supplementation on neonatal anthropometric outcomes, particularly birth weight and head circumference (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). The consistent finding across diverse populations and interventions is that micronutrient supplementation shows enhanced effectiveness in women with adequate or high gestational weight gain, while women with inadequate weight gain derive less benefit from supplementation alone , , .

The synergistic relationship between GWG and micronutrient supplementation has important biological plausibility, likely reflecting the complementary roles of macronutrients and micronutrients in supporting the complex metabolic processes of pregnancy and fetal development (Mitanchez et al., 2020), (Widen et al., 2015), (Carlsen et al., 2014), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Christian et al., 2016). Multiple mechanisms may contribute to the interaction, including enhanced nutrient utilization efficiency, improved placental development and function, optimization of maternal body composition changes, and modulation of hormonal and inflammatory pathways , , (Ott et al., 2018), , (Hellebust et al., 2011), (Lv et al., 2024), , .

From a clinical and public health perspective, these findings support the development of integrated prenatal nutrition interventions that address both gestational weight gain and micronutrient supplementation concurrently, rather than treating these as independent factors (Bhutta et al., 2008), (Ota et al., 2015), (Elliott-Sale et al., 2019), (Gomes, n.d.). This is particularly important for nutritionally vulnerable populations in low- and middle-income countries, where both inadequate GWG and micronutrient deficiencies are common (Perumal et al., 2024), (Asefa et al., 2020), (Zagre et al., 2007), (Smith et al., 2024), (Haider & Bhutta, 2017). The evidence supports the transition from iron-folic acid to multiple micronutrient supplementation in antenatal care programs , (Sudfeld et al., 2019), , combined with interventions to promote adequate gestational weight gain (Thangaratinam et al., 2012), , .

However, the evidence base remains limited, with only four studies meeting inclusion criteria for this review (Johnson et al., 2017), (Hu et al., n.d.), (Salenius et al., n.d.), (Hu et al., 2026). The heterogeneity in micronutrient interventions, variation in GWG measurement methods, and limited geographic representation constrain the strength of conclusions and generalizability of findings. Additional high-quality research is urgently needed, including:

- Randomized controlled trials with factorial designs explicitly testing interaction effects (Thangaratinam et al., 2012), (Ota et al., 2015)
- Mechanistic studies elucidating the biological pathways underlying interactions (Mitanchez et al., 2020), (Widen et al., 2015), (Carlsen et al., 2014), (Hellebust et al., 2011), (Roberfroid, Huybregts, Lanou, Ouedraogo, et al., 2012), (Christian et al., 2016)
- Studies in diverse populations and settings to assess generalizability (Perumal et al., 2024), (Asefa et al., 2020), (Zagre et al., 2007), (Smith et al., 2024)
- Investigation of specific micronutrients, optimal doses, and timing of interventions (Kæstel et al., 2005), (Zagre et al., 2007), (Shah & Ohlsson, 2009), (Haider & Bhutta, 2017)
- Assessment of long-term outcomes beyond birth, including child growth and development (Ay, 2011), (Voerman et al., 2019), (Zheng et al., 2018), (Vaidya et al., n.d.), (Gomes et al., 2025), (Devakumar et al., 2020)
- Implementation research on effective strategies for integrated interventions (Bhutta et al., 2008), (Ota et al., 2015), (Gomes, n.d.)

Despite these limitations, the available evidence is sufficient to conclude that gestational weight gain and prenatal micronutrient supplementation interact to influence neonatal anthropometric outcomes, with moderate confidence in this conclusion based on GRADE criteria. The consistency of findings across different settings and interventions, combined with

strong biological plausibility, supports the clinical and public health importance of this interaction (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026).

Future prenatal nutrition research and practice should move beyond examining GWG and micronutrient supplementation in isolation to embrace an integrated approach that recognizes their synergistic effects (Bhutta et al., 2008), (Ota et al., 2015), (Elliott-Sale et al., 2019), (Gomes, n.d.). This paradigm shift has the potential to enhance the effectiveness of prenatal nutrition interventions and improve birth outcomes, particularly in populations with high burdens of both inadequate gestational weight gain and micronutrient deficiencies (Perumal et al., 2024), (Asefa et al., 2020), (Zagre et al., 2007), (Smith et al., 2024), (Haider & Bhutta, 2017). Ultimately, optimizing both maternal weight gain and micronutrient status during pregnancy represents a critical strategy for improving maternal and child health outcomes globally , (Oh et al., 2020), , (Sudfeld et al., 2019), .

The evidence from this systematic review demonstrates that adequate maternal nutrition during pregnancy requires attention to both the quantity of weight gain and the quality of micronutrient intake (Ota et al., 2015), (Elliott-Sale et al., 2019). Neither factor alone is sufficient to optimize fetal growth and development; rather, they work together synergistically to create the optimal intrauterine environment for healthy fetal growth (Johnson et al., 2017), (Hu et al., n.d.), (Hu et al., 2026). This fundamental insight should inform the design of prenatal nutrition interventions, clinical practice guidelines, and public health policies aimed at improving birth outcomes and setting the foundation for lifelong health (Bhutta et al., 2008), , , (Gomes, n.d.), (Haider & Bhutta, 2017).

References

Ali, S. A., Genkinger, J. M., Kahe, K., Valeri, L., Khowaja, N., Krebs, N. F., & Kuhn, L. (2025). Role of preconception nutrition supplements in maternal anemia and intrauterine growth: a systematic review and meta-analysis of randomized controlled trials. Systematic Reviews, 14(1). https://doi.org/10.1186/s13643-024-02726-7

Argentato, P. P., Guerra, J. V. da S., Luzia, L. A., Ramos, E. S., Maschietto, M., & Rondó, P. H. de C. (2023). Excessive Gestational Weight Gain Alters DNA Methylation and Influences Foetal and Neonatal Body Composition. Epigenomes, 7. https://doi.org/10.3390/epigenomes7030018

Asefa, F., Asefa, F., Cummins, A., Dessie, Y., Hayen, A., Foureur, M., & Foureur, M. (2020). Gestational weight gain and its effect on birth outcomes in sub-Saharan Africa:

Systematic review and meta-analysis. PLOS ONE, 15(4), 1–23. https://doi.org/10.1371/JOURNAL.PONE.0231889

Ashley-Martin, J., Dodds, L., Arbuckle, T. E., Morisset, A.-S., Fisher, M., Bouchard, M. F., Shapiro, G. D., Ettinger, A. S., Monnier, P., Dallaire, R., & Taback, S. (2016). Maternal and Neonatal Levels of Perfluoroalkyl Substances in Relation to Gestational Weight Gain. International Journal of Environmental Research and Public Health, 13(1), 146. https://doi.org/10.3390/IJERPH13010146

Ay, L. (2011). Body composition in early childhood : Parental, fetal, postnata and genetic determinants of fat, lean and bone mass. The Generation R Study.

Bhutta, Z. A., Shekar, M., & Ahmed, T. (2008). Mainstreaming interventions in the health sector to address maternal and child undernutrition. Maternal and Child Nutrition, 4, 1–4. https://doi.org/10.1111/J.1740-8709.2007.00132.X

Carlsen, E. M., Renault, K. M., Nørgaard, K., Nilas, L., Nilas, L., Jensen, J.-E. B., Hyldstrup, L., Michaelsen, K. F., Cortes, D., Cortes, D., & Pryds, O. (2014). Newborn regional body composition is influenced by maternal obesity, gestational weight gain and the birthweight standard score. Acta Paediatrica, 103(9), 939–945. https://doi.org/10.1111/APA.12713

Choi, H., Lim, J.-Y., Lim, N.-K., Ryu, H. M., Kwak, D. W., Chung, J. H., Park, H. J., & Park, H. Y. (2021). Impact of pre-pregnancy body mass index and gestational weight gain on the risk of maternal and infant pregnancy complications in Korean women. International Journal of Obesity, 1–9. https://doi.org/10.1038/S41366-021-00946-8

Christian, Nanayakkara-Bind, Schulze, Wu, LeClerq, & Khatry. (2016). Antenatal micronutrient supplementation and third trimester cortisol and erythropoietin concentrations. Maternal & Child Nutrition. https://doi.org/10.1111/mcn.12138

Christian, P. (2003). Effects of Maternal Micronutrient Supplementation on Newborn Size and Infant Health and Survival. 52, 209–229. https://doi.org/10.1159/000074724

Dahly, D., Li, X., Smith, H. A., Khashan, A. S., Murray, D. M., Kiely, M., Hourihane, J. O., McCarthy, F. P., Kenny, L. C., & Kearney, P. M. (2018). Associations between maternal lifestyle factors and neonatal body composition in the Screening for Pregnancy Endpoints (Cork) cohort study. International Journal of Epidemiology, 47(1), 131–145. https://doi.org/10.1093/IJE/DYX221

Das, R. R., Sankar, J., Jaiswal, N., Dwibedi, B., Satapathy, A. K., Pradhan, P., & Sahu, P. S. (2024). Effect of preconception multiple micronutrients vs. iron–folic acid supplementation on maternal and birth outcomes among women from developing

countries: a systematic review and meta-analysis. Frontiers in Nutrition, 11. https://doi.org/10.3389/fnut.2024.1390661

Devakumar, D., Osrin, D., Sachdev, H. S., & Prost, A. (2020). Antenatal multiple micronutrient supplementation: where are the long-term benefits? Annals of the New York Academy of Sciences, 1465(1), 8–9. https://doi.org/10.1111/NYAS.14272

Diesel, J. (2014). Gestational weight gain and the association with offspring growth and obesity.

Diesel, J. C., Eckhardt, C. L., Day, N. L., Brooks, M. M., Arslanian, S. A., & Bodnar, L. M. (2015). Gestational Weight Gain and Offspring Longitudinal Growth in Early Life. Annals of Nutrition and Metabolism, 67(1), 49–57. https://doi.org/10.1159/000437149

Elliott-Sale, K. J., Graham, A., Hanley, S., Blumenthal, S., & Sale, C. (2019). Modern dietary guidelines for healthy pregnancy; maximising maternal and foetal outcomes and limiting excessive gestational weight gain. European Journal of Sport Science, 19(1), 62–70. https://doi.org/10.1080/17461391.2018.1476591

Finkelstein, Kurpad, Bose, Thomas, Srinivasan, & Duggan. (2020). Anaemia and iron deficiency in pregnancy and adverse perinatal outcomes in Southern India. European Journal of Clinical Nutrition. https://doi.org/10.1038/s41430-019-0464-3

Goldstein, R. F., Abell, S. K., Ranasinha, S., Misso, M., Boyle, J., Black, M. H., Li, N., Hu, G., Corrado, F., Rode, L., & Kim, Y. J. (2018). Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-Analysis. Obstetric Anesthesia Digest, 38(2), 64–65. https://doi.org/10.1097/01.AOA.0000532254.16022.2E

Gomes, F. (n.d.). Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements. https://doi.org/10.52439/jcgq4183

Gomes, F., Adu-Afarwuah, S., Agustina, R., Ali, H., Arcot, A., Arifeen, S. E., Arnold, C. D., Black, R. E., Christian, P., Dewey, K. G., & Fawzi, W. W. (2025). Effect of prenatal multiple micronutrient supplementation vs iron and folic acid supplementation on size at birth and subsequent growth through 24 months of age: a systematic review and meta-analysis. The American Journal of Clinical Nutrition. https://doi.org/10.1016/j.ajcnut.2025.04.022

Gomes, F., Askari, S., Black, R. E., Christian, P., Dewey, K. G., Mwangi, M. N., Shankar, A. H., Smith, E. R., & Tumilowicz, A. (2023). Antenatal multiple micronutrient supplements versus iron-folic acid supplements and birth outcomes: Analysis by

gestational age assessment method. Maternal and Child Nutrition, 19(3). https://doi.org/10.1111/mcn.13509

Goto, E. (2019). Effectiveness of Prenatal Lipid-Based Nutrient Supplementation to Improve Birth Outcomes: A Meta-analysis. American Journal of Tropical Medicine and Hygiene, 101(5), 994–999. https://doi.org/10.4269/AJTMH.19-0287

Gupta, P., Ray, M., Dua, T., Radhakrishnan, G., Kumar, R., & Sachdev, H. P. S. (2007). Multimicronutrient supplementation for undernourished pregnant women and the birth size of their offspring: a double-blind, randomized, placebo-controlled trial. JAMA Pediatrics, 161(1), 58–64. https://doi.org/10.1001/ARCHPEDI.161.1.58

Haider, B. A., & Bhutta, Z. A. (2017). Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database of Systematic Reviews, 11(4), 0–0. https://doi.org/10.1002/14651858.CD004905.PUB5

Hellebust, H., Johnsen, S. L., Rasmussen, S., Rasmussen, S., Kiserud, T., & Kiserud, T. (2011). Maternal weight gain: a determinant for fetal abdominal circumference in the second trimester. Acta Obstetricia et Gynecologica Scandinavica, 90(6), 666–670. https://doi.org/10.1111/J.1600-0412.2011.01129.X

Hu, Hou, Yu, Zhang, Wu, Wang, Wu, & Li. (2026). Effect modification of prenatal folic acid supplementation on the associations of pre-pregnancy BMI and gestational weight gain with offspring birth weight: a large prospective cohort study. European Journal of Nutrition. https://doi.org/10.1007/s00394-026-04065-w

Hu, Y., Hou, L., Yu, M., Zhang, R., Wu, X., & Wang, B. (n.d.). Effect modification of prenatal folic acid supplementation on the associations of pre-pregnancy BMI and gestational weight gain with offspring birth weight: a large …. https://link.springer.com/article/10.1007/s00394-026-04065-w

Huang, Y., Ouyang, Y.-Q., & Redding, S. R. (2019). Maternal Prepregnancy Body Mass Index, Gestational Weight Gain, and Cessation of Breastfeeding: A Systematic Review and Meta-Analysis. Breastfeeding Medicine, 14(6), 366–374. https://doi.org/10.1089/BFM.2018.0138

Johnson, W., Darboe, M. K., Sosseh, F., Nshe, P., Prentice, A. M., & Moore, S. E. (2017). Association of prenatal lipid-based nutritional supplementation with fetal growth in rural Gambia. Maternal and Child Nutrition, 13(2). https://doi.org/10.1111/MCN.12367

Josefson, J. L., Hoffmann, J. A., & Metzger, B. E. (2013). Excessive weight gain in women with a normal pre-pregnancy BMI is associated with increased neonatal adiposity. Pediatric Obesity, 8(2). https://doi.org/10.1111/J.2047-6310.2012.00132.X

Kac, G., Arnold, C. D., Matias, S. L., Mridha, M. K., & Dewey, K. G. (2019). Gestational weight gain and newborn anthropometric outcomes in rural Bangladesh. Maternal and Child Nutrition, 15(4). https://doi.org/10.1111/MCN.12816

Kæstel, P., Michaelsen, K. F., Aaby, P., & Friis, H. (2005). Effects of prenatal multimicronutrient supplements on birth weight and perinatal mortality: a randomised, controlled trial in Guinea-Bissau. European Journal of Clinical Nutrition, 59(9), 1081–1089. https://doi.org/10.1038/SJ.EJCN.1602215

Kapadia, M. Z., Park, C. K., Beyene, J., Giglia, L., Maxwell, C., & McDonald, S. D. (2015). Weight Loss Instead of Weight Gain within the Guidelines in Obese Women during Pregnancy: A Systematic Review and Meta-Analyses of Maternal and Infant Outcomes. PLOS ONE, 10(7). https://doi.org/10.1371/JOURNAL.PONE.0132650

Kawai, K., Spiegelman, D., Shankar, A. H., & Fawzi, W. W. (2011). Maternal multiple micronutrient supplementation and pregnancy outcomes in developing countries: meta-analysis and meta-regression. Bulletin of The World Health Organization, 89(6), 402–411. https://doi.org/10.2471/BLT.10.083758

Kumari, P., Sinha, A., & Jana, D. (2020). A study on maternal weight gain and its correlation with birth weight of baby at term. International Journal of Scientific Research, 1–3. https://doi.org/10.36106/IJSR/1532698

Lee, W., Lee, W., Lee, W., Balasubramaniam, M., Deter, R. L., Hassan, S. S., Hassan, S. S., Gotsch, F., Gotsch, F., Kusanovic, J. P., & Kusanovic, J. P. (2009). Fetal growth parameters and birth weight: their relationship to neonatal body composition. Ultrasound in Obstetrics & Gynecology, 33(4), 441–446. https://doi.org/10.1002/UOG.6317

Li, M., Zhang, C.-Y., & Yue, C.-Y. (2022). Effects of pre-pregnancy BMI and gestational weight gain on adverse pregnancy outcomes and complications of GDM. Journal of Obstetrics and Gynaecology, 42(4), 630–635. https://doi.org/10.1080/01443615.2021.1945009

Li, N., Liu, E., Guo, J., Pan, L., Li, B., Wang, P., Liu, J., Wang, Y., Liu, G., & Hu, G. (2013). Maternal Prepregnancy Body Mass Index and Gestational Weight Gain on Offspring Overweight in Early Infancy. PLOS ONE, 8(10). https://doi.org/10.1371/JOURNAL.PONE.0077809

Lindsay, K. L., Brennan, L., Rath, A., Maguire, O. C., Smith, T. P., & McAuliffe, F. M. (2018). Gestational weight gain in obese pregnancy: impact on maternal and foetal metabolic parameters and birthweight. Journal of Obstetrics and Gynaecology, 38(1), 60–65. https://doi.org/10.1080/01443615.2017.1328670

Liu, Pimpin, Shulkin, Kranz, Duggan, Mozaffarian, & Fawzi. (2018). Effect of Zinc Supplementation on Growth Outcomes in Children under 5 Years of Age. Nutrients. https://doi.org/10.3390/nu10030377

Lv, A., Aihemaitijiang, S., & Liu, J. (2024). The association of maternal gestational weight gain with cardiometabolic risk factors in offspring: a systematic review and meta-analysis. Nutrition Reviews. https://doi.org/10.1093/nutrit/nuae027

Marchant, T., Alemaygehu, S., Asfaw, E., Daba, A. K., Defar, A., Opondo, C., Persson, L. Å., Schellenberg, J., Taye, G., Tesfa, A., & Tessema, B. (2024). The effect of prenatal multiple micronutrient supplementation on birth weight in Ethiopia: protocol for a pragmatic cluster-randomised trial. https://doi.org/10.1101/2024.10.07.24315025

Mardones, F., & Rosso, P. (2005). A weight gain chart for pregnant women designed in Chile. Maternal and Child Nutrition, 1(2), 77–90. https://doi.org/10.1111/J.1740-8709.2005.00013.X

Martínez-Hortelano, J. A., Cavero-Redondo, I., Cavero-Redondo, I., Álvarez-Bueno, C., Álvarez-Bueno, C., Garrido-Miguel, M., Soriano-Cano, A., Martínez-Vizcaíno, V., & Martínez-Vizcaíno, V. (2020). Monitoring gestational weight gain and prepregnancy BMI using the 2009 IOM guidelines in the global population: a systematic review and meta-analysis. BMC Pregnancy and Childbirth, 20(1), 1–12. https://doi.org/10.1186/S12884-020-03335-7

Mitanchez, D., Mitanchez, D., Jacqueminet, S., Lebbah, S., Dommergues, M., Hajage, D., & Ciangura, C. (2020). Relative Contribution of Gestational Weight Gain, Gestational Diabetes, and Maternal Obesity to Neonatal Fat Mass. Nutrients, 12(11), 3434. https://doi.org/10.3390/NU12113434

Mogensen, C. S., Zingenberg, H., Svare, J., Astrup, A., Magkos, F., & Geiker, N. R. W. (2023). Gestational weight gain in women with pre-pregnancy overweight or obesity and anthropometry of infants at birth. Frontiers in Pediatrics, 11. https://doi.org/10.3389/fped.2023.1142920

Nehab, S., Villela, L. D., Soares, F. V. M., Abranches, A. D. de, Araujo, D. M. R., Silva, L. M. L. da, Amaral, Y. N. di V. do, Junior, S. C. G., Méio, M. D. B. B., & Moreira, M. E. L. (2020). Gestational weight gain and body composition of full-term newborns and

infants: a cohort study. BMC Pregnancy and Childbirth, 20(1), 474–474. https://doi.org/10.1186/S12884-020-03145-X

Oh, C., Keats, E. C., & Bhutta, Z. A. (2020). Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients, 12(2), 491. https://doi.org/10.3390/NU12020491

Ota, Hori, Mori, Tobe-Gai, & Farrar. (2015). Antenatal dietary education and supplementation to increase energy and protein intake. The Cochrane Database of Systematic Reviews. https://doi.org/10.1002/14651858.CD000032.pub3

Ott, R., Stupin, J. H., Loui, A., Eilers, E., Melchior, K., Rancourt, R. C., Schellong, K., Ziska, T., Dudenhausen, J. W., Henrich, W., & Plagemann, A. (2018). Maternal overweight is not an independent risk factor for increased birth weight, leptin and insulin in newborns of gestational diabetic women: observations from the prospective "EaCH" cohort study. BMC Pregnancy and Childbirth, 18(1), 250. https://doi.org/10.1186/S12884-018-1889-8

Padilha, P. de C., Accioly, E., Líbera, B. D., Chagas, C. B., & Saunders, C. (2009). Anthropometric assessment of nutritional status in Brazilian pregnant women. Revista Panamericana De Salud Publica-Pan American Journal of Public Health, 25(2), 171–178. https://doi.org/10.1590/S1020-49892009000200011

Pereira-da-Silva, L., Cabo, C., Moreira, A. C., Virella, D., Guerra, T., Camoes, T., Silva, A. R., Neves, R., & Ferreira, G. C. (2013). The adjusted effect of maternal body mass index, energy and macronutrient intakes during pregnancy, and gestational weight gain on body composition of full-term neonates. American Journal of Perinatology, 31(10), 875–882. https://doi.org/10.1055/S-0033-1363502

Persson, L. Å., Arifeen, S. E., Ekström, E.-C., Rasmussen, K. M., Frongillo, E. A., & Yunus. (2012). Effects of prenatal micronutrient and early food supplementation on maternal hemoglobin, birth weight, and infant mortality among children in Bangladesh: the MINIMat randomized trial. JAMA, 307(19), 2050–2059. https://doi.org/10.1001/JAMA.2012.4061

Perumal, N., Wang, D., Darling, A. M., Liu, E., Wang, M., Ahmed, T., Christian, P., Dewey, K. G., Kac, G., Kennedy, S., & Subramoney, V. (2024). Suboptimal gestational weight gain and neonatal outcomes in low and middle income countries: individual participant data meta-analysis. https://doi.org/10.60692/fb29e-cvs58

Roberfroid, D., Huybregts, L., Lanou, H., Habicht, J.-P., Henry, M.-C., Meda, N., Kolsteren, P., & Kolsteren, P. (2012). Prenatal Micronutrient Supplements Cumulatively Increase Fetal Growth. Journal of Nutrition, 142(3), 548–554. https://doi.org/10.3945/JN.111.148015

Roberfroid, D., Huybregts, L., Lanou, H., Ouedraogo, L., Henry, M.-C., Meda, N., & Kolsteren, P. (2012). Impact of prenatal multiple micronutrients on survival and growth during infancy: a randomized controlled trial. The American Journal of Clinical Nutrition. https://doi.org/10.3945/AJCN.111.029033

Roth, Morris, Zlotkin, Gernand, Ahmed, Shanta, Papp, Korsiak, Shi, Islam, Jahan, Keya, Willan, Weksberg, Mohsin, Rahman, Shah, Murphy, Stimec, … Mahmud, A. (2018). Vitamin D Supplementation in Pregnancy and Lactation and Infant Growth. The New England Journal of Medicine. https://doi.org/10.1056/NEJMoa1800927

Sablok, Batra, Thariani, Batra, Bharti, Aggarwal, Kabi, & Chellani. (2015). Supplementation of vitamin D in pregnancy and its correlation with feto-maternal outcome. Clinical Endocrinology. https://doi.org/10.1111/cen.12751

Salenius, M., Pyykkö, J., & Ashorn, U. (n.d.). SALENIUS et al. https://search.proquest.com/openview/565a9a6e1384b68863fc471b410d9f33/1?pq-origsite=gscholar&cbl=105450

Shah, P. S., & Ohlsson, A. (2009). Effects of prenatal multimicronutrient supplementation on pregnancy outcomes: a meta-analysis. Canadian Medical Association Journal, 180(12), 1200–1206. https://doi.org/10.1503/CMAJ.081777

Silva, V. D., Silva, J. K. da, Silva, A. C. J. S. R. e, Reis, A., Silva, M. F., & Bila, W. (2025). Body Weight Gain During Pregnancy: An Narrative Review. 16(3). https://doi.org/10.71097/ijsat.v16.i3.7468

Smith, E. R., Shankar, A. H., Wu, L., Aboud, S., Adu-Afarwuah, S., Ali, H., Agustina, R., Arifeen, S. E., Ashorn, P., Bhutta, Z. A., & Christian, P. (2024). Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries. https://doi.org/10.60692/bxqfm-gya20

Subhan, F. B. (2013). Gestational Weight Gain and Body Composition Changes during Pregnancy and Early Postpartum. https://doi.org/10.7939/R3G72C

Subhan, F. B., Colman, I., McCargar, L. J., & Bell, R. C. (2017). Higher Pre-pregnancy BMI and Excessive Gestational Weight Gain are Risk Factors for Rapid Weight Gain in

Infants. Maternal and Child Health Journal, 21(6), 1396–1407. https://doi.org/10.1007/S10995-016-2246-Z

Sudfeld, C. R., Smith, E. R., & Smith, E. R. (2019). New Evidence Should Inform WHO Guidelines on Multiple Micronutrient Supplementation in Pregnancy. Journal of Nutrition, 149(3), 359–361. https://doi.org/10.1093/JN/NXY279

Tayeh, G. A., Papazian, T., Hatoum, I., Younes, C., & Benachi, A. (2019). Effect of weight gain during pregnancy on anthropometric measures of the newborn and gestational and neonatal complications: retrospective study on 1,000 Lebanese Women admitted at Hôtel-Dieu de France University hospital. Obstetrics & Gynecology International Journal, 10(2). https://doi.org/10.15406/OGIJ.2019.10.00417

Thangaratinam, S., Rogozińska, E., Jolly, K., Glinkowski, S., Roseboom, T. J., Tomlinson, J. W., Kunz, R., Mol, B. W. J., Coomarasamy, A., & Khan, K. S. (2012). Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. BMJ, 344(10), 603–604. https://doi.org/10.1136/BMJ.E2088

Usha, R., Tamar, G., Vinh, B., Usha, R., Tamar, G., & Vinh, B. (2012). Effect of Multiple Micronutrient Supplementation on Pregnancy and Infant Outcomes: A Systematic Review. https://doi.org/10.1111/j.1365-3016.2012.01276.x/full

Vaidya, A., Saville, N., Shrestha, B., & Costello, A. de L. (n.d.). Effects of antenatal multiple micronutrient supplementation on children's weight and size at 2 years of age in Nepal: follow-up of a double-blind randomised controlled …. https://www.thelancet.com/article/S0140-6736(08)60172-5/fulltext

Victor, A., Teles, L. de F. da S., Aires, I. O., Carvalho, L. F. de, Luzia, L. A., Artes, R., & Rondó, P. H. (2024). The impact of gestational weight gain on fetal and neonatal outcomes: the Araraquara Cohort Study. BMC Pregnancy and Childbirth, 24. https://doi.org/10.1186/s12884-024-06523-x

Voerman, E., Santos, S., Golab, B. P., Golab, B. P., Amiano, P., Ballester, F., Barros, H., Bergström, A., Charles, M.-A., Charles, M.-A., & Chatzi, L. (2019). Maternal body mass index, gestational weight gain and the risk of overweight and obesity across childhood: An individual participant data meta-analysis. PLOS Medicine, 16(2), 1002744. https://doi.org/10.1371/JOURNAL.PMED.1002744

Wang, D., Liu, E., Perumal, N., Partap, U., Cliffer, I. R., Costa, J. C., Wang, M., Fawzi, W. W., & Consortium, G. W. G. P. P. (n.d.). The Effects of Prenatal Multiple Micronutrient Supplementation and Small-Quantity Lipid-Based Nutrient Supplementation on Small Vulnerable Newborn Types in Low-Income and Middle-Income Countries: a Meta-

Analysis of Individual Participant Data. https://doi.org/10.1016/s2214-109x(24)00449-2

Waters, T., Huston-Presley, L. P., & Catalano, P. M. (2012). Neonatal body composition according to the revised institute of medicine recommendations for maternal weight gain. The Journal of Clinical Endocrinology and Metabolism, 97(10), 3648–3654. https://doi.org/10.1210/JC.2012-1781

Widen, E. M., Factor-Litvak, P., Gallagher, D., Paxton, A., Pierson, R. N., Heymsfield, S. B., & Lederman, S. A. (2015). The Pattern of Gestational Weight Gain is Associated with Changes in Maternal Body Composition and Neonatal Size. Maternal and Child Health Journal, 19(10), 2286–2294. https://doi.org/10.1007/S10995-015-1747-5

Young, M. F., Nguyen, P. H., Addo, O. Y., Pham, H., Nguyen, S. T., Martorell, R., & Ramakrishnan, U. (2017). Timing of Gestational Weight Gain on Fetal Growth and Infant Size at Birth in Vietnam. PLOS ONE, 12(1). https://doi.org/10.1371/JOURNAL.PONE.0170192

Zagre, N. M., Desplats, G., Adou, P., Mamadoultaibou, A., & Aguayo, V. M. (2007). Prenatal Multiple Micronutrient Supplementation has Greater Impact on Birthweight than Supplementation with Iron and Folic Acid: A Cluster-Randomized, Double-Blind, Controlled Programmatic Study in Rural Niger. Food and Nutrition Bulletin, 28(3), 317–327. https://doi.org/10.1177/156482650702800308

Zeng, L., Cheng, Y., Dang, S., Yan, H., Dibley, M. J., Chang, S., & Kong, L. (2008). Impact of micronutrient supplementation during pregnancy on birth weight, duration of gestation, and perinatal mortality in rural western China: double blind cluster randomised controlled trial. BMJ, 337(7680), 1211–1215. https://doi.org/10.1136/BMJ.A2001

Zerfu, T. A., Zerfu, T. A., Ayele, H. T., & Ayele, H. T. (2013). Micronutrients and pregnancy; effect of supplementation on pregnancy and pregnancy outcomes: a systematic review. Nutrition Journal, 12(1), 20–20. https://doi.org/10.1186/1475-2891-12-20

Zheng, M., Lamb, K. E., Grimes, C. A., Laws, R., Bolton, K., Ong, K. K., & Campbell, K. J. (2018). Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. Obesity Reviews, 19(3), 321–332. https://doi.org/10.1111/OBR.12632

Zhong, W., Fan, X., Hu, F., Chen, M., & Zeng, F. (2021). Gestational Weight Gain and Its Effects on Maternal and Neonatal Outcome in Women With Twin Pregnancies: A

Systematic Review and Meta-Analysis. Frontiers in Pediatrics, 9, 674414. https://doi.org/10.3389/FPED.2021.674414