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A landscape of micronutrient status in women through the reproductive years: Insights from seven regions in Asia

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Abstract
Optimal micronutrient status is critical to the health of women, particularly during their reproductive years. A woman's health and nutritional status during the preconception stage thus has significant implications for pregnancy outcomes and her offspring's health later in life. In this review, we evaluated micronutrient intakes and status (iron, folate, and vitamin B12) of women in their reproductive years and during pregnancy, along with associated health consequences and dietary causes, across seven regions in Asia, namely, Hong Kong, Indonesia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam. A structured literature search, targeting peer-reviewed publication databases, as well as data from international and national sources in the public domain, was conducted. Our review of the nutritional landscape demonstrates that micronutrient deficiency–related conditions, especially anemia and its associated health consequences, are common among Asian women of reproductive age, yet the dietary causes are poorly studied. Inadequate or borderline dietary intake of micronutrients and low consumption of micronutrient supplements were evident, despite existing recommendations, food fortification, and supplementation strategies. Evaluation of current programs through nutrition monitoring and improvement of supplementation strategies, such as supplementing with multiple micronutrients, alongside food-based programs, will help better support the health of women through their reproductive years.

Keywords
anemia, Asia, deficiency, micronutrient, supplementation, women of reproductive age

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Introduction

According to the Developmental Origin of Health and Disease (DOHaD) theory, the prenatal environment profoundly influences health and disease in childhood and adulthood.[1] The "fetal origins" hypothesis proposed by Professor David Barker[1] states that poor nutrition in utero results in developmental changes in the body's structure, function, and metabolism, increasing the risk of diseases such as coronary heart disease in later life.[2] As such, the International Federation of Gynecology and Obstetrics (FIGO) advocates the importance of getting optimal nutrition from an adequate diet comprising all essential micronutrients and macronutrients in the correct amounts and proportions during pregnancy and even at preconception, to equip women for future motherhood.[3]

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Micronutrients are essential components of cells and tissues, as well as key metabolic enzyme co-factors. Consequently, deficiencies in important micronutrients, such as iron and folate, are well-known drivers of adverse health and pregnancy outcomes, including anemia and various birth defects.[3,4] Cetin and colleagues[4] recently showed that inadequate maternal micronutrient status can exist even in pregnant women consuming a balanced diet, resulting in health consequences for both mother and child in the short and long term. More recently, the importance of women's health status before conception was highlighted due to its strong link to pregnancy outcomes.[5] Findings suggest that while micronutrient supplementation started during pregnancy may help correct key maternal nutrient deficiencies, it may be insufficient to fundamentally improve child health.[5] Taken together, the current evidence points to the need to evaluate the health status of women not only during pregnancy but also from as early as adolescence.

In many parts of Asia, advances in public health and economic development have markedly improved diet and nutrition in the past decades.[6] Nevertheless, suboptimal maternal micronutrient intake remains a significant factor contributing to increased risk of adverse maternal and fetal health outcomes. For example, while considered a "moderate" public health problem globally,[7] anemia is still of particular concern in low-/middle-income countries.[7,8] Insufficient intake of iron and other micronutrients, such as folate and vitamin B12, can result in anemia[7–10] and consequently increases the risk of serious pregnancy complications such as pre-term birth, low birth weight, pre-eclampsia, and mortality.[11,12] Fetal development is also affected.

In infants and young children, unaddressed deficiencies in iron, vitamin B12, and other critical micronutrients can contribute to anemia, suboptimal growth, delayed development, low birth weight, and neural tube defects with profound and long-term impacts on health.[3,4] In the face of the double burden of malnutrition in developing regions, such as those in Asia, micronutrient deficiencies are recognized as a problem facing both underweight and overweight mothers.[13]

Up-to-date, nationally representative data on micronutrient intake, status, and associated health outcomes in Asia appear limited. Although international as well as national recommendations on supplementation exist, it is unclear how these are being implemented in terms of programs or initiatives within individual regions. In this review, we first examined the prevalence of key maternal and fetal health outcomes in seven regions in Asia and provided a snapshot of the intake levels and status of a few specific micronutrients, namely, iron, folate, and vitamin B12, which can contribute to these adverse health outcomes. Finally, we reviewed supplementation recommendations and programs from these regions and highlighted important research gaps, challenges, and opportunities for improvement.

The seven regions selected were Singapore, Indonesia, Thailand, Vietnam, Philippines, Hong Kong, and Taiwan, which allowed us to cover both developing and developed regions in Asia. A structured search was conducted in PubMed in December 2018 to identify peer-reviewed publications on the target topics. In parallel, an Internet search was performed to identify relevant and publicly available reports published or hosted by public health organizations, national health authorities, and non-governmental organization; additional sources were identified and retrieved by the authors via their research networks. No restrictions were imposed on the literature search time period and publication or study type. Articles relating to the following topics in pregnant women and those of reproductive age were retrieved: (1) prevalence of maternal and fetal conditions related to micronutrient status or deficiency (maternal anemia, pre-eclampsia, low birth weight, pre-term birth, and neural tube defects); (2) dietary intake levels and blood concentrations of iron, folate, and vitamin B12; and (3) ongoing micronutrient supplementation strategies. The retrieved publications and reports were searched for data on these topics, and data were tabulated for each of the seven regions.

Micronutrient-related adverse maternal and fetal outcomes are prevalent in Asia

Table 1 summarizes the prevalence of five common maternal and fetal health outcomes in each of the seven Asian regions, with statistics from the United States (US) or Europe shown for comparison. We chose to focus on maternal anemia, pre-eclampsia, low birth weight, preterm birth, and neural tube defects; outcomes that are associated with one or more of the micronutrients of interest (iron, folate, and vitamin B12).[3–5,9,10,12,32,33] Data were extracted from World Health Organization (WHO) databases, national surveys, sub-national cohort studies, and systematic reviews. Of the outcomes examined, maternal anemia was by far the most prominent (Table 1). For maternal outcomes, it was notable that in almost all seven Asian regions, the estimated prevalence of anemia (1990–2016) was over 30%, nearly twice that of the US and European countries. The exception was Hong Kong, where the lower published estimates (2% and 8%) were based on earlier data (1992 study)[22] and data collected from a small sample of women attending maternal and child health centers for ante-natal care in 2009, respectively.[23] For pre-eclampsia, the estimated incidence in Indonesia (9%) was two to three times higher than the other Asian regions, as well as the US and Europe (Table 1). For fetal outcomes, low birth weight affected almost one in five live births in the Philippines, which was around two to three times higher than the other Asian regions and US/Europe (Table 1). For regions where data were available, the reported

Table 1. Maternal and fetal health outcomes in selected regions.

Conditions	Reported	United States[14–19a]	Europe[14,17,19–21a]	Hong Kong[22,23a]	Indonesia[14,16,18,24,25a]	Philippines[16,18,20,26–28a]	Singapore[14,16,18,19,23,24a]	Taiwan[19,29a]	Thailand[14,16,18–20,30a]	Vietnam[16,18–20,31a]
Anemia[b]	Prevalence (%)	16	23–26	2[c]–8[d]	42	26–30	32		40	37
Pre-eclampsia	Incidence (%)	2	4		9		4	1–2	2	
Low birth weight[e]	Prevalence (%)	8	7	5	9	20	9		8	6
Pre-term birth[f]	Prevalence (%)	10	9		10–16	13	10–12		13	7
Neural tube defects	Prevalence, per 10,000 births	5	2–36			2	1	3	2–7	4

Grayed out cells indicate no data reported.
[a]Data were extracted from WHO databases, national surveys, and systematic reviews.
[b]Hb < 110 g/L for pregnant women unless otherwise stated.
[c]Data from Department of Health. Patients who attended maternal and child health centers for ante-natal checkups; anemia was defined as Hb < 100 g/L.
[d]Data from a study conducted in two hospitals.
[e]Newborn infants weighing <2500 g at birth.
[f]<37 completed weeks.

prevalence of pre-term birth and neural tube defects was generally similar to that of the US and Europe (Table 1).

Micronutrient status during the reproductive years

Data on iron, folate, and vitamin B12 intake and status in non-pregnant women of reproductive age were retrieved from nine national-level surveys[34–42] and three sub-national cohort studies[43–45] (Table 2). We described the reported intake levels as "inadequate" or "borderline" with respect to the FIGO-recommended thresholds or ranges for each micronutrient.[3]

The iron intake levels varied widely across regions, with the lowest of 7.8 mg/day in the Philippines and highest of 18.4 mg/day in Singapore. Relative to the daily intake level recommended by FIGO (15–18 mg/day),[3] reported iron intake levels of women of reproductive age in the seven Asian regions were either inadequate or borderline optimal. Daily iron intake in Hong Kong ranged from inadequate to borderline optimal (7.9–15 mg/day),[34,42] whereas the levels in the Philippines,[41] Taiwan,[38] and Thailand[40] were suboptimal (6.4–12.9 mg/day). In Singapore,[36] Indonesia,[44] and Vietnam,[37,39] iron intake levels were between 15 and 18 mg/day, just at the level recommended by FIGO. Vietnam was the only region with available data for blood iron status. Of note, iron deficiency was prevalent among 13.7% of women of reproductive age in Vietnam[37] despite the mean plasma ferritin level (48.5 µg/L) above the cut-off level for deficiency (<15 µg/L according to WHO guidelines).[46]

Data on folate intake (one region) and status (three regions) in women of reproductive age were only available from four of the regions (Table 2). In Thailand,[45] the reported mean folate intake of 172 µg/day was less than half the minimum recommended by FIGO (400 µg/day).[3] The mean serum/plasma folate levels reported for Taiwan[35] (20.2–22.0 nmol/L) and Vietnam[37] (17.6 nmol/L) were almost twofold above the cut-off levels for deficiency (<10 nmol/L)[47]. However, substantial proportions of women in both regions were folate-insufficient: 21.9% in Taiwan[35] and 25.1% in Vietnam.[37] Similarly, although the mean RBC folate level reported for women of reproductive age in Indonesia (872 nmol/L) was above the cut-off level for deficiency (<305 nmol/L),[48] borderline folate insufficiency (RBC folate < 906 nmol/L) may be common.[49]

Data on vitamin B12 intake and status in women of reproductive age were scarce (Table 2). Only Vietnam had data for vitamin B12 intake (mean: 1.5 µg/day),[39] which was below that recommended by FIGO (2.4 µg/day), and mean plasma vitamin B12 level, which was reported as 630.3 pmol/L, above the cut-off level for deficiency (<150 pmol/L).[48,50]

Overall, intake of these three micronutrients (iron, folate, and vitamin B12) was low or at best borderline sufficient among women in these regions; this was true even

Table 2. Nutrition status for each key micronutrient in women of reproductive age.

		RDI[a]	Hong Kong[34,42a]	Indonesia[43,44a]	Philippines[41a]	Singapore[36a]	Taiwan[35,38a]	Thailand[40,45a]	Vietnam[37,39a]
Iron	Intake level (mg/day)	15–18	*7.9[c]–15*	15–17[d]	*7.8–8.0*	15.9–18.4	*12.9*	*6.4–9.2[d]*	15.7[d]
	Serum/plasma ferritin level (µg/L)[e]	–							48.5
Folate	Intake level (µg/day)	400						*172*	
	Serum/plasma folate level (nmol/L)[f]	–		872[g]			20.2–22.0		17.6
Vitamin B12	Intake level (µg/day)	2.4							*1.5*
	Plasma Vitamin B12 level (pmol/L)[h]								630.3

RDI: recommended daily intake.
Grayed out cells indicate no data reported.
Data for each region are mean unless otherwise stated.
Intake levels below RDI are marked in italics.
[a]RDIs are those recommended by FIGO.
[b]Data are mostly obtained from national studies, except for three sub-national cohort studies.[43–45]
[c]Based on analysis of samples of commonly consumed food combined into food composites, dietary exposures were estimated by computer modeling.
[d]Median.
[e]Cut-off level for iron deficiency: plasma ferritin <15 µg/L.[46]
[f]Cut-off level for folate deficiency: serum/plasma folate <10 nmol/L.[47]
[g]Red cell folate level.
[h]Cut-off level for vitamin B12 deficiency: plasma vitamin B12 <150 pmol/L.[48]

for iron, whose role in anemia is well-recognized. This is despite local intake recommendations in all seven regions being largely consistent with those of FIGO (Table S1 of Supplemental material).[3,50–62] The data also point to insufficiencies or outright deficiencies in a substantial proportion of women of reproductive age (even where mean levels were above-threshold), especially for iron and folate. If uncorrected, the effects of insufficiencies or deficiencies will be magnified in pregnancy, which places even greater demands on the mother.[63] Taken together, these observed nutritional deficits are likely to contribute to the high prevalence of maternal anemia in these regions (Table 1). The clear gaps in the national data on micronutrient intake and status (iron, folate, and vitamin B12) are of concern as these could hinder effective management of these and other micronutrient deficiencies.

Micronutrient status during pregnancy

Data on iron, folate, and vitamin B12 intake and status in pregnant women were predominantly from sub-national cohort studies (Table 3).[44,64–68] Data on iron intake were available only for Vietnam, Thailand, and Indonesia.[40,66,68] Indeed, in these regions, which had a high reported prevalence of anemia (37%–42%; Table 1), iron intake was suboptimal. Daily iron intake levels in Vietnam[68] (mean: 9.4 mg) and Thailand[40] (median: 15 mg) were well below the level recommended by FIGO for pregnant women (27 mg/day).[3] For Indonesia, reported mean daily iron intake was variable and ranged between 9.6 and 30.4 mg, depending on study setting.[44,66] Only the Philippines[65] and Singapore[67] had data for iron status, with median serum ferritin level reported as 15.7 µg/L (only slightly above the WHO cut-off level for deficiency (<15 µg/L[46])) and 24.2 µg/L, respectively (Table 3). Of note, iron deficiency was still prevalent among 34% of pregnant women in the Philippines.[65]

Data on folate intake and status in pregnant women were scarce and only available from Vietnam and Singapore (Table 3).[67,68] The mean daily intake of folate (440.8 µg) in Vietnam[68] was within the range recommended by FIGO (400–600 µg/day). Only Singapore[64] had data for median plasma folate level, which was reported as 34.4 nmol/L and above the WHO cut-off level for deficiency (<10 nmol/L).[47] Nonetheless, folate deficiency was still reported in 3% of pregnant women in Singapore; 8% were folate-insufficient.[64]

Similarly, data on vitamin B12 intake and status were scarce (Table 3). Only Vietnam had data for vitamin B12 intake (mean: 4.4 µg/day)[68] which was above that recommended by FIGO (2.6 µg/day)[3] (Table 3). Only Singapore had data for median plasma vitamin B12 level, which was reported as 209 pmol/L[64] and above the cut-off level for deficiency (<150 pmol/L).[48] No data were available for vitamin B12 deficiency in these Asian regions.

Table 3. Nutritional intake and status for each key micronutrient in pregnant women.

		RDI[a]	Hong Kong	Indonesia[44,66b]	Philippines[65b]	Singapore[64,67b]	Taiwan	Thailand[40b]	Vietnam[68b]
Iron	Intake level (mg/day)	27		*9.6–30.4*				*15*[c]	*9.4*
	Serum/plasma ferritin level (µg/L)[d]	–			15.7[c]	24.2[c]			
Folate	Intake level (µg/day)	400–600							440.8
	Serum/plasma folate level (nmol/L)[e]	–				34.4[c]			
Vitamin B12	Intake level (µg/day)	2.6							*4.4*
	Plasma Vitamin B12 level (pmol/L)[f]					209[c]			

RDI: recommended daily intake.
Grayed out cells indicated no data reported.
Data for each region are mean values unless otherwise stated.
Intake levels below RDI are marked in italics.
[a]RDIs are those recommended by FIGO
[b]Data are mostly obtained from sub-national cohort studies, except for one national study.[40]
[c]Median.
[d]Cut-off level for iron deficiency: plasma ferritin <15 µg/L.[46]
[e]Cut-off level for folate deficiency: serum/plasma folate <10 nmol/L.[47]
[f]Cut-off level for vitamin B12 deficiency: plasma vitamin B12 <150 pmol/L.[48]

The scarcity of micronutrient data is more prominent in pregnant women than in women of reproductive age. Despite the sparseness of these data, the trends for iron intake and status were somewhat similar to those in women of reproductive age (Table 2), with substantial proportions of women having outright deficiencies. The lack of data on folate and vitamin B12 makes it challenging to come to any conclusive findings, although one can probably infer data from existing trends found in women of reproductive age. With the increased nutrient demands in pregnancy, it is likely that such deficits contribute heavily to the high maternal anemia prevalence in these regions (Table 1).

Managing micronutrient inadequacies or deficiencies

A review of the literature and regional recommendations showed that dietary intake recommendations (Table S1), food fortification,[69] and other strategies[70–72] currently exist in the seven regions to improve nutrition and intake of key micronutrients—particularly iron and folate. In Indonesia, the Philippines, and Thailand, fortification of staple foods, such as flour or rice with specific micronutrients (iron, folate, or B vitamins), is mandatory, and iodization of salt is mandatory in most Southeast Asian regions.[69] Provisions for voluntary fortification of other micronutrients vary across regions. This is encouraging considering the extent of micronutrient deficiencies in women of reproductive age and in pregnant women. However, the success of implementing these strategies does not appear to have been formally evaluated. The coverage of large-scale or commercial food fortification for target populations also needs to be considered, especially for low-income families or those in rural areas with limited access to markets.

FIGO recommends additional daily iron and/or folate supplementation in women planning for a pregnancy, during pregnancy, and the first 3 months postpartum.[3] In addition, FIGO recommends to supplement vitamin B12 and other nutrients as required throughout these three stages.[3] While supplementation recommendations and/or programs are available across the regions, the supplementation strategies often focus on only iron and/or folate supplementation during preconception and pregnancy (Table 4). Even then, only a handful of regions (e.g. Indonesia, Philippines, Thailand, and Vietnam) have implemented supplementation programs to support such recommendations.[69] Supplementation strategies for other micronutrients, such as vitamin B12 are rare (Table 4) despite FIGO's recommendation. For example, among the seven regions, vitamin B12 supplementation is recommended only in Vietnam (in women across all stages) and in Hong Kong (in pregnant women who are vegetarians; Table 4). The direct impact of supplementation-related programs is also largely unknown.

Our search for information on supplement use in pregnancy and women of reproductive age revealed further

Table 4. Supplementation recommendations or programs in the Asian regions.

Nutrient	Stage	Hong Kong[51,52a]	Indonesia[73a]	Philippines[56,74a]	Singapore[75a]	Taiwan[58,70a]	Thailand[76–80]	Vietnam[60,81a]
Iron	Reproductive age			R			P	P
	Pregnant	R	P	P, R	R	R	P, R	R
	Lactating			R		R		R
Folate	Reproductive age	R		R	R	R	P, R	P
	Pregnant	R	P	P, R	R	R	P, R	R
	Lactating	R						R
Vitamin B12	Reproductive age							R
	Pregnant	R[b]						R
	Lactating							R

P: program; R: recommendation.
Grayed out cells indicated no data reported.
[a]Data gathered are not exhaustive.
[b]For vegetarians only.

data gaps. Despite widespread recommendations for additional iron and/or folate supplementations, use of these micronutrient supplements appears to vary greatly across regions and reproductive stages. Even during pregnancy, supplement use appears low or moderate, and varies from between 25% and 87% reported among pregnant women in the Philippines[82] to 33% reported in a study in Indonesia and 73% (for folate supplementation) in a Singapore-based study.[83,84] In the preconception and lactation stages, supplementation of micronutrients may be even less common.[43,44,85] Two studies in urban Indonesia reported 2%−16% of non-pregnant women who took supplements, and a study in rural Vietnam reported around 25% of lactating mothers taking supplements.[43,44,85] This is a potential issue, since early nutrition deficits are likely to persist into later life,[4] creating a cycle that is hard to break out of.

Current supplementation strategies often focus on just one or two micronutrients (such as iron–folate supplements), which could limit their effectiveness in view of multiple nutrient deficiencies and associated adverse outcomes.[86] Indeed, multiple micronutrient supplements have been shown to provide greater benefits than iron–folate supplements for some birth outcomes, with no increased risk of harm to the mother or child.[87,88] A Cochrane review of 17 trials involving 137,791 women reported greater risk reduction of low birth weight and small-for-gestational age births with multiple micronutrient supplements compared with iron–folate supplements.[87] Another meta-analysis reported greater reduction in pre-term birth with early initiation of multiple micronutrient supplements before 20 weeks gestation, compared with iron–folate supplements.[88] Furthermore, a recent publication reported that presumptively replacing iron–folate supplements with multiple micronutrient supplements in pregnant women for 1 year would reduce the number of deaths and number of cases of pre-term birth and reduce the costs associated with adverse outcomes.[89] These findings support the use of supplements containing multiple micronutrients beyond iron and folate, especially in settings where multiple micronutrient deficiencies are common.[87,88,90]

Monitoring micronutrient status

Although FIGO recommends that nutritional assessments should be incorporated into routine healthcare for women throughout their reproductive years,[3] we noted that nutritional assessment among in women in Asia is still limited. National surveys yielded some information on the nutritional status of women in the general population,[35,36,38,40–42,91] but data were much more sparse for pregnant or lactating women.[40,41] Often, only selected micronutrients were evaluated, and the methods of assessing intake or blood levels of individual micronutrients varied across the regions and study settings (Tables 2 and 3). It is possible that strategies advocating routine supplementation may play a part in influencing the perceived need for nutritional assessment.

Broad-based nutrition surveillance systems are required to identify nutritional risk, inadequacy and deficiency in women throughout the reproductive years, preferably using standardized methodology. Although dedicated national micronutrient status surveys have been conducted in a number of countries, such as Bangladesh and Nepal,[92,93] resource limitations may make it challenging to implement and sustain such survey programs. Linking micronutrient status data collection to another national-level survey, such as the well-established Demographic and Health Surveys (DHS) in > 90 countries,[94] has been explored in Cambodia and Malawi[95] as a way to incorporate micronutrient status assessment into national surveys. In regions where nationwide surveys are not feasible, conducting regular smaller surveys with standardized methodology in different areas in these regions can also provide important information to guide regional policy makers and governments in developing programs and interventions.

Summary

Our review of the nutritional landscape demonstrates that micronutrient deficiency-related conditions—most notably anemia and its associated health consequences—are common among Asian women of reproductive age, yet this public health issue is inadequately studied.

There are a few limitations to this review. Even for the well-known micronutrients, such as iron and folate, the data were often limited, heterogeneous (a mixture of national-level and sub-national cohort data and differences in study settings within regions such as those between rural and urban populations), and especially sparse for specific populations, such as pregnant women and lactating women. Our review included both peer-reviewed journal publications in English and research reports published by national and international organizations. As such, there was variation in the type and level of detail of reported data. Across studies reporting intake data, a range of dietary assessment methods were employed, and this may also account for some of the variation observed. Commonly used micronutrient status indicators were reported, such as serum/plasma ferritin for iron status, but the lack of information provided do not allow us to evaluate the quality of the micronutrient status data.

Although a complete picture of the status in the selected regions could not be drawn, this review reveals the scarcity of relevant data in these regions and points out an urgent need to address this. It is envisioned that this review would serve as an important evidence-based justification to support future initiatives, such as conducting regular surveys to monitor the status of multiple micronutrients and identify vulnerable areas, ongoing assessment of program impact, or designing targeted supplementation programs to complement other types of interventions in a country or region. For example, an iron/folic acid supplementation program for pregnant women has been implemented in Indonesia since the 1990s, providing supplements through ante-natal clinics, pharmacies, and midwives.[73] More recently, the Southeast Asian Ministers of Education Regional Center for Food and Nutrition (SEAMEO RECFON) initiated a program in Indonesia aimed at preventing stunting in children. A model for early childhood care, nutrition and education was developed through research on providing complementary feeding recommendations and educating nutritionists and mothers of young children on preventing stunting and anemia.[96] Findings from the SMILING project, a large multinational collaboration, underscore the importance of country- and region-specific knowledge and priorities in shaping policy and interventions, particularly the value of data on the nutritional content of locally available foods and habitual diets of target populations.[97]

Across the regions, we found evidence of inadequate or borderline dietary intake of micronutrients and low use of micronutrient supplements, despite consistent intake recommendations from both international and national bodies. With the high prevalence of maternal anemia and other conditions, this motivates our call for greater attention to women's nutritional status in this region, through combined strategies of improved monitoring of dietary intake or nutritional biomarkers, and evaluation and subsequent improvement of supplementation strategies.

Nutrition-sensitive and nutrition-specific interventions both have a role in supporting health and nutrition.[98] Besides multiple micronutrient deficiencies, infection burden can also contribute to anemia; an analysis of risk factors for anemia in non-pregnant women of reproductive age in 10 low-/middle-income countries suggests that the extent to which iron deficiency contributes to anemia is strongly influenced by a country's infection burden.[99] Diarrhea and intestinal parasitic infections can interfere with digestion and nutrient absorption, contributing to deficiencies in iron and other micronutrients that can also increase individuals' susceptibility to infections. Therefore, it is important to consider nutrition-specific interventions such as dietary modification/diversification and supplementation alongside nutrition-sensitive interventions including disease control, water supply, or agriculture. For example, in rural Vietnam, a population-based intervention combining weekly iron/folic acid supplementation with regular deworming has shown sustained effectiveness in reducing both iron deficiency anemia and soil-transmitted helminth infections.[100] Such combined programs have demonstrated a positive impact on the nutritional status of mothers and children.

In addition, socioeconomic factors strongly and directly influence diet quality and nutrition status. As an example, anemia is disproportionately concentrated in low socioeconomic groups.[8] Poverty is a major cause of poor diet and malnutrition in low-/middle-income countries in Asia. In households where resources are stretched, meeting basic macronutrient and energy requirements tends to be prioritized over nutrient quality; this problem may be compounded by limited availability or affordability of micronutrient-rich fresh foods or commercial fortified foods.

For supplementation, our recommendations are twofold. Since micronutrient deficiencies frequently co-exist in the context of poor diet, consideration should be given to supplementing with multiple micronutrients (in addition to iron and folate) particularly early in pregnancy, to further reduce risk of key birth outcomes. Ideally, overlapping public health concerns, such as infection burden, should be addressed in tandem to maximize the impact of each intervention. Second, in the pre-/peri-conceptional period or earlier, multiple micronutrient supplementation should also be considered, when necessary, to correct suboptimal nutrition or deficiency, as these will likely persist into later stages if not addressed. Along with other interventions, such as nutrition monitoring and food-based programs, multiple micronutrient supplementation will support optimal health of women throughout their reproductive years, and offer every child a better chance of a healthy start in life.

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Author contributions

All authors were involved in conceptualization, interpretation of data, writing-review and editing; read and approved the final article; and take responsibility for the integrity of the work as a whole.

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Supplemental material

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References

1. Barker DJ, Eriksson JG, Forsen T, et al. Fetal origins of adult disease: strength of effects and biological basis. *Int J Epidemiol* 2002; 31(6): 1235–1239.
2. Barker M, Dombrowski SU, Colbourn T, et al. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet* 2018; 391: 1853–1864.
3. Hanson MA, Bardsley A, De-Regil LM, et al. The international federation of gynecology and obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First." *Int J Gynaecol Obstet* 2015; 131(Suppl. 4): S213–S253.
4. Cetin I, Buhling K, Demir C, et al. Impact of Micronutrient Status during Pregnancy on Early Nutrition Programming. *Ann Nutr Metab* 2019; 74(4): 269–278.
5. Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet* 2018; 391: 1830–1841.
6. Cavalli-Sforza LT. Public health & nutrition in the Asia-Pacific: reflections on a quarter century. *Asia Pac J Clin Nutr* 2015; 24: 1–9.
7. Haemoglobin concentrations for the diagnosis of anaemia assessment of severity, https://apps.who.int/iris/handle/10665/85839 (accessed 26 August 2020).
8. Balarajan Y, Ramakrishnan U, Ozaltin E, et al. Anaemia in low-income and middle-income countries. *Lancet* 2011; 378: 2123–2135.
9. Nutritional anaemias tools for effective prevention control, https://apps.who.int/iris/bitstream/handle/10665/259425/9789241513067-eng.pdf;jsessionid=0B1D33BF6E81F2504F46BF97D7556AF2?sequence=1 (accessed 28 March 2019).
10. Aljaadi AM, How RE, Loh SP, et al. Suboptimal biochemical riboflavin status is associated with lower hemoglobin and higher rates of anemia in a sample of Canadian and Malaysian women of reproductive age. *J Nutr* 2019; 149: 1952–1959.
11. Sifakis S and Pharmakides G. Anemia in pregnancy. *Ann N Y Acad Sci* 2000; 900: 125–136.
12. Roberts JM, Balk JL, Bodnar LM, et al. Nutrient involvement in preeclampsia. *J Nutr* 2003; 133: 1684S–1692S.
13. Haddad L, Cameron L and Barnett I. The double burden of malnutrition in SE Asia and the Pacific: priorities, policies and politics. *Health Policy Plan* 2015; 30: 1193–1206.
14. Abalos E, Cuesta C, Grosso AL, et al. Global and regional estimates of preeclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2013; 170(1): 1–7.
15. Martin JA, Hamilton BE, Osterman MJ, et al. Births: final data for 2015. *Natl Vital Stat Rep* 2017; 66(1): 1.
16. Global preterm birth estimates, https://www.who.int/reproductivehealth/global-estimates-preterm-birth/en/ (accessed 16 April 2019).
17. Prevalence of anemia among pregnant women (%) 1990–2016, https://data.worldbank.org/indicator/SH.PRG.ANEM?end=2011&start=1990 (accessed 23 April 2019).
18. Prevalence of anemia among pregnant women (%) 1990–2011, https://data.worldbank.org/indicator/SH.PRG.ANEM. Accessed 28 March 2019
19. Zaganjor I, Sekkarie A, Tsang BL, et al. Describing the prevalence of neural tube defects worldwide: a systematic literature review. *PLoS ONE* 2016; 11: e0151586.
20. Chawanpaiboon S, Vogel JP, Moller AB, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019; 7(1): e37–e46.
21. State of the World's children, childinfo, and demographic and health surveys: low-birthweight babies of births, https://data.worldbank.org/indicator/SH.STA.BRTW.ZS?end=2012&start=2012&view=bar (accessed 23 April 2019).
22. WHO Global Database on Anaemia, https://www.who.int/vmnis/anaemia/data/database/countries/chn_ida.pdf?ua=1 (accessed 26 May 2019).
23. Western pacific country health information profiles: 2010 revision, http://www.wpro.who.int/publications/CHIPS2010.pdf (accessed 27 March 2019).
24. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates

in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 2012; 379: 2162–2172.
25. Indonesia Food Nutrition Security Profiles, http://www.fao.org/3/a-at707e.pdf (accessed 20 March 2019).
26. Nutritional status of Filipino adolescents >10-19 years old, https://www.fnri.dost.gov.ph/images//sources/eNNS2018/ADOLESCENTS_and_WRA.pdf (accessed 8 August 2019).
27. Padilla CD, Cutiongco EM and Sia JM. Birth defects ascertainment in the Philippines. *Southeast Asian J Trop Med Public Health* 2003; 34(Suppl. 3): 239–243.
28. UNICEF-WHO, Low birthweight estimates: Levels trends 2000-2015. Geneva: World Health Organization, https://www.unicef.org/media/53711/file/UNICEF-WHO%20Low%20birthweight%20estimates%202019%20.pdf (accessed 23 August 2019).
29. You SH, Cheng PJ, Chung TT, et al. Population-based trends and risk factors of early- and late-onset preeclampsia in Taiwan 2001-2014. *BMC Pregnancy Childbirth* 2018; 18: 199.
30. Thailand Multiple Indicator Cluster Survey, 2012, https://mics-surveys-prod.s3.amazonaws.com/MICS4/East%20Asia%20and%20the%20Pacific/Thailand/2012-2013/Final/Thailand%202012%20MICS_English.pdf (accessed 19 March 2019).
31. Viet Nam Multiple Indicator Cluster Survey, 2014, Final Report. Ha Noi, Viet Nam, https://mics-surveys-prod.s3.amazonaws.com/MICS5/East%20Asia%20and%20the%20Pacific/Viet%20Nam/2013-2014/Final/Viet%20Nam%202013-14%20MICS_English.pdf (accessed 21 March 2019).
32. Stevens GA, Finucane MM, De Regil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. *Lancet Glob Health* 2013; 1: e16–e25.
33. Schaefer E. Micronutrient deficiency in women living in industrialized countries during the reproductive years: is there a basis for supplementation with multiple micronutrients? *J Nutr Disord Ther* 2016; 6: 4.
34. The First Hong Kong Total Diet Study Report No. 9. The First Hong Kong Total Diet Study: Minerals, https://www.cfs.gov.hk/english/programme/programme_firm/files/Report_on_the_1st_HK_Total_Diet_Study_Minerals_e.pdf (accessed 6 May 2019).
35. Chen KJ, Pan WH, Lin YC, et al. Trends in folate status in the Taiwanese population aged 19 years and older from the Nutrition and Health Survey in Taiwan 1993-1996 to 2005-2008. *Asia Pac J Clin Nutr* 2011; 20(2): 275–282.
36. Report of the National Nutrition Survey, 2010, https://www.hpb.gov.sg/docs/default-source/pdf/nns-2010-report.pdf?sfvrsn=18e3f172_2 (accessed 22 March 2019).
37. Laillou A, Pham TV, Tran NT, et al. Micronutrient deficits are still public health issues among women and young children in Vietnam. *PLoS ONE* 2012; 7(4): e34906.
38. National Nutrition Health Survey (2013-2016) in Taiwan, https://www.hpa.gov.tw/Cms/File/Attach/6201/File_12811.pdf (accessed 18 July 2019).
39. Nguyen PH, Nguyen H, Gonzalez-Casanova I, et al. Micronutrient intakes among women of reproductive age in Vietnam. *PLoS ONE* 2014; 9: e89504.
40. Maternal dietary intake nutritional status in Thailand, http://ilsisea-region.org/wp-content/uploads/sites/21/2017/08/Session-1-06-Tippawan-Pongcharoen.pdf (accessed 25 March 2019).
41. Maternal Dietary Intake Nutritional Status in the Philippines: The 8th National Nutrition Survey Results, http://ilsisea-region.org/wp-content/uploads/sites/21/2017/08/Session-1-05-Marina-Vargas.pdf (accessed 22 March 2019).
42. Woo J. Nutrition and health issues in the general Hong Kong population. *Hong Kong Med J* 1998; 4(4): 383–388.
43. Green TJ, Skeaff CM, Venn BJ, et al. Red cell folate and predicted neural tube defect rate in three Asian cities. *Asia Pac J Clin Nutr* 2007; 16: 269–273.
44. Madanijah S, Briawan D, Rimbawan R, et al. Nutritional status of pre-pregnant and pregnant women residing in Bogor district, Indonesia: a cross-sectional dietary and nutrient intake study. *Br J Nutr* 2016; 116(Suppl. 1): S57–S66.
45. Sirikulchayanonta C, Madjupa K, Chongsuwat R, et al. Do Thai women of child bearing age need pre-conceptional supplementation of dietary folate? *Asia Pac J Clin Nutr* 2004; 13: 69–73.
46. Serum ferritin concentrations for the assessment of iron status iron deficiency in populations, https://www.who.int/vmnis/indicators/ferritin/en/ (accessed 26 August 2020).
47. Serum red blood cell folate concentrations for assessing folate status in populations, https://www.who.int/vmnis/indicators/serum_RBC_folate_update2015/en/ (accessed 26 August 2020).
48. Allen L, de Benoist B, Dray O, et al. Guidelines on food fortification with micronutrients. *WHO/FAO*, 2006, https://www.who.int/nutrition/publications/guide_food_fortification_micronutrients.pdf
49. Rogers LM, Cordero AM, Pfeiffer CM, et al. Global folate status in women of reproductive age: a systematic review with emphasis on methodological issues. *Ann N Y Acad Sci* 2018; 1431: 35–57.
50. Vitamin mineral requirements in human nutrition, 2nd ed., https://apps.who.int/iris/bitstream/handle/10665/42716/9241546123.pdf (accessed 22 March 2019).
51. Eat smart to prevent iron deficiency, https://www.fhs.gov.hk/english/health_info/woman/30069.html (accessed 21 March 2019).
52. Healthy eating during pregnancy breastfeeding, https://www.fhs.gov.hk/english/health_info/woman/20036.pdf (accessed 15 March 2019).
53. Meeting your calcium needs, https://www.fhs.gov.hk/english/health_info/woman/30120.html (accessed 21 March 2019).
54. Nutrients definition function, https://www.cfs.gov.hk/english/nutrient/nutrient.php (accessed 21 March 2019).
55. Ministerial Regulation No. 75. 2013: Dietary Reference Intake recommended for the Indonesian Population, https://peraturan.bkpm.go.id/jdih/userfiles/batang/PMK%20No.%2075%20ttg%20Angka%20Kecukupan%20Gizi%20Bangsa%20Indonesia.pdf (accessed 30 March 2019).

56. Philippine Dietary Reference Intakes, 2015, http://www.fnri.dost.gov.ph/images/images/news/PDRI-2018.pdf (accessed 30 March 2019).
57. Recommended dietary allowances for normal healthy persons in Singapore (Children Adolescents), https://www.healthhub.sg/live-healthy/192/recommended_dietary_allowances (accessed 30 March 2019).
58. Food and Drug Administration, Health Promotion Administration (Ministry of Health Welfare). Chinese Dietary Reference Intakes (DRIs) Seventh Edition (100 years revision). 2012.
59. Food Nutrition: Knowledge for all ages. In: Wathanee K, et al. The Food and Drug Administration of Thailand, http://www.inmu.mahidol.ac.th/th/freebook_01.pdf (accessed 30 March 2019).
60. National Nutrition Guide for Pregnant Women Nursing Mothers, https://cvdvn.files.wordpress.com/2017/04/hdqg_dinh-dc6b0e1bba1ng.pdf (accessed 30 March 2019).
61. Thai Recommended Daily Intakes, http://food.fda.moph.go.th/Rules/dataRules/4-4-2ThaiRDI.pdf (accessed 30 March 2019).
62. Table of daily reference intake for Thai BE. 2546, http://www.fda.moph.go.th/sites/food/Permission/4.4.8-DRI.pdf (accessed 30 March 2019).
63. Wilson RL, Gummow JA, McAninch D, et al. Vitamin and mineral supplementation in pregnancy: evidence to practice. *J Pharma Pract Res* 2018; 48: 186–192.
64. Chen LW, Lim AL, Colega M, et al. Maternal folate status, but not that of vitamins B-12 or B-6, is associated with gestational age and preterm birth risk in a multiethnic Asian population. *J Nutr* 2015; 145: 113–120.
65. de Jong N, Romano AB and Gibson RS. Zinc and iron status during pregnancy of Filipino women. *Asia Pac J Clin Nutr* 2002; 11: 186–193.
66. Hartriyanti Y, Suyoto PS, Muhammad HF, et al. Nutrient intake of pregnant women in Indonesia: a review. *Malays J Nutr* 2012; 18(1): 113–124.
67. Loy SL, Lim LM, Chan SY, et al. Iron status and risk factors of iron deficiency among pregnant women in Singapore: a cross-sectional study. *BMC Public Health* 2019; 19: 397.
68. Nguyen CL, Hoang DV, Nguyen PTH, et al. Low dietary intakes of essential nutrients during pregnancy in Vietnam. *Nutrients* 2018; 10: 1025.
69. Report on Regulatory Status of Micronutrient Fortification in Southeast Asia, http://ilsisea-region.org/wp-content/uploads/sites/21/2016/06/ILSI-SEA-Region-Report-Micronutrient-Fortification-Regulations.pdf (accessed 28 March 2019).
70. Maternal Health Booklet, https://www.hpa.gov.tw/Pages/ashx/File.ashx?FilePath=~/File/Attach/725/File_9166.pdf (accessed 29 March 2019).
71. Ministry of Health (MOH). *Maternal and child health handbook*. Jakarta: Ministry of Health, 2003 (in Indonesian).
72. PPD Compendium of Phillippine Medicine 18th Edition, Food Nutrition Research Institute (Department of Science Technology). Nutritional Guidelines for Filipinos 2012.
73. Dibley MJ, Titaley CR, d'Este C, et al. Iron and folic acid supplements in pregnancy improve child survival in Indonesia. *Am J Clin Nutr* 2012; 95(1): 220–230.
74. Philippines: Improving nutrition health for pregnant women newborns young children, https://www.nutritionintl.org/content/user_files/2016/05/philipinnes-right-start-infographic-web.pdf (accessed 28 March 2019).
75. Perinatal Society of Singapore. Guidelines on optimal perinatal nutrition—summary statements. *SJOG* 2019; 50: 21.
76. Bureau of Nutrition; Department of Health Ministry of Public Health. *The Handbook of Nutritional Health Promotion in Antenatal Clinic for Public Health Personel*, 2015.
77. Marulee S. The handbook of preconception care. Maternal and Child Group of Health, 7th Health Center (Ubon Ratchathani), Department of Health, 2014.
78. Ministry of Public Health. Thai women with red cheeks 2017-2026. 2nd National Reproductive Health Development Strategy (2017-2026) on Promoting Birth and Quality Growth, https://www.thaihealth.or.th/Content/44460-%E0%B9%82%E0%B8%84%E0%B8%A3%E0%B8%87%E0%B8%81%E0%B8%B2%E0%B8%A3%E0%B8%AA%E0%B9%88%E0%B8%87%E0%B9%80%E0%B8%AA%E0%B8%A3%E0%B8%B4%E0%B8%A1%E0%B8%AA%E0%B8%B2%E0%B8%A7%E0%B9%84%E0%B8%97%E0%B8%A2%E0%B9%81%E0%B8%81%E0%B9%89%E0%B8%A1%E0%B9%81%E0%B8%94%E0%B8%87.html
79. Subcommittee of explicit knowledge of food and nutrition for consumer. *Explicit knowledge of food and nutrition for all ages*. Nonthaburi, Thailand: Secretary Unit of National Food Committee, Bureau of Food, Thai Food and Drug Administration, 2016.
80. Winichagoon P. Thailand nutrition in transition: situation and challenges of maternal and child nutrition. *Asia Pac J Clin Nutr* 2013; 22: 6–15.
81. Maternal Child Nutrition in Viet Nam, http://www.un.org.vn/en/feature-articles-press-centre-submenu-252/339-maternal-and-child-nutrition-in-viet-nam.html (accessed 28 March 2019).
82. Maternal Health Nurtition Infant Young Child Feeding Surveys-2015. Updating of the Nutritional Status of Filipino Children and Other Population Groups, http://enutrition.fnri.dost.gov.ph/site/uploads/2015_MATERNAL_AND_IYCF_SURVEY.pdf (accessed 14 August 2019).
83. Asia the Pacific regional overview of food security nutrition, 2018-accelerating progress towards the SDGs, http://www.fao.org/3/CA0950EN/ca0950en.pdf (accessed 28 March 2019).
84. Chen LW, Fung SM, Fok D, et al. The development and evaluation of a diet quality index for Asian toddlers and its Perinatal correlates: the GUSTO cohort study. *Nutrients* 2019; 11: 535.
85. Nakamori M, Ninh NX, Isomura H, et al. Nutritional status of lactating mothers and their breast milk concentration of iron, zinc and copper in rural Vietnam. *J Nutr Sci Vitaminol* 2009; 55(4): 338–345.
86. Bailey RL, West KP Jr and Black RE. The epidemiology of global micronutrient deficiencies. *Ann Nutr Metab* 2015; 66(Suppl. 2): 22–33.
87. Haider BA and Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2017; 4: CD004905.
88. Smith ER, Shankar AH, Wu LS, et al. 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. *Lancet Glob Health* 2017; 5: e1090–1e100.

89. Engle-Stone R, Kumordzie SM, Meinzen-Dick L, et al. Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness. *Ann N Y Acad Sci* 2019; 1444: 35–51.
90. Sudfeld CR and Smith ER. New evidence should inform WHO guidelines on multiple micronutrient supplementation in pregnancy. *J Nutr* 2019; 149: 359–361.
91. Wu SJ, Pan WH, Yeh NH, et al. Trends in nutrient and dietary intake among adults and the elderly: from NAHSIT 1993-1996 to 2005-2008. *Asia Pac J Clin Nutr* 2011; 20(2): 251–265.
92. Nepal National Micronutrient Status Survey Report, 2016, https://www.unicef.org/nepal/reports/nepal-national-micronutrient-status-survey-report-2016 (accessed August 2020).
93. Bangladesh National Micronutrients Status Survey 2011-12 Final Report, https://www.gainhealth.org/resources/reports-and-publications/national-micronutrients-status-survey-2011-12-final-report (accessed August 2020).
94. The DHS Program: Demographic Health Surveys, https://dhsprogram.com/
95. Rhodes EC, Hennink M, Jefferds MED, et al. Integrating micronutrient status assessment into the 2015-2016 Malawi demographic and health survey: a qualitative evaluation. *Matern Child Nutr* 2019; 15(Suppl. 1): e12734.
96. SEAMEO RECFON. 2018/2019 annual report: SEAMEO RECFON, https://drive.google.com/file/d/1lG-i1RWhRe-nl6wO1nXgE4DD5G0P-ons/view
97. Berger J, Roos N, Greffeuille V, et al. Driving policy change to improve micronutrient status in women of reproductive age and children in southeast Asia: the SMILING project. *Matern Child Health J* 2019; 23(Suppl. 1): 79–85.
98. Ruel MT and Alderman H; Maternal and Child Nutrition Study Group. Nutrition-sensitive interventions and programmes: how can they help to accelerate progress in improving maternal and child nutrition? *Lancet* 2013; 382: 536–551.
99. Wirth JP, Woodruff BA, Engle-Stone R, et al. Predictors of anemia in women of reproductive age: biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. *Am J Clin Nutr* 2017; 106(Suppl. 1): 416S–427S.
100. Casey GJ, Montresor A, Cavalli-Sforza LT, et al. Elimination of iron deficiency anemia and soil transmitted helminth infection: evidence from a fifty-four month iron-folic acid and de-worming program. *PLoS Negl Trop Dis* 2013; 7(4): e2146.