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REVIEW ARTICLE

Micronutrient needs and supplementation strategies during pregnancy

Maria Cemortan*, Irina Sagaidac, Olga Cernetchi

Department of Obstetrics and Gynecology, *Nicolae Testemițanu* State University of Medicine and Pharmacy, Chișinău, Republic of Moldova

ABSTRACT

Introduction. Micronutrient deficiencies during pregnancy remain a major global public health concern, with implications for maternal health, fetal development, and long-term child outcomes. International organizations such as the WHO and FIGO have issued evidence-based guidelines on micronutrient supplementation, which are increasingly being adapted into national protocols.

Material and methods. This narrative review was based on literature searches in PubMed, Scopus, Web of Science, and Google Scholar, covering January 2000 to May 2025. Peer-reviewed studies, systematic reviews, and clinical guidelines from WHO, FIGO, and the Moldovan Ministry of Health were included. The review focused on iron, folic acid, iodine, calcium, vitamin D, and selected trace elements.

Results. Iron and folic acid emerged as the most consistently recommended supplements across guidelines, with proven efficacy in reducing maternal anemia and neural tube defects. Iodine and calcium are also emphasized, particularly in regions with documented dietary insufficiency. Moldova's antenatal care protocol largely aligns with WHO and FIGO recommendations, prioritizing targeted over universal supplementation for nutrients beyond iron and folate. Evidence on routine supplementation with multivitamin complexes remains inconclusive.

Conclusions. Evidence-based micronutrient supplementation is essential to optimizing pregnancy outcomes. Universal iron and folic acid supplementation remain the cornerstone of antenatal nutrition strategies. Context-specific approaches, as exemplified by the Moldovan model, can enhance implementation in resource-limited settings.

Keywords: micronutrient supplementation, pregnancy nutrition, antenatal care, iron deficiency anemia, folic acid, iodine.

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***Corresponding author: Maria Cemortan**, MD, PhD, assistant professor
Department of Obstetrics and Gynecology
Nicolae Testemițanu State University of Medicine and Pharmacy
bd. Ștefan cel Mare și Sfânt 165, Chișinău, Republic of Moldova, MD-2004
e-mail: mariacemortan@yahoo.com

Authors' ORCID IDs
Maria Cemortan – https://orcid.org/0000-0003-3137-7524
Irina Sagaidac – https://orcid.org/0000-0003-2491-9612
Olga Cernetchi – https://orcid.org/0000-0002-9229-8080

Key messages

What is not yet known on the issue addressed in the submitted manuscript

Despite global recommendations, there is limited understanding of how international micronutrient supplementation strategies are adapted and implemented within national antenatal care protocols, including Moldova. The impact of context-specific modifications on maternal and fetal outcomes remains insufficiently explored.

The research hypothesis

Adherence to evidence-based, targeted micronutrient supplementation strategies, aligned with WHO and FIGO guidelines and adapted to local contexts, can optimize maternal and neonatal outcomes more effectively than non-individualized, multivitamin-based supplementation during pregnancy.

The novelty added by the manuscript to the already published scientific literature
This review uniquely integrates global guidelines with national policies from the Republic of Moldova to illustrate how targeted supplementation strategies are operationalized in practice. It highlights the clinical rationale for Moldova's tailored approach.

Introduction

Adequate nutrition during pregnancy is a cornerstone of maternal and fetal health, with micronutrients playing a critical role in ensuring optimal outcomes for both mother and child. Pregnancy increases metabolic demands and physiological needs, making women more susceptible to deficiencies in essential vitamins and minerals. These deficiencies can have significant short- and long-term effects on maternal health, fetal development, and the overall trajectory of child growth [1].

To address the high burden of micronutrient deficiencies, numerous international organizations, including the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO), have developed evidence-based guidelines recommending both population-level and targeted supplementation strategies [1-3]. National authorities, such as the Ministry of Health of the Republic of Moldova, have adapted these strategies to their epidemiological context by integrating supplementation and counseling into routine antenatal care [4-6].

This narrative review explores the current evidence on the physiological roles and public health significance of key micronutrients in pregnancy. It also examines global and national recommendations on supplementation strategies, aiming to inform clinical practice and guide future interventions to improve maternal and neonatal health outcomes.

Material and methods

This article was designed as a narrative review, aimed at synthesizing current scientific evidence and relevant public health guidance concerning the physiological importance, intake requirements, and supplementation strategies for key micronutrients during pregnancy. The review places particular emphasis on iron, folic acid, iodine, calcium, vitamin D, and other essential micronutrients implicated in maternal and fetal health outcomes.

A comprehensive, non-systematic literature search was conducted using the databases PubMed, Scopus, Web of Science, and Google Scholar, covering publications from January 2000 to May 2025. Search terms included combinations of "pregnancy", "micronutrients", "maternal nutrition", "supplementation", "iron deficiency", "folic acid", "iodine in pregnancy", "antenatal care", "maternal outcomes", and "public health nutrition". The search strategy prioritized peer-reviewed literature, including randomized controlled trials, systematic reviews, meta-analyses, Cochrane reviews, and high-quality observational studies. In addition, official documents issued by international bodies such as the World Health Organization and the International Federation of Gynecology and Obstetrics, as well as national-level protocols and guidelines from the Republic of Moldova, were included to ensure the integration of global and local policy perspectives.

Inclusion criteria focused on studies involving human pregnancy and micronutrient intake or supplementation with defined maternal or neonatal outcomes. Eligible sources included clinical trials, systematic reviews, meta-analyses, Cochrane reviews, and national or international policy documents. Non-peer-reviewed materials, animal studies, case reports, and studies not addressing micronutrient-related outcomes in pregnancy were excluded.

Given the narrative nature of this review, the selection of sources may be subject to selection bias. No formal quality assessment tool was applied, and the inclusion of references was guided by relevance, citation frequency in guidelines, and alignment with the Moldovan clinical context. This approach may limit the reproducibility and objectivity of the findings. Additionally, the review does not include quantitative data synthesis or statistical comparison between interventions, which is inherent to the narrative design.

Despite these limitations, the narrative format allows for a comprehensive and policy-oriented synthesis of scientific literature, offering a practical and comparative overview of international and national strategies for micronutrient supplementation during pregnancy.

This review does not constitute a systematic review or meta-analysis and does not include quantitative data synthesis. Rather, it presents a qualitative integration of current knowledge and practice standards, with the aim of providing clinicians, public health professionals, and policy-makers with an up-to-date overview of the rationale, scope, and implementation of micronutrient interventions during pregnancy.

Results

The findings from the literature and national and international guidelines converge on the critical importance of specific micronutrients during pregnancy. Iron, folic acid, iodine, calcium, and vitamin D were consistently identified as the most essential micronutrients with significant clinical and public health implications [7].

Iron deficiency anemia is among the most prevalent conditions during pregnancy, affecting over 30% of pregnant women globally and up to 40% in low- and middle-income countries [8]. Iron deficiency anemia is recorded in 8-15% of women of reproductive age, while iron deficiency is found in every third woman. Approximately 50-60% of pregnant women suffer from iron deficiency anemia, and in 70% of these cases, iron deficiency is detected. In the Republic of Moldova, over 10,000 women give birth each year with diagnosed iron deficiency anemia, representing 56.4% of all births, and the incidence is increasing [9].

Iron-deficiency anemia (IDA) in pregnant women is increasingly recognized as a common and persistent problem, even in high-income countries. Several modern lifestyle, dietary, and physiological factors contribute to its rising prevalence today compared to past generations. Pregnancy significantly increases the body's iron requirements due to the expansion of maternal blood volume, fetal growth, and placental development. It is estimated that a woman needs approximately 1,000-1,200 mg of iron throughout pregnancy, with the majority required in the second and third trimesters. When iron stores are already depleted before conception, these demands quickly outpace supply, leading to iron deficiency.

Contemporary diets contribute substantially to this issue. Many pregnant women consume less red meat or follow plant-based diets, which are lower in heme iron – the most bioavailable form. Additionally, widespread consumption of highly processed foods, which are often poor in micronutrients, combined with inhibitors of iron absorption such as calcium, tea, and phytates, further reduces dietary iron availability. At the same time, short intervals between pregnancies and pre-existing conditions like heavy menstrual bleeding or chronic inflammation (e.g., obesity, infections) impair iron absorption or increase iron loss.

Lastly, health system practices play a role. In many settings, iron supplementation is offered only when anemia is detected, rather than as a preventive strategy. Moreover, preconception care often overlooks iron status, and antenatal screening may be delayed until mid-pregnancy, missing opportunities for early intervention.

In this context, rising rates of IDA reflect a mismatch between physiological needs and current dietary and healthcare patterns, highlighting the importance of timely assessment, individualized counseling, and context-sensitive supplementation strategies.

Insufficient iron intake is associated with fatigue, increased risk of infections, low birth weight, and preterm birth. Supplementation has been shown to reduce the risk of maternal anemia and improve perinatal outcomes when appropriately initiated and monitored [10]. Iron was universally recognized as a key nutrient for the prevention and management of maternal anemia. WHO, FIGO, and national guidelines recommend routine iron supplementation in all pregnant women, especially in regions with a high prevalence of anemia [1, 3]. The Moldovan national protocol mandates the administration of 100 mg elemental iron every second day starting from 12 weeks' gestation, aligned with WHO's recommendation of 30-60 mg daily where anemia is prevalent [1, 5, 6]. Iron supplementation has been shown to reduce the incidence of maternal anemia at term, lower the risk of preterm birth, and improve infant iron stores at birth.

International recommendations on iron supplementation during pregnancy vary significantly, reflecting differences in anemia prevalence, nutritional status, and healthcare infrastructure across regions. The World Health Organization and the International Federation of Gynecology and Obstetrics (FIGO) advocate for universal daily supplementation with 30-60 mg of elemental iron and 400 μg of folic acid for all pregnant women (Table 1).

Table 1. Summary of iron supplementation guidelines in pregnancy

Organization	Universal Supplementation?	Dose	Screening	When to Supplement
WHO	Yes	30-60 mg/day	Not emphasized	All pregnant women
ACOG	No	60-120 mg/day (if IDA)	Yes	Only if anemic
RCOG	No	100-200 mg/day (if IDA)	Yes	Only if anemic
NICE	No	Based on need	Yes	Only if anemic
CDC	Yes	30 mg/day	Yes	All pregnant women
FIGO	Yes (in most settings)	30-60 mg/day	Recommends screening but supports universal supplementation where anemia is prevalent	All pregnant women, especially in LMICs
Moldova	Yes	100 mg elemental iron every second day starting from 12 weeks' gestation	Yes	All pregnant women

Note: WHO – World Health Organization, ACOG – American College of Obstetricians and Gynecologists, RCOG – Royal College of Obstetricians and Gynaecologists, NICE – National Institute for Health and Care Excellence, CDC – Centers for Disease Control and Prevention, FIGO – International Federation of Gynecology and Obstetrics, IDA – Iron-deficiency anemia

This approach is particularly emphasized in low- and middle-income countries (LMICs), where iron-deficiency anemia is highly prevalent and screening services may be limited. FIGO also supports this universal strategy but acknowledges that in settings with well-developed health systems, targeted supplementation based on screening results may be appropriate.

In contrast, organizations based in high-income countries tend to recommend a screen-and-treat approach. The American College of Obstetricians and Gynecologists (ACOG) and the Royal College of Obstetricians and Gynaecologists (RCOG) both advise routine anemia screening during pregnancy, with iron supplementation reserved for women diagnosed with iron-deficiency anemia [11, 12]. Similarly, the National Institute for Health and Care Excellence (NICE) discourages routine supplementation for non-anemic women and emphasizes dietary management and monitoring. An exception is the Centers for Disease Control and Prevention (CDC) in the United States, which supports low-dose daily iron supplementation (30 mg) for all pregnant women, beginning at the first prenatal visit, regardless of anemia status.

This variation in recommendations illustrates a broader public health debate between preventive universal supplementation and individualized treatment, shaped by local epidemiology and healthcare capabilities. As global dietary patterns shift and concerns grow regarding declining nutrient density in modern diets, some experts suggest that even in high-income settings, universal or semi-universal supplementation strategies may merit reconsideration.

In low- and middle-income countries (LMICs), where iron deficiency is highly prevalent (>40% of pregnant women), organizations like the WHO and Centers for Disease Control and Prevention recommend universal daily iron supplementation during pregnancy [13]. This is seen as a cost-effective population-level strategy to reduce adverse outcomes like maternal mortality, preterm birth, and low birth weight.

In contrast, high-income countries (HICs) like the USA (ACOG), UK (RCOG, NICE), where IDA prevalence is lower due to better baseline nutrition and access to healthcare, promote a screen-and-treat approach. This minimizes unnecessary supplementation and potential side effects [13]. Routine supplementation is beneficial in settings with poor access to health services, as many women may not receive timely testing or follow-up. However, in settings where anemia screening is feasible, targeted treatment is preferred to avoid risks such as:

- Gastrointestinal side effects (nausea, constipation)
- Iron overload in women with adequate stores or undiagnosed conditions (e.g., hemochromatosis)
- Poor adherence due to side effects in women who do not need iron

In LMICs, universal supplementation simplifies logistics and ensures that iron reaches all women regardless of access to testing. In HICs, healthcare systems can afford individualized care based on blood tests (hemoglobin, ferritin), enabling personalized supplementation.

The debate between universal vs. targeted iron supplementation reflects a balance between population-level public health strategies and individualized clinical care. While global nutritional transitions and changes in food quality may suggest a need for broader supplementation, recommendations continue to be tailored based on local epidemiology, health system capacity, and risk-benefit assessments.

Folic acid is another critical micronutrient. Its periconceptional and early pregnancy supplementation is strongly associated with a reduced risk of neural tube defects (NTDs), as it supports DNA synthesis and cellular replication. A daily intake of 400 µg of folic acid, initiated before conception and continued through the first trimester, can reduce NTD risk by up to 85% [14, 15].

Despite strong recommendations from global authorities, many pregnancies remain unplanned, and supplementation is often delayed or insufficient [3]. Folic acid supplementation emerged as a cornerstone of periconceptional and early pregnancy care. Both WHO and FIGO recommend a daily intake of 400 µg folic acid, starting at least one month before conception and continuing through the first trimester, to prevent neural tube defects (NTDs) [1, 3]. In Moldova, standard practice includes 1 mg folic acid every second day throughout pregnancy for all women, and 5 mg/day up to the 12th week of pregnancy for those with elevated risk (e.g., history of NTDs, diabetes, antiepileptic use) [4-6]. Although this differs from the internationally recommended dose of 400 µg daily, it is likely influenced by the limited availability of low-dose folic acid formulations in pharmacies, making 1 mg tablets a more practical choice for routine use. Despite the strength of evidence, global adherence to preconceptional folic acid use remains suboptimal. This has led some countries to adopt mandatory folic acid food fortification programs, which have been associated with significant reductions in NTD prevalence. However, such programs are not universally implemented, and targeted supplementation remains a critical strategy (Table 2).

Table 2. Folic acid supplementation guidelines during pregnancy

Organization	Recommended Dose	Timing	High-Risk Groups
WHO	400 µg/day	Preconception to 12 weeks' gestation	4 mg/day if history of NTDs
FIGO	400-800 µg/day	Preconception to first trimester	Higher doses for high-risk groups
ACOG	400-800 µg/day	≥1 month before conception to 12 weeks	4 mg/day for high-risk women
RCOG	400 µg/day	Preconception to week 12	5 mg/day for high-risk groups
NICE	400 µg/day	From preconception to 12 weeks	5 mg/day if high-risk
Moldova National Protocol	400 µg/day	Start ≥1 month before pregnancy, continue through first trimester	4 mg/day if previous NTDs or other risk factors

Note: WHO – World Health Organization, FIGO – International Federation of Gynecology and Obstetrics, ACOG – American College of Obstetricians and Gynecologists, RCOG – Royal College of Obstetricians and Gynecologists, NICE – National Institute for Health and Care Excellence, NTDs – neural tube defects

Mandatory folic acid food fortification is a public health policy in which governments require the addition of folic acid (the synthetic form of folate) to certain staple foods – most commonly wheat flour, maize flour, or rice – to improve the population's folate status. The rationale is to reduce the incidence of neural tube defects (NTDs) by ensuring that all women of childbearing age, including those with unplanned pregnancies, receive adequate folic acid intake regardless of supplement use.

This strategy is particularly effective in addressing the limitations of preconceptional supplementation, such as lack of awareness, late initiation of prenatal care, and high rates of unplanned pregnancies.

As of 2023, over 85 countries have implemented mandatory folic acid fortification policies. These include the United States, Canada, Australia, Chile, South Africa, and several countries in Latin America and the Middle East. In these

countries, significant reductions in NTD rates have been reported—up to 30–70%, depending on baseline prevalence and adherence to fortification standards. For example, in the United States, mandatory fortification of enriched grain products began in 1998 and has been associated with a 36% decline in NTD prevalence. In Chile, after wheat flour fortification was introduced, NTD rates dropped by approximately 50%.

Despite this success, many European countries, including Moldova, have not adopted mandatory folic acid fortification, often due to concerns about overexposure in the general population, possible masking of vitamin B12 deficiency, and a preference for voluntary supplementation strategies.

Overall, mandatory fortification is considered a cost-effective and equitable intervention, especially in settings where supplement coverage is low and dietary folate intake is insufficient. The World Health Organization and FIGO support the implementation of food fortification as a complementary strategy to supplementation for the primary prevention of NTDs.

Folic acid supplementation is safe, inexpensive, and effective. Ensuring adequate intake before and during early pregnancy is a critical component of maternal and child health. Public health efforts must continue to promote awareness and access, particularly for populations with limited healthcare engagement or poor nutritional status.

Iodine is vital for fetal brain development and maternal thyroid function. Even mild-to-moderate iodine deficiency in pregnancy is linked to lower cognitive scores in offspring and increased risk of goiter and hypothyroidism, miscarriage, and cretinism in severe cases [16]. Strategies like universal salt iodization have improved iodine status globally, but gaps persist in some regions, especially in areas with limited dietary diversity [1, 16, 17]. Iodine was highlighted for its critical role in fetal neurodevelopment. Mild-to-moderate iodine deficiency remains a concern in many regions, including parts of Europe, despite the implementation of universal salt iodization programs.

During pregnancy, iodine requirements increase by approximately 50% due to increased maternal thyroid hormone production, enhanced renal iodine clearance, and fetal needs. The World Health Organization recommends a daily iodine intake of 250 µg for pregnant and lactating women, which often cannot be met through diet alone, especially in regions without universal salt iodization (USI). The Moldovan guidelines endorse iodine sufficiency but do not currently recommend routine iodine supplementation beyond dietary measures (Table 3).

Table 3. Iodine supplementation guidelines during pregnancy

Organization	Recommended Dose	Supplementation Approach	Target Groups
WHO	250 µg/day (total intake)	150 µg/day if salt iodization is inadequate	All pregnant/lactating women
FIGO	150-250 µg/day	Preferably via iodized salt or supplements	Women in low-iodine areas
ACOG	150 µg/day	As part of daily prenatal multivitamin	All pregnant and breastfeeding women
NICE	No specific guideline on iodine	Emphasizes dietary intake and public health measures	General population-level iodine sufficiency
Moldova National Protocol	Do not currently recommend routine iodine supplementation beyond dietary measures		

Note: WHO – World Health Organization, FIGO – International Federation of Gynecology and Obstetrics, ACOG – American College of Obstetricians and Gynecologists, NICE – National Institute for Health and Care Excellence

WHO, FIGO, and other international bodies recommend iodine supplementation (150–250 µg/day) for pregnant and breastfeeding women living in areas with inadequate iodine intake or where USI is not reliably implemented. Iodine is commonly provided through potassium iodide (KI) or potassium iodate (KIO_3) in the form of multivitamin supplements. The goal is to ensure adequate maternal and fetal thyroid function throughout gestation.

Calcium plays a vital role in fetal skeletal development, muscle contraction, vascular function, and neuromuscular signaling [18]. During pregnancy, calcium demands increase to support the growth of the fetal skeleton, especially in the third trimester, when fetal bone mineralization is most active. While maternal physiological adaptations (e.g., increased intestinal calcium absorption) help meet this demand, insufficient calcium intake can lead to maternal bone demineralization and elevated risks of hypertensive disorders, particularly preeclampsia.

The World Health Organization recommends daily calcium supplementation (1.5-2 g of elemental calcium) for all pregnant women in populations with low dietary calcium intake (<1,000 mg/day). This recommendation is based on evidence showing that calcium supplementation significantly reduces the risk of preeclampsia, especially in high-risk women and those with low baseline calcium intake. WHO also advises dividing the dose into 2-3 daily administrations to enhance absorption and avoid gastrointestinal discomfort.

Organizations in high-income countries, such as ACOG and NICE, do not universally recommend calcium supplementation for all pregnant women [11, 19]. Instead, they encourage meeting calcium needs through diet, unless deficiency is suspected or dietary intake is inadequate. Dietary sources include dairy products, fortified plant-based milk, leafy greens, almonds, and small fish with bones. Moldova's standard antenatal care package does not recommend routine supplementation with calcium, which instead emphasizes dietary counseling (Table 4).

Table 4. Calcium supplementation guidelines during pregnancy

Organization	Universal Supplementation?	Recommended Dose	Target Population
WHO	Yes (in low-intake settings)	1.5-2 g/day (divided doses)	All pregnant women in populations with <1,000 mg/day calcium intake
FIGO	Yes (in high-risk or low-intake settings)	1.5-2 g/day	Women at risk of preeclampsia or with low dietary calcium
ACOG	No universal supplementation	Through diet; supplement if needed	High-risk or insufficient intake
NICE	No universal supplementation	Emphasis on dietary intake	High-risk groups only
Moldova National Protocol	Yes (selected cases)	Typically 1 g/day	Recommended for women at risk of preeclampsia or low calcium intake

Note: WHO – World Health Organization, FIGO – International Federation of Gynecology and Obstetrics, ACOG – American College of Obstetricians and Gynecologists, NICE – National Institute for Health and Care Excellence

Vitamin D, vitamin B12, zinc, and other trace micronutrients were addressed more variably across sources. While deficiencies are associated with adverse pregnancy outcomes, such as impaired bone development, immune dysfunction, and intrauterine growth restriction, there is insufficient evidence to support universal supplementation in the absence of individual risk factors. The Moldovan antenatal protocol explicitly advises against routine supplementation with multivitamin or multimineral complexes, except in documented deficiency states.

Discussion

This review confirms that evidence-based micronutrient supplementation during pregnancy is essential to optimizing maternal and neonatal outcomes. Iron and folic acid remain the most consistently recommended supplements worldwide, backed by strong evidence demonstrating reductions in maternal anemia and neural tube defects. Iodine and calcium also play crucial roles, particularly in fetal neurodevelopment and preeclampsia prevention, respectively, though recommendations for their supplementation are more variable and context-dependent.

Global guidelines, including those from WHO and FIGO, generally support universal supplementation with iron and folic acid, especially in populations where deficiencies are prevalent. In contrast, iodine and calcium supplementation are often recommended only in populations with known insufficiencies or specific risk factors, such as low dietary intake, inadequate food fortification policies, or increased risk of hypertensive disorders. This stratification allows for efficient resource allocation and minimizes unnecessary supplementation [20].

The Republic of Moldova's antenatal care protocol reflects this targeted, pragmatic approach, aligning closely with international recommendations while tailoring interventions to local resource availability and population health data. The country mandates iron and folic acid supplementation – though in formulations and schedules that diverge slightly from WHO dosing, possibly due to formulation availability. Meanwhile, calcium and iodine supplementation are advised only under certain clinical conditions, with dietary counseling forming the foundation of care.

Despite clear clinical guidelines, several challenges persist. Adherence to preconceptional folic acid supplementation remains low globally due to high rates of unplanned pregnancies. Similarly, gaps in iodine sufficiency persist in regions without robust salt iodization programs. The limited use of calcium supplementation in Moldova may reflect an underestimation of preeclampsia risk or insufficient dietary assessment. There is also a lack of consensus on the use of broad-spectrum multivitamins, with Moldova explicitly discouraging their routine use except in cases of diagnosed deficiency.

Emerging tools, such as the FIGO Nutrition Checklist, may enhance individual risk assessment and improve the integration of micronutrient strategies into routine antenatal care [21]. Future research should evaluate the effectiveness and cost-efficiency of targeted versus universal supplementation approaches, as well as the long-term impacts of national protocols on maternal and child health indicators.

Conclusions

Adequate intake of key micronutrients during pregnancy – particularly iron and folic acid – is critical for maternal and neonatal health. While universal supplementation with these two nutrients remains a global standard, recommendations for iodine and calcium vary according to dietary sufficiency and risk factors. Moldova's antenatal care model offers a context-sensitive strategy that aligns with international guidelines while accommodating local resource constraints and nutritional realities.

This review underscores the importance of combining evidence-based protocols with individualized clinical judgment. Integration of supplementation, nutritional counseling, and screening within routine antenatal visits enables more effective and equitable care. Moving forward, strengthening adherence to periconceptional folic acid use, expanding iodine sufficiency programs, and tailoring calcium and vitamin D strategies based on risk will be essential for advancing maternal nutrition and birth outcomes.

Competing interests

None declared.

Authors' contributions

All authors participated in the study design and contributed to drafting the manuscript. The authors critically reviewed the work and approved the final version of the manuscript.

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