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A qualitative study of factors influencing adherence with micronutrient supplementation among women of reproductive age in Viet Nam

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Abstract

A qualitative study of factors influencing adherence with micronutrient supplementation among women of reproductive age in Viet Nam
By Meredith Nechitilo

Objective: To identify factors that influence adherence to consumption of micronutrient supplements before and during pregnancy among participants of a double-blind randomized controlled trial (PRECONCEPT) assessing the impact of weekly preconceptional multiple micronutrient supplements on maternal and child health outcomes in 20 rural communes in northern Viet Nam.

Methods: In-depth interviews were conducted with current and former PRECONCEPT participants, including 15 pre-pregnant women receiving weekly micronutrient supplements, 8 pregnant women receiving daily iron-folate supplements, 8 women who had delivered and 8 drop-outs. Domains of interest included participants' experiences with supplements and knowledge about nutritional needs, micronutrient deficiencies, and the study. Four focus groups (one per participating district) were also conducted with Village Health Workers who distributed the supplements. Data were transcribed, translated, and coded and analyzed using MAXQDA software, applying the principles of grounded theory.

Results: Basic knowledge about anemia is high, and most women recognize that it is important to take iron supplements during pregnancy. Anemia is universally conflated with iron-deficiency anemia, though recent surveys suggest that less than half of all anemia in this population is caused by iron deficiency. There is very low knowledge of micronutrient deficiencies other than anemia, and low awareness of the health benefits of taking micronutrient supplements other than iron. Outside of pregnancy, women sometimes take iron or certain B or C vitamins on a curative basis only, terminating use when symptoms fade. The primary barriers to consistent adherence are forgetting and adverse side effects. Functional support and positive reinforcement from health workers and family members may improve adherence.

Conclusions: Initiation of supplement use requires recognition of the health consequences of micronutrient deficiencies and perceived personal susceptibility to those deficiencies, while maintaining consistent use requires a defined cue to action and minimization of attrition due to side effects. Increased awareness of micronutrient deficiencies among health center staff and Village Health Workers may improve women's valuation of micronutrient supplementation outside of pregnancy, and therefore increase initiation. Once supplement use is initiated, functional support from health workers and the cultivation of social support mechanisms can maximize adherence.

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Chapter 1: Introduction

Introduction and rationale

In recent years, there has been increasing recognition of the critical role of micronutrients in development and immune function. Pregnant women and children under the age of 2 are considered to be the groups most vulnerable to micronutrient deficiencies, particularly of iron, vitamin A, zinc, and folic acid. Poor maternal nutritional status is associated with adverse pregnancy outcomes including anemia, maternal hemorrhage, preterm birth, poor fetal development, and low birth weight (Ramakrishnan, Grant, Goldenberg, Zongrone, & Martorell, 2012; Wu, Imhoff-Kunsch, & Girard, 2012). Low birth weight in turn is strongly correlated with childhood stunting. Stunted children have a higher risk of morbidity and mortality, and are likely to go on to finish fewer years of school, have reduced productivity, and earn less money than their peers (Victora et al., 2008).

In Viet Nam, micronutrient deficiencies are common among women of reproductive age (WRA). Zinc deficiency is widespread, affecting nearly three-quarters of rural WRA (Laillou et al., 2012). Nationally, iron deficiency prevalence is a relatively modest 16 percent, but anemia rates among WRA have been reported to top 40 percent in the northern provinces (Aikawa, Ngyen, Sasaki, & Binns, 2006). Child nutritional status is equally troubling. The prevalence of stunting in children under 5 is 29 percent, or one of every three children, making Viet Nam one of the 36 countries that collectively share 90 percent of the global stunting burden (National Institute of Nutrition & United Nations Children's Fund, 2012; World Health Organization, 2011).

Iron and folic acid are widely recommended as prenatal supplements, and have been shown to reduce the incidence of low birth weight babies, neural tube defects, and infant and

maternal mortality. More recently, there has been a move toward prenatal multiple micronutrient (MM) supplementation, which may have an additional positive impact on pregnancy outcomes beyond that of traditional iron-folate supplements (Haider & Bhutta, 2012; Shrimpton, Huffman, Zehner, Darnton-Hill, & Dalmiya, 2009). Indeed, a recent study in northern Viet Nam indicated that prenatal MM supplements may reduce rates of low birth weight and stunting more effectively than iron-folate (Huy, Le Hop, Shrimpton, & Hoa, 2009).

Problem statement

While micronutrient supplements have been shown to have high efficacy in preventing and treating nutritional deficiencies, supplementation interventions often suffer from poor adherence (Klemm et al., 2011; Victora et al., 2012). Low adherence rates may be due to a variety of dynamic factors –personal, cultural, or logistical – which are unique to the particular setting of the intervention. Recognition of these factors is a necessary step toward improving the effectiveness of supplementation programs.

To date, there has been little qualitative research on supplement adherence in pregnant women, and virtually none on adherence among non-pregnant WRA. This gap in the research has limited the effectiveness and consequently the health impact of supplementation interventions targeting WRA, as existing programs lack insight into the factors influencing a woman's choice and ability to adhere to a supplement regimen. The most efficacious supplement will have only a limited impact if the target population does not use it.In order to bridge the gap between efficacy and effectiveness of supplementation programs in northern Viet Nam and elsewhere, we must understand the factors that facilitate or discourage women's adherence to them.

Purpose statement

This study aims to examine influences on adherence among women participating in the PRECONCEPT study, a double-blind randomized control trial where non-pregnant women were assigned to one of three weekly micronutrient supplements until becoming pregnant, at which point they were switched to a daily prenatal supplement. In-depth interviews were conducted with current and former participants from each of the four districts included in the study. In addition, focus group discussions were conducted with Village Health Workers, who are responsible for supplement distribution, monitoring of supplement use, and follow-up.

The objectives of this study are (1) to understand women's perceptions of dietary needs, causes and consequences of micronutrient deficiency, and nutritional supplements, (2) to identify practical, cultural and other factors associated with women's supplement use, and (3) to identify factors associated with partial and non-adherence to the PRECONCEPT supplementation program.

Significance statement

The impact of supplementation programs depends heavily on individual adherence. By understanding the factors that influence adherence, future programs can improve the effectiveness of their messaging and activities, which in turn will maximize health gains among women and children. The results of this study can be used to improve future effectiveness trials and supplementation programs in northern Viet Nam, as well as contributing to the nascent body of research around supplement adherence among WRA.

Abbreviations

ANC: Antenatal care

CHC: Commune Health Center

HBM: Health Behavior Model

IDA: Iron-deficiency anemia

IFA: Iron-folic acid

LBW: Low birthweight

MM: Multiple micronutrient

MNP: Micronutrient powder

SGA: Small for gestational age

VHW: Village Health Worker

WRA: Women of reproductive age

Chapter 2: Literature review

Micronutrient status and health outcomes for WRA and infants

Poor maternal micronutrient status during pregnancy is associated with a range of adverse health outcomes for mother and child, including increased risk of maternal hemorrhage, preterm birth, and intrauterine growth restriction (IUGR) (Mason et al., 2012; Wu et al., 2012). In particular, anemia is well-recognized as a significant cause of maternal mortality, partially through its contribution to postpartum hemorrhage; together, anemia and hemorrhage are estimated to account for two of every five maternal deaths in Asia (Khan, Wojdyla, Say, Gülmezoglu, & Van Look, 2006). Consequently, programming in South-East Asia has prioritized the reduction of maternal anemia through daily iron-folate (IFA) supplementation during pregnancy. However, there is increasing evidence to suggest that prenatal IFA supplementation is insufficient to fully address anemia, particularly for women who enter pregnancy already anemic, and also fails to address other nutrient deficiencies which contribute to adverse pregnancy outcomes (Haider & Bhutta, 2012; Wu et al., 2012).

Recent research indicates the potential for significant health gains through two strategies: preconception IFA supplementation, and prenatal multiple micronutrient (MM) supplementation. There is also emerging evidence of possible benefits from preconception MM supplementation.

Why preconception?

There is increasing evidence of the need for women to enter pregnancy with adequate nutrient levels. Micronutrients such as iodine and folate are critical to fetal development

processes early in pregnancy, before a woman realizes she is pregnant. Animal studies indicate that micronutrient deficiencies during the early stages of pregnancy have the greatest detrimental effect on fetal development (Wu et al., 2012). In addition, nutrient requirements increase dramatically during pregnancy, and women who enter pregnancy with poor nutrient status may be unable to meet these demands even with optimal diets.

Anemia and iron deficiency

Iron needs nearly double during pregnancy, and the body's ability to absorb dietary iron may be insufficient to meet iron requirements in later pregnancy (Stoltzfus, 2011; Wu et al., 2012). Anemia is common even among women who begin their pregnancies with adequate iron stores. Women who enter pregnancy already anemic are at increased risk for adverse pregnancy outcomes (Klemm et al., 2011). The WHO has advocated weekly IFA supplementation of women of reproductive age to combat both anemia and folate deficiency, particularly during early pregnancy (World Health Organization, 2009).

Ronnenberg et al. (Ronnenberg et al., 2004) found that moderate anemia before pregnancy was significantly associated with fetal growth restriction (OR: 4.6, $p = 0.006$) and low birthweight (OR: 6.5, $p = 0.009$) among Chinese women. Correspondingly, an intervention in northern Viet Nam found that deworming and weekly IFA supplements pre-pregnancy significantly reduced the prevalence of low birthweight (OR: 0.29, $p = 0.017$) (Passerini et al., 2012).

Other deficiencies

Folate deficiency is strongly associated with the occurrence of neural tube defects

(NTDs), which develop in the first month of pregnancy (Imdad, Yakoob, & Bhutta, 2011). A 2010 Cochrane Review supported the widely-promoted practice of periconceptional folate supplementation to reduce risk of NTDs, beginning at least one month before pregnancy (De-Regil Luz, Fernández-Gaxiola Ana, Dowswell, & Peña-Rosas Juan, 2010).

Iodine deficiency during early pregnancy is associated with maternal hypothyroxinemia and impaired fetal neurodevelopment, and in severe cases can lead to cretinism (Morreale de Escobar, Obregon, & Escobar del Rey, 2004; Zimmermann, 2012).

Why multiple micronutrient supplements?

Daily IFA supplementation during pregnancy is widely practiced in many countries to reduce the prevalence of maternal anemia and associated negative health outcomes. However, while iron and folate status are both critical before and during pregnancy, these are not the only deficiencies that can negatively impact maternal and child health. Vitamin A, B12, iodine, zinc, and other nutrients are critical to fetal development, particularly during early pregnancy (Wu et al., 2012). Many women are deficient in multiple micronutrients, which cannot be resolved by supplementation with iron and folate alone. To address this spectrum of deficiencies, there has been a push in recent years for multiple micronutrient (MM) supplementation. The most common formulation for MM supplements is the UNICEF/WHO/UNU international multiple micronutrient preparation, which includes 15 micronutrients and has been widely used and adapted (United Nations Children's Fund, World Health Organization, & United Nations University, 1999).

To date, most of the research comparing the impact of MM and IFA supplements on

maternal and child health has focused on supplementation during pregnancy (hereinafter referred to as "prenatal"). The current body of research suggests that MM supplementation has a significant impact on intrauterine growth, as indicated by reductions in low birthweight (LBW) and small for gestational age (SGA), while reported effects on other pregnancy outcomes are mixed. However, given the available evidence on the importance of nutrient status before and during early pregnancy, it is possible that preconception MM supplementation could show more significant reductions in adverse pregnancy outcomes.

Anemia

A 12-week efficacy trial among anemic adolescent girls in Bangladesh found that twice-weekly MM supplements were not significantly more efficacious in improving hemoglobin levels than IFA (Ahmed et al., 2005). However, the authors noted that many of the girls remained deficient in several nutrients, and speculated that more frequent supplementation may lead to a more significant difference in efficacy.

More recently, Hanieh et al. (Hanieh et al., 2013) conducted a randomized controlled trial in northern Viet Nam comparing the impact of intermittent prenatal IFA and MM supplements with daily IFA supplementation on maternal and child outcomes. The daily IFA group had higher ferritin levels than the intermittent groups, but the study found no significant difference in hemoglobin levels across treatment groups. The authors argue that the results support adoption of intermittent IFA supplementation among WRA, with doses doubled during pregnancy. This strategy could lead to increased adherence and lower costs (which could in turn increase both coverage and adherence). However, the implications for MM supplementation are limited, as there was no group receiving daily MM supplements; as in the Ahmed et al. trial, the authors

note that it is uncertain whether intermittent MM supplementation is sufficient to correct deficiencies and potentially improve hemoglobin levels.

Pregnancy outcomes and early child development

The strongest evidence for MM supplementation is its impact on intrauterine growth. A recent review of 16 randomized controlled trials found that prenatal MM supplementation was significantly associated with a 17% reduction of SGA and 14% reduction in LBW compared to IFA (Ramakrishnan, Grant, Imdad, Bhutta, & Martorell, 2013). This corroborates the 2012 Cochrane Review by Haider and Bhutta, which showed that prenatal MM supplementation was associated with reduced rates of SGA (10%) and LBW (11%) (Haider & Bhutta, 2012). No significant effects were found for other pregnancy outcomes, including preterm birth, miscarriage and stillbirth, pre-eclampsia, or maternal or infant mortality.

A systematic review by Shrimpton et al. also found a reduction in SGA and LBW among women supplemented with MMS compared to IFA (Shrimpton et al., 2009). In addition, the authors note that MM supplementation was equally effective as IFA in reducing anemia, despite frequently containing less iron, and suggest that the inclusion of vitamin C in MMS may have improved iron absorption. Given that anemia can have many nutrient-related etiologies, it is also possible that other nutrients included in the MM supplements improved hemoglobin status.

There is some evidence of the advantage of MMS over IFA for other pregnancy outcomes and for early childhood development, though the existing evidence is mixed. A 2002-2003 effectiveness trial in northern Viet Nam (Huy et al., 2009) found that weight gain during pregnancy was higher among women taking MMS than those taking IFA, and prevalence of low birthweight was significantly lower ($p < 0.05$). Anthropometric data collected two years after the

trial showed that children of mothers who had taken MMS were significantly less likely to be stunted ($p < 0.05$).

Similarly, a randomized controlled trial in Burkina Faso found that prenatal MMS was associated with a 27% reduction in stunting during infancy compared to IFA ($p = 0.002$), though this gap narrowed after the first year (Roberfroid et al., 2012). Children of mothers in the MMS group were also less likely to have episodes of fever ($p = 0.04$), though there was no significant difference in infant mortality.

By contrast, Shankar et al. found an 18% reduction in early infant mortality among children of mothers who had taken prenatal MMS compared to IFA ($p = 0.010$) (Shankar et al., 2008). The effects were significantly greater for infants of women who had been undernourished or anemic at enrollment, with reductions of 25% ($p = 0.0021$) and 38% ($p < 0.0001$) respectively.

Effectiveness of IFA and MM supplementation

In order to positively impact maternal and child health, supplement programs must be not only efficacious, but effective. Along with coverage, adherence is commonly identified as a primary barrier to the effectiveness of supplementation interventions. Most research on adherence has focused on prenatal IFA supplementation, but there is increasing data on adherence to intermittent supplementation strategies and MM supplementation.

In the effort to combat maternal anemia, daily IFA supplementation during pregnancy is now standard practice in many countries. The WHO recommends six months or 180 days of IFA supplementation during pregnancy.

A cross-country comparison of data from DHS surveys found that most countries fell

short of the WHO recommendation on both coverage and adherence (Klemm et al., 2011). Among the included Asian countries, between 43 and 78 percent of women received or purchased any iron supplements during their pregnancy, and fewer than 35 percent of women in any of these countries took iron for 90 days or more. Median use ranged between 30 and 66 days. The report noted that ANC coverage and frequency of visits was positively (though non-significantly) associated with receipt and consumption of iron tablets among pregnant women.

Galloway et al. conducted formative research in eight countries to assess barriers to and facilitators of adherence to iron supplementation during pregnancy (Galloway et al., 2002). They found that inadequate supplement supply was the greatest barrier to effective supplementation programs. Other barriers included additional challenges around coverage and access (including poor distribution and limited access to antenatal care), reluctance to take medications during pregnancy, and fear of the danger of delivering a large baby. Side effects were another barrier, though far from the greatest; approximately one-third of women reported experiencing negative side effects from iron supplements, and one-tenth terminated supplement use because of these side effects. Positive influences on adherence included perceived improved health, reduction of anemia symptoms, and perceived positive impact on the health of their baby. Women were more willing to tolerate temporary side effects if they valued these positive effects of the supplements.

A mixed-methods study in Cambodia (Lacerte, Pradipasen, Temcharoen, Imamee, & Vorapongsathorn, 2011) found that age and income were not good predictors of adherence to IFA supplementation among pregnant women. The use of a reminding technique ($p = 0.014$), support from family ($p < 0.001$), and attending 4 or more ANC visits ($p < 0.001$) were significantly and positively associated with adherence. In the interviews, women identified “lack of information, difficulty of access to ANC, and insufficient support from their families” as

barriers to adherence. Most interviewees had low knowledge about anemia and the preventive value of iron supplements, and said that they had not received information about these topics during their ANC visits. Coverage issues (inadequate supply and distribution) also negatively affected adherence. Contrary to the findings of other studies, side effects were not significantly associated with non-adherence.

Begum (Begum, 2012) used survey data to consider the association of demographic and socioeconomic factors with adherence to a prenatal IFA supplementation program in Uttar Pradesh. The husband's presence during ANC appointments was significantly associated with adherence (OR: 1.88, $p = 0.001$). Poor women and illiterate women were less likely to meet the adherence standard (OR: 0.65, $p = 0.001$), while urban women were more likely (OR: 1.35, $p = 0.001$). Because of the limitations of the research tool, the study does not explain why these associations exist, nor does it provide insight into influences on adherence at a personal or individual level; as a result, the author's discussion of the results is mainly speculative, and the data do not identify specific points to target for improvement, nor suggest strategies for improved effectiveness of future programs.

In their review of large-scale maternal nutrition programs, Victora et al. (Victora et al., 2012) identified factors that positively influenced adherence to micronutrient supplementation programs, as well as barriers to adherence, as shown in Table 1.

Table 1: Factors with positive and negative influence on adherence to large-scale maternal supplementation programs (Victora et al., 2012).

Barriers to adherence	**Positive influences on adherence**
• Lack of recognition of anemia as a serious health problem • Poor knowledge about why iron tablets are prescribed	• Well-being after alleviation of anemia • Improved appetite • Appreciation of a positive effect

• Beliefs against taking medicines during pregnancy • Fear that supplements might cause a large baby and make delivery difficult	for the fetus

Most of the existing research on adherence focuses on prenatal supplementation. To date, there has been no research on adherence to MM supplements among non-pregnant women.

Viet Nam

Micronutrient status of WRA in Viet Nam

Micronutrient deficiencies are common in Viet Nam, particularly in the mountainous, rural provinces in the north. A 2003 cross-sectional survey conducted in the northern province of Nghe An found that 43% of pregnant women had mild anemia, and 0.5% were severely anemic (Aikawa, Ngyen, et al., 2006). More recent surveys indicate that the prevalence of anemia has decreased in the past decade. The 2009-2010 General Nutrition Survey by the National Institute of Health and UNICEF that iron-deficiency anemia affected 29% of non-pregnant women and 36.5% of pregnant women (National Institute of Nutrition & United Nations Children's Fund, 2012). This represents a significant decrease from prevalence figures from the 1995 survey, but a slight increase from 2000 (Ninh, Khan, Vinh, & Khoi, 2003).

Table 2: Prevalence of anemia among pregnant and non-pregnant women in Viet Nam, 1995-2010 (NIN & UNICEF, 2012; Ninh et al, 2003).

Survey year	Pregnant women (%)	Non-pregnant women (%)
1995	52.7	40.2
2000	32.2	24.3

2009-2010	36.5	29.0

The 2010 survey showed that 35% of lactating women had subclinical Vitamin A deficiency, down from 58% in 1998 (Ninh et al., 2003). National coverage of maternal iron supplementation was low, with only 18% of mothers reporting having taken iron in the past six months. Coverage of Vitamin A supplementation was higher, reaching 62% of post-partum women. In all cases, coverage rates were a few points higher in the northern midland and mountain region, where Thai Nguyen is located.

A national 2010 study found lower rates of iron-deficiency anemia among WRA than those found by the General Nutrition Survey, but higher rates of Vitamin A deficiency (Laillou et al., 2012). The survey results suggested that iron deficiency and anemia had decreased in prevalence in recent years, but there was still high prevalence of deficient or marginal status in zinc, vitamin A, folate, and B12, all of which are associated with negative health outcomes for mothers and/or children. Relevant prevalences are shown in Table 3.

Table 3: Prevalence of micronutrient deficiencies and associated health outcomes among WRA in Viet Nam, 2010 (Laillou et al., 2012).

	Prevalence (%)
Anemia	11.6
Iron deficiency	13.7
Iron-deficiency anemia (IDA)	5.4
Zinc deficiency	67.2
Vitamin A	
Deficient	1.6
Marginal	13.6
Folate	
Deficient	2.7
Marginal	25.1
B12	
Deficient	11.7

Marginal	3.8

Less than half of anemia among women was classified as IDA, suggesting that the majority of anemia cases had etiologies other than iron deficiency. Almost a third of WRA had deficient or marginal folate status, and roughly one in six had deficient or marginal B12 status. Deficiency in these nutrients is associated with increased risk of neural tube defects, and adequate levels of both are strongly recommended one month before pregnancy and for the first trimester. At a population level, zinc deficiency was found to affect half of children and two-thirds of WRA. Zinc deficiency is associated with stunting, though the authors note that the prevalence of stunting is not a suitable stand-in for measuring zinc deficiency in a population. The 2009-2010 nutrition found a national stunting prevalence of 29.3%, and 33.7% in the northern midland and mountain region.

Previous supplementation interventions in Viet Nam

The past 15 year have seen multiple efforts to improve micronutrient status among women and children in Viet Nam, particularly in the northern provinces. Most interventions have focused on IFA supplementation during pregnancy in order to reduce the prevalence of maternal anemia.

Nguyen et al. (Nguyen et al., 2005) coupled IFA distribution to WRA and pregnant women with a social marketing and mobilization campaign. IFA tablets were distributed to non-pregnant women through the Women's Union, while pregnant women received tablets directly from the Commune Health Center, as was standard practice in the province. Awareness of anemia as a health concern was high at baseline (90.8%), but knowledge about specific causes and preventive measures was limited. Over the 12 months of the intervention, knowledge of

certain causes of anemia increased significantly, including dietary lack (categorized as "poor nutrition"), menstruation, increased iron needs during pregnancy, and hookworm infection ($p<0.001$). There was also a significant increase in knowledge of anemia as a serious health concern, and of IFA supplements as a means of preventing anemia ($p<0.001$). Self-reported purchasing and usage of the supplements among non-pregnant women increased from 54.5% to 92% in the first six months of the intervention, then dropped after the ninth month. The authors found that this drop was likely attributable to the circulation of an untrue rumor about negative health effects of the supplements, as well as increased forgetting during the harvest season when women were very busy. The authors point out that iron supplements had long been perceived as medicine, which conveyed a negative image.

Casey et al. (Casey et al., 2010) assessed the impact of weekly IFA supplements and periodic deworming medication on anemia prevalence. Supplement distribution was integrated into the existing healthcare system, through VHWs and CHC staff. At baseline, 34% of women were identified as anemic; however, only 14% had IDA. Over the course of the intervention, anemia prevalence was cut in half (38% → 19%), and iron deficiency and IDA decreased significantly (19% → 6% and 14% → 4%, respectively). The authors further noted that while supplement coverage decreased over the course of the study, from an initial 99% to 81% in April 2009, adherence (defined as taking 75% or more of the supplements) increased over the same period from 51% to 87%. The authors report that participants said the IFA tablets made them feel better after a few months of use, and that this had a positive influence on their adherence; however, it is unclear how widespread or common this sentiment was, and therefore its reliability as an influence on adherence is uncertain.

Influences on adherence

Influences on adherence are touched on to varying extents in the Viet Nam interventions. Hanieh et al.'s randomized controlled trial found that adherence was significantly lower in the daily IFA group than in the twice-weekly IFA group ($p = 0.01$), and still lower in the MM group ($p < 0.001$). Notably, the MM group reported significantly higher prevalence of nausea and vomiting as side effects compared to the IFA groups. While the authors do not discuss side effects as a potential negative influence on adherence, it is reasonable to consider as a possibility (Hanieh et al., 2013).

Nguyen et al. and Casey et al. both reported that perceived improved health had a positive effect on adherence. Nguyen et al. also found that forgetting and the circulation of negative rumors reduced adherence.

The most comprehensive examination of supplement adherence in Viet Nam is a 2003 mixed-methods study by Aikawa et al. (Aikawa, Jimba, et al., 2006), which utilized surveys, focus groups, and workshops with commune leaders to examine factors affecting adherence among pregnant women taking daily IFA. Over two-thirds of women surveyed received information about anemia from their CHC, approximately a third received information from a VHW or the Women's Union, and between 4 and 15 percent received information from radio or TV. The duration of supplement use was significantly longer among women who received information about anemia from media sources ($p < 0.01$) and who did not experience side effects ($p < 0.005$). Conversely, women who identified that a diet lacking in iron-rich foods was a cause of anemia took supplements for a shorter duration ($p < 0.005$). The authors propose that these women may have relied more on dietary intake of iron and therefore had a lower perceived need for the supplements, which reduced their adherence. This may be associated with a preference

for traditional medicine, which emphasizes diet over supplementation.

Survey results indicated that the two primary motivations for continued adherence were decreased dizziness (50% of respondents) and concern for the health of their baby (54%). Similarly, focus groups reported that the supplements reduced headaches and dizziness, and noted this as a motivation for continued adherence. All the focus groups indicated bad smell and vomiting as side effects of the supplements. None of the groups specifically mentioned family encouragement as a factor in their supplement use. Low prioritization of IDA prevention by commune leaders was commonly mentioned as a barrier to regular supplement use.

In the decade since the Aikawa et al. study was conducted, the prevalence of iron deficiency and IDA have decreased in northern Viet Nam, while awareness has increased, so this study may not be a fully accurate reflection of the most common channels of receiving information about anemia or the current prioritization of IDA prevention. However, motivations and other influences on adherence may be the same.

Table 4: Factors associated with supplement adherence among women of reproductive age in Viet Nam.

Study	Study population	Methodology	Positive influences on adherence	Barriers to adherence
Nguyen et al. 2005	Pregnant and non-pregnant women receiving weekly IFA tablets	Survey	• Feeling "stronger"	• Iron supplements perceived as medicine • Forgetting • Negative rumors about supplements
Aikawa et al. 2006	Pregnant women receiving daily IFA	Survey, focus groups, workshops with commune leaders	• Improved health • Reduced dizziness and headaches • Concern for health of baby • Receiving anemia information from media	• Bad smell • Side effects (vomiting) • Low prioritization of IDA prevention • Preference for traditional medicine
Casey et al. 2010	Pregnant and non-pregnant women receiving weekly IFA and periodic deworming tablets	Unclear	• Improved health	N/A
Hanieh et al. 2013	Pregnant women receiving daily IFA, intermittent IFA, or intermittent MMS	Randomized controlled trial	• Intermittent use (for IFA only)	• Side effects (nausea and vomiting)

Limitations of Viet Nam studies

There are several gaps in the current body of research on supplementation in Viet Nam. To date, there have been few interventions or studies focusing on MM supplementation, with the exceptions of the aforementioned effectiveness trial by Huy et al. and randomized controlled trial by Hanieh et al. There is also no published research on pre- or periconceptional supplementation, or of the effect of micronutrient supplementation among WRA on later pregnancy outcomes and early childhood development.

Another limitation of the studies assessed above is the common conflation of anemia and iron deficiency. Current estimates (Casey et al., 2010; Laillou et al., 2012) suggest that less than half of anemia among WRA in Viet Nam is IDA. Vitamin A, B12, and folate deficiencies are all known to cause anemia, and the Laillou et al. and NIN surveys indicate that there is high prevalence of deficient or marginal status of these nutrients in Viet Nam. Several studies considered hookworm infection as a cause of anemia (Aikawa, Ngyen, et al., 2006; Casey et al., 2010; Nguyen et al., 2005), but did not consider other micronutrient deficiencies or alternative etiologies such as genetic blood disorders.

Nguyen et al. primarily assessed knowledge about iron-related causes and prevention of anemia. Huy et al. tested blood samples for hemoglobin, but not ferritin levels, making it impossible to determine the proportion of anemia cases caused by iron deficiency. The three districts included in the randomized controlled trial in Huy et al. had varying anemia prevalences at baseline from 18% in the district that received MM supplements to 28.4% in the district that received IFA (Huy et al., 2009); it is possible that the primary causes of anemia were not the same in each district, given that they belonged to three different provinces, and differences of anemia prevalence and etiology may have impacted the effects of the supplements in each

district. The authors note that women who received 30 mg of iron in MM supplements saw a similar reduction in anemia to women taking 60 mg of iron in IFA, and conclude that MM is equally effective as IFA at controlling anemia, and the most important factor is the initial prevalence of anemia. This ignores the effect that IFA and MM supplements may have on anemia caused by different or coexisting deficiencies.

Much of the quantitative research on anemia in Viet Nam has focused disproportionately on iron deficiency as a cause, and iron supplementation as an intervention. If the literature is an accurate reflection of recent interventions, it appears that programs to address iron deficiency far outnumber those targeting other micronutrient deficiencies in pregnant and non-pregnant women. More specifically, previous efforts in Viet Nam have focused primarily on IFA supplementation during pregnancy. However, in recent years, there has been increasing awareness of the importance of ensuring adequate nutrient levels before pregnancy, as well as the value of addressing multiple micronutrient deficiencies.

Research on adherence is similarly limited primarily to prenatal IFA supplementation. There is little data available on adherence among non-pregnant women or women taking MM supplements, and to date, there have been no qualitative studies assessing influences on adherence among these populations. Future interventions targeting non-pregnant and periconceptional women will require further information regarding the factors that may affect these women's adherence to a supplementation program.

Filling the gaps

The PRECONCEPT study

The PRECONCEPT study is a double-blind randomized controlled trial which aims to fill some of the gaps in the literature around preconception and MM supplementation by evaluating the impact of preconception micronutrient supplements on pregnancy outcomes and early childhood development. Study participants are women of reproductive age in four districts of Thai Nguyen province, in the northern mountainous region of Viet Nam. Participants were randomly assigned to one of three weekly supplements (folic acid, IFA, or MM), which they took until becoming pregnant, at which point all participants were switched to daily IFA. All preconception supplements were taken on the same schedule, and the iron content was identical in the IFA and MM supplements (60 µg), allowing for valid comparisons between the treatment groups.

The PRECONCEPT study also offered an opportunity to assess influences on non-pregnant women's adherence to a long-term supplementation regimen. Using cross-sectional qualitative methods, the current study evaluated perceptions of dietary needs, micronutrient deficiencies, and supplements among women at various stages of participation in the PRECONCEPT trial. The purpose of this study is to identify factors associated with MM supplement adherence among non-pregnant women in Viet Nam in order to inform the development and delivery of future nutrition programs targeting this population.

Chapter 3: Methods and Results

METHODS

Overview

The objectives of this study were to understand perceptions of dietary needs, causes and consequences of micronutrient deficiency, and nutritional supplements among women of reproductive age (WRA) in northern Viet Nam, and to identify practical, cultural and other factors associated with adherence to a nutritional supplementation regimen. The study used cross-sectional qualitative methods to assess influences on women's adherence to the PRECONCEPT supplementation regimen in Thai Nguyen province. In-depth interviews were conducted with current and former PRECONCEPT participants, including pre-pregnant, pregnant, and post-partum women, as well as drop-outs. Focus group discussions were conducted with the Village Health Workers (VHWs) responsible for supplement distribution and follow-up.

PRECONCEPT study

Research was conducted among participants of the PRECONCEPT study in Thai Nguyen province, implemented by a study team at the Thai Nguyen University of Medicine and Pharmacy (TUMP). PRECONCEPT is a double-blind randomized controlled trial assessing the impact of multiple micronutrient (MM) supplements given to non-pregnant women of reproductive age on later pregnancy outcomes and early childhood development. Enrollment was restricted to married women who were planning to get pregnant within the next year.

Severely anemic women and those with a history of high-risk pregnancy were excluded from the study. Women who had regularly taken iron-folate (IFA) or MM supplements in the two months prior to enrollment were also excluded (Nguyen et al., 2012).

Most participants (88.1%) had one child at the time of enrollment. Of those who had been pregnant before, most reported attending at least one prenatal check-up (90.0%) and taking IFA or MM supplements (78.0%) during their last pregnancy. Approximately one in five participants were anemic at baseline.

Table 5: Characteristics of PRECONCEPT participants at baseline (n=5011) (P. Nguyen et al., 2012).

Mean age ±SD	26.2 ± 4.6
Ethnic minority (%)	49.5
Work as farmers (%)	80.6
Number of children (%)	
0	9.4
1	88.1
≥2	2.5
Attended prenatal check-up during last pregnancy (%)	90.0
Took IFA or MM during last pregnancy (%)	78.0
Underweight (BMI<18.5) (%)	31.4
Anemic (%)	19.7

Participants were assigned to one of three weekly oral supplements: folic acid, IFA, or MMS. They were instructed by their Village Health Worker (VHW) to take these supplements

until they became pregnant, at which point they were switched to daily IFA supplements for the duration of their pregnancy. Supplements were distributed to participants by VHWs, initially on a weekly and later on a biweekly basis. The VHWs were also responsible for monitoring supplement consumption and providing basic support to participants, and received a small stipend for their work. Participants, VHWs, and TUMP staff were blinded to the individual participant's supplement, as were the researchers on this qualitative study of adherence.

The VHWs held an initial meeting in their village with all participating women, at which each VHW was instructed to briefly describe the PRECONCEPT project, to make a distribution plan together with the participants, to go over the guidelines for supplement storage, and to have the participants take their first supplement. At this meeting, participants were told that they should only take one kind of supplement before pregnancy. They were instructed to take the PRECONCEPT supplements either one hour before or two hours after the main meal of the day, at a fixed time every week, and to keep the empty supplement containers for the VHWs to check later.

Research design

The study used a cross-sectional qualitative approach to identify influences on women's adherence to the PRECONCEPT supplement program. In-depth interviews with current and former participants were used to obtain information on women's perceptions of nutritional supplements and identify influences on women's adherence to the PRECONCEPT program. Focus groups were conducted with the VHWs responsible for supplement distribution and follow-up, in order to provide additional insight into barriers to supplement adherence, as well as contributing to a broader understanding of factors associated with adherence and partial or non-

adherence.

Study Site, Population and Recruitment

This study targeted women and VHWs in four districts of Thai Nguyen province who were involved in the PRECONCEPT study before or during the summer of 2013. Thai Nguyen is a mountainous province in northern Vietnam. Its population is 70 percent rural, and agriculture plays an important role in the province's economy. Districts are sub-divided into communes, which each have one Commune Health Center (CHC) with 10-20 associated VHWs. The PRECONCEPT study included four districts, each with five participating communes. For this sub-study on adherence, data collection was conducted in one commune randomly selected from the five participating communes in each district. Baseline characteristics for these communes are shown in Table 6.

Table 6: Characteristics of PRECONCEPT participants in selected communes at baseline.

	Phan Me (n=175)	Binh Long (n=75)	Khoi Ky (n=42)	Lam Vy (n=69)
Ethnic minority (%)	36.6	57.3	21.4	84.1
Work as farmers (%)	72.6	86.7	73.8	82.6
Underweight (BMI<18.5) (%)	27.6	27.4	23.8	30.4
Anemic (%)	5.8	18.7	0.0	10.1

In accordance with PRECONCEPT eligibility criteria, at the time of their enrollment in the trial, all in-depth interview participants were married women between the ages of 18 and 35 who planned to become pregnant in the next year. Most of the participants were farmers and had

at least one child before enrolling in PRECONCEPT. These traits are representative of women of reproductive age living in rural northern Viet Nam, and are shared by many women in developing countries who may be targeted by supplementation interventions.

All VHWs participating in focus groups were responsible for PRECONCEPT supplement distribution and participant follow-up. The majority of these VHWs were women.

Instruments

One focus group discussion guide and four in-depth interview guides (tailored to participation status) were developed in collaboration with the PRECONCEPT study team. The interview guides shared a base of common questions, and included additional questions based on participation status. The interview guides focused on the participants' individual experiences and motivations, while the discussion guide assessed VHWs' perceptions of influences on adherence at the commune level.

The guides were translated into Vietnamese and reviewed with the co-principal investigator on the PRECONCEPT study. The guides were then piloted by the research assistant team, and revisions were made to improve clarity, flow, and appropriateness for the study population. Small clarification edits were made between the first and second rounds of interviews in response to feedback from participants and the interviewers.

Procedures

In each of the four communes, trained research assistants conducted in-depth interviews with approximately 10 participants: four pre-pregnant women currently taking one of the three PRECONCEPT supplements, two pregnant women, two post-partum women, and two women

who had dropped out of the study. In one commune, only three interviews with pre-pregnant women were conducted, resulting in a total of 39 interviews across all four communes. Participants in in-depth interviews were purposively recruited by VHWs, CHC staff, and the TUMP liaison for each commune. Domains of interest included participants' knowledge about nutritional needs and micronutrient deficiencies, knowledge about the PRECONCEPT study, individual experience with supplements, and perceived effectiveness and side effects of nutritional supplements in general and PRECONCEPT in particular.

In addition, one focus group discussion with six participating VHWs was conducted in each commune. VHWs for focus group discussions were recruited purposively by CHC staff and the TUMP liaison. Domains of interest included VHWs' knowledge about nutritional needs and micronutrient deficiencies, knowledge about the PRECONCEPT study, the logistics of supplement distribution, and VHWs' perceptions of factors influencing participants' adherence.

Data were collected over three days in each commune. All interviews and focus groups were conducted in Vietnamese in private rooms at the CHC. Interviews and focus groups were digitally recorded with the consent of participants. These recordings were later transcribed and translated prior to analysis.

Data analysis

Verbatim transcripts of all interviews and focus groups were translated into English. These translations were coded using MAXQDA and analyzed according to the principles of grounded theory. Comparative analysis was conducted across commune and participation status, as well as by inductive sub-groups identified during the coding process.

Ethical Considerations

This study was determined by the Emory University Institutional Review Board to be closely aligned with the goals and aims of the previously-approved PRECONCEPT study, and was added as an amendment to that study (IRB #51384).Written informed consent was secured from participants before all interviews and focus groups.

Limitations

The primary limitation of this study is the potentially skewed representation of the primary reasons for dropping out of the study. According to PRECONCEPT survey data, the most common reason given for withdrawing from the study is the participant's moving out of the project area. Because of their relocation, these participants were inaccessible for the purposes of this study. Furthermore, participants who harbored distrust or ill will toward the study or project team were unlikely to agree to an interview. As a result, the results may offer an incomplete picture of non-adherence.

The results of this study may not be fully transferrable to women who do not meet the inclusion/exclusion criteria of the PRECONCEPT study. Specifically, these results may not reflect the perspectives of women with certain severe micronutrient deficiencies, those not consciously intending to become pregnant in the near future, or those with a greater awareness of their nutritional status or knowledge about supplements than those included in the PRECONCEPT study.

Given that PRECONCEPT is an efficacy trial, adherence is likely higher than it would be for a broader intervention among the general population. In addition, the decision to participate in the study may be associated with differences in financial motivation, interest in prenatal

health, or women's relationships with their VHWs.

RESULTS

Reported adherence among PRECONCEPT participants

Commune-level adherence figures for the four communes included in this study are listed in Table 7.Adherence was notably lower in Binh Long and Lam Vy, two of the most remote and rural communes in the study.

Table 7: Adherence rates for PRECONCEPT in participating communes.

Commune	Adherence
Phan Me	97.2%
Binh Long	87.5%
Khoi Ky	97.4%
Lam Vy	87.0%

Knowledge and attitudes around nutrient deficiencies

Anemia and iron deficiency

The interview data suggest that basic understanding of anemia is high. A significant majority of women were familiar with the term "anemia," and most of these were able to explain that it had to do with blood volume, and that pregnant women were at higher risk. Many women reported having been diagnosed as anemic in the past, and understood symptoms such as dizziness and headache as consequences of insufficient blood supply to the brain. Dizziness was

the most common symptom associated with anemia.

The baseline data presented in Table 6 show that anemia prevalence at baseline varied greatly between the four communes selected for this study, with significantly higher prevalence in the rural communes of Binh Long and Lam Vy. However, interview participants across all four communes demonstrated similar knowledge of and concern for anemia, with no noticeable distinction between urban and rural communes.

A majority of women received information about anemia from Commune Health Center (CHC) staff and Village Health Workers (VHWs). Many also reported learning about anemia from various forms of media, including books, magazines, newspapers, and television and radio programs.

Anemia was almost universally conflated with iron-deficiency anemia. Most women discussing anemia associated the condition with iron deficiency. Not all women explicitly linked anemia to iron deficiency; however, no other etiologies were mentioned.

With very few exceptions, women who reported any supplement use prior to PRECONCEPT had taken iron, frequently as their only experience with supplements. Iron supplements were taken most commonly during pregnancy, occasionally coupled with calcium supplements, but most frequently taken alone. In addition, some women took iron to treat symptoms of anemia such as dizziness and headaches, most commonly after being diagnosed (with or without a hemoglobin test) by a doctor.

Most participants reported having taken iron supplements during their first pregnancy. Some took Obimin, a common prenatal multivitamin that contained iron and several micronutrients, but referred to it only as “iron.” Most women who took iron did so on the advice of a CHC health worker or VHW, while some were advised by other women or, in a few cases,

by pharmacists.

Iron was by far the most commonly named supplement that participants said they would consider taking in the future, as well as the most widely recommended for use by other women. Most participants agreed that iron should be taken during pregnancy in order to ensure sufficient blood for both mother and child. Many expressed the opinion that iron was the only supplement required during this time.

> "Some women know that during pregnancy, they must supplement iron. They don't know that they must take other supplements to have adequate minerals." (A9 - Pre-pregnant, Phan Me)

Participants who had previously been diagnosed with anemia were more likely to say that all women should take iron, and to believe that anemia was widely prevalent among women.

> "[Women] should take supplements because most women are anemic. No one isn't - only a few." (C1 - Post-partum, Khoi Ky)

The high valuation of prenatal iron supplementation may have led to unintended double-dosing among some PRECONCEPT participants. A few women reported taking iron supplements or Obimin during their pregnancy in addition to the GESTCARE provided by the study. This suggests that there is incomplete awareness of the contents of the GESTCARE supplements, which contain the full recommended amount of iron for prenatal use. This doubling up of supplements may increase the risk for side effects or overdose.

B and C vitamins

Following iron, the most common supplements women had taken previously were

vitamin C and a range of B vitamins, particularly B1, B6, and B12. Unlike iron, which participants noted could serve both to prevent and treat anemia, B and C vitamins were considered to serve an exclusively curative purpose. Women took them when they felt tired or weak, or when they had headaches, and terminated use when these symptoms stopped:

> "In the past, I sometimes took vitamin 3B [a supplement which includes B1, B6, and B12]. [...] Whenever I felt ill or tired or in pain, I would take this supplement. I bought it myself, or went to the Commune Health Center to ask for advice. When I felt that I had my strength back, I stopped." (A10 - Pre-pregnant, Phan Me)

A few participants stated explicitly that they didn't view these as nutrient supplements, but as medicine:

> "*Interviewer*: When you took vitamin B1, did you think that was a nutrient?
> *Participant*: No, I didn't. I think it's a kind of medicine. A medicine for better appetite, to become healthier and less tired." (B8 - Pre-pregnant, Binh Long)

In some cases, these supplements were recommended by CHC doctors; in others, women took them on the advice of pharmacists or other women, or because they had seen them advertised.

Calcium

A few women reported having taken prenatal calcium supplements. These women discussed calcium as having similar importance to iron for a healthy pregnancy. Several other women mentioned calcium as an important nutrient in food. Valuation of both dietary and supplementary calcium was significantly higher in Khoi Ky than in other communes, which

suggests a difference in nutrition programming.

Other nutrients and deficiencies

Knowledge of other nutrients and their associated deficiencies was quite low. While many women recognized a general association between the mother's nutritional status and her child's health, there was little discussion of specific ways that maternal deficiencies could impact fetal or early childhood development.

Folic acid was mentioned very rarely, and only once as an ingredient in a supplement (Obimin) women had taken or were aware of. Folate was never mentioned as an ingredient in iron supplements, despite the fact that the prenatal supplements most participants reported taking can reasonably be expected to have contained folate. There was no discussion of the consequences of folate deficiency, or its role in fetal development.

Similarly, despite the high prevalence of zinc deficiency among both WRA and children in Viet Nam, zinc was mentioned by only one woman, and then only in passing. A few women expressed the belief that babies of women who took PRECONCEPT and GESTCARE were bigger and stronger than other babies, but did not draw an explicit link between maternal nutritional status and the child's physical development.

Recognition and valuation of vitamin A was low, though slightly higher than that of folic acid and zinc. A few women knew that it could be found in some fruits, and that it was generally good to consume. Vitamin A was never mentioned in women's supplement experience or future plans, nor in their recommendations for other women.

Fortified milk

Several women reported drinking fortified “pregnancy” milk during a previous pregnancy, most commonly the brand “Materna”. Women who had consumed this product knew generally that it was good for health and contained nutrients, but were unable to list specific ingredients. This milk contained the same micronutrients as a prenatal multivitamin; however, it was considered more as a healthful addition to the prenatal diet, rather than a form of supplementation. Women who reported drinking fortified milk did not count this in their previous supplement experience.

Summary

Anemia (equated with iron deficiency) is by far the best recognized and understood health outcome associated with micronutrient deficiencies. Most women believe that pregnant women are susceptible to anemia, that it can negatively impact the health of both mother and child, and that prenatal iron supplements are an effective method of preventing anemia and reducing the risk of adverse health outcomes. A minority of women view sub-optimal nutrition status before pregnancy as contributing to a woman’s susceptibility to anemia and its negative health consequences during pregnancy.

Beyond anemia, there is very low awareness of negative health consequences related to micronutrient deficiencies. Most women do not appear to feel that they are susceptible to other nutrient deficiencies, or that these deficiencies have a serious impact on their own health or the health of their child. As a result, valuation of supplements other than iron is low. Some vitamins are valued in a medicinal capacity, as they are believed to reduce fatigue and weakness, but are not considered to have preventive benefit for either the woman or her pregnancy.

Women who had past experience taking supplements on a curative basis generally said

that they would continue taking them when they felt weak or ill. Several women expressed the opinion that strong, healthy women did not need to take supplements.

> "I won't take supplements before pregnancy. My health is already good, so it isn't necessary to take supplements. If my health is weak, I will take them as needed." (B2 - Pre-pregnant woman, Binh Long)

> "I think [other women] are stronger than me, so it isn't necessary for them to take supplements." (B6 - Post-partum woman, Binh Long)

While most women said that they did not intend to take supplements in the future, many said that they would take supplements if they were recommended to do so by their doctor or VHW. They felt that they did not know what nutrients they lacked, and therefore would not know what supplement to take, but would trust the advice of their health workers.

> "I think that doctors usually advise us well. If we lack nutrients, we should take them. (...) If we want to take medicine or have any problems, we should go to see the doctor and then take medicine after." (A3 - Post-partum woman, Phan Me)

> "I will just ask the doctor about what I should take if I don't feel well. I will buy whatever they advise me to." (C6 - Pregnant, Khoi Ky)

Influences on adherence

Overall, adherence to the weekly PRECONCEPT supplements was relatively high. The most common barriers to adherence among both drop-outs and current participants were forgetting and side effects.

Forgetting

Many women mentioned that it was difficult to remember to take the PRECONCEPT supplements. Several women felt that this was due to the once-weekly supplement schedule, and felt that it was easier to remember to take the GESTCARE supplement because it became part of their daily routine. One post-partum woman (C6) said that she had forgotten to take her PRECONCEPT supplement around 10 times, but had never forgotten to take GESTCARE, "not even once."

> "*Interviewer*: What was your main reason for dropping out of the project?
> *Participant*: I didn't remember the schedule of taking the medicine. It wasn't taken continuously, just one tablet per week, so I didn't remember. [...] If I were taking the medicine continuously, I could remember." (B9 - Drop-out, Binh Long)

> "I took [GESTCARE] every day, I didn't forget. I remembered very well, since I had to take it every day. I took the pre-pregnancy supplement every week, so it was easier to forget." (C1 - Post-partum, Khoi Ky)

The majority of participants reported having forgotten to take the PRECONCEPT supplement at least once. Roughly half of these women said they took the supplement when they remembered, and the other half omitted the tablet for that week. This appears to be the result of inconsistent advice from VHWs, and has some relationship with how much flexibility the participants viewed the supplement schedule. Participants who considered the schedule to be very strict tended to omit that week's supplement if they forgot, while women who viewed the schedule as more flexible were likely to take the supplement when they remembered.

> "For instance, if I forgot one night, I would remember it and take it the following day. I

> didn't forget for several days. (...) I didn't take it on a scheduled day or hour. For example, today is Saturday and I am supposed to take the supplement. This week I might take it in the morning, but next week I will take it at noon, since whenever I see it, I remember and take it." (A9 - Pre-pregnant, Phan Me)

> "I skip a week [when I forget]. I was told to take the supplement at the exact time every week. I'm afraid that taking it at the wrong time is not good." (B8 - Pre-pregnant, Binh Long)

> "I did not take the supplement after I forgot, because the health workers told us that we did not need to do so. (...) I don't know the reason clearly. I just think taking the medicine in the right way, at the right time, is good for our health, for any treatment." (D1 - Post-partum, Lam Vy)

> "Many women don't remember to take the supplements at a certain time. It would be simpler to take them at any time. For example, they take the supplement on Sunday. However, they will forget if they have to take the supplement one hour before or two hours after the meal." (C9 - Pre-pregnant, Khoi Ky)

A few women discussed strategies for remembering the supplements, such as hanging the supplement bag over their beds or setting a reminder on their phone, which served as cues to action. These women said that they rarely if ever forgot to take their supplements, and attributed this to their reminder strategies.

Side effects

Study records indicate that participants moving out of the project area is the primary reason for dropping out of the study; for practical reasons, those women were not included in this study. Among the drop-outs interviewed, side effects were reported as the most common reason

for dropping out. Side effects were also mentioned by many women who did not drop out.

The most frequently reported side effects among all participants were gastrointestinal problems, including constipation, indigestion, and nausea. A few women reported itching; it is likely that this is a side effect of iron, as it was also reported as a side effect of previous iron usage, and in one case began only when the participant switched to GESTCARE after becoming pregnant.

In some cases, women experienced side effects at the start of their supplement use, but the symptoms disappeared within the first month. These women understood this as their bodies getting accustomed to the supplement, and many said that they had been counseled along these lines by their VHW. For other women, their side effects continued throughout the duration of their supplement use. Women were more willing to tolerate these side effects if they were relatively mild and lasted only a short time (less than an hour after taking the supplement), especially if they had been reassured by their VHW that the symptoms were not serious and would pass. Women who felt that their side effects endangered their health or interfered with their daily life were likely to discontinue use.

Chapter 4: Discussion and recommendations

Future supplementation programs will face two related but distinct challenges: first, to encourage initiation of preconception supplementation, and second, to ensure adherence once the behavior has been initiated. The results from this study, the first of multiple micronutrient supplement adherence in non-pregnant women, suggest that initiation of supplement use is heavily influenced by perceived health threats and valuation of supplements, while continued adherence, in the presence of an adequate supply chain, is affected by barriers such as side effects and forgetting.

Perceived threats and valuation of supplements

According to the Health Behavior Model (HBM), health behavior is determined by an individual's perceptions about both a disease and the proposed preventive or curative behavior. These perceptions include the perceived seriousness of the disease and the individual's perceived susceptibility, and perceived benefits of and barriers to the new behavior (Glanz, Rimer, & Lewis, 2002).

The interviews with PRECONCEPT participants show that perceived threats to nutritional health among this population do not align with the threats indicated by survey data. The 2010 survey by Laillou et al. found that less than half of all anemia among WRA in Viet Nam is caused by iron deficiency (Laillou et al., 2012). However, PRECONCEPT participants universally equate anemia with iron deficiency. There is very low awareness of other causes of the condition, such as hookworm infection or other nutrient deficiencies. Furthermore, anemia is perceived as a threat of similar risk and severity across all four communes, despite the

significantly lower prevalence of the condition in Phan Me and Khoi Ky.

The perceived severity of anemia during pregnancy is high, and most women consider themselves susceptible during that period. Anemia before pregnancy is considered less dangerous, manifesting as dizziness or fatigue. Visibly healthy, "strong" women are generally not considered at risk of anemia outside of pregnancy, while thin or weak women are more susceptible. In all cases, iron supplements are considered the primary means of both prevention and treatment, and are believed to be highly effective. Other supplements are not believed to have an impact on anemia.

A baseline survey of PRECONCEPT participants assessed micronutrient intake through a semi-quantitative food frequency questionnaire (P. H. Nguyen et al., 2014). Results from this survey suggest that a quarter of participants (24.8%) had insufficient dietary intake of iron, and approximately the same number (27.1%) had insufficient vitamin A intake. However, while interviewed participants perceived iron deficiency anemia as a serious threat to health during pregnancy, vitamin A deficiency was not recognized as a threat to either maternal or child health.

Similarly, the food consumption data suggest that B vitamin deficiencies are highly prevalent in this population, but there was little recognition of these as threats. An estimated two-thirds of study participants consumed insufficient vitamin B12. Along with B1 and B6, B12 supplements were used by some women on a curative basis to treat fatigue or weakness, but were perceived as a medical treatment, rather than a means of addressing deficiency. In addition, more than half of participants consumed inadequate folate, and 40% consumed inadequate vitamin B2; however, there was very low awareness of these nutrients among interviewed participants, and no perception of deficient status as having an impact on health.

Another key construct of the HBM is that behavior relies on defined cues to action.

Among PRECONCEPT participants, supplements are widely viewed as medicine, serving a curative purpose rather than a preventive one. Consequently, the cue to action to take supplements is when a woman experiences distinct symptoms such as dizziness, headaches, or weakness. If these symptoms are diagnosed as anemia by a health care provider, women will generally initiate iron supplementation. Depending on the provider's instructions and their own financial position, they may either continue taking iron indefinitely, or stop once their symptoms improve.

If anemia is not diagnosed, women may take vitamin C or certain B vitamins to treat their symptoms, whether on the advice of a health worker or pharmacist, other women, or advertisements. These vitamin supplements are taken on an exclusively curative basis: women take them until their symptoms improve, and then terminate use. The sole exception to this curative view of supplements is iron. In addition to the curative use described above, there is some appreciation for the preventive value of iron taken during pregnancy. Most women agree that all women should take some iron during pregnancy, regardless of whether or not they experience symptoms of anemia. As a result, there are two separate cues for action for iron supplementation: first, when a woman experiences symptoms of anemia (most commonly dizziness or headaches), and second, when a women knows that she is pregnant.

With the exception of prenatal iron, there is very low awareness of the benefits of preventive micronutrient supplementation. Supplements are considered medicine, and medicine is taken only when one becomes sick. Therefore, preventive supplementation is considered unnecessary: not harmful, but with no tangible benefits, and a waste of resources for women with limited financial resources. Because physical symptoms serve as the cue to action for most women, women with subclinical or asymptomatic deficiencies are unlikely to take supplements.

Preconception supplementation is similarly regarded as unnecessary. Most women recognize that iron requirements increase during pregnancy, necessitating supplementation, but are less concerned with pre-pregnancy nutritional status, due to low awareness of the consequences of entering pregnancy with nutrient deficiencies. Furthermore, most women do not perceive themselves to be at risk of entering pregnancy with poor nutrient status. In the absence of distinct symptoms, women consider themselves strong and healthy, and therefore having adequate nutrition. As a result, preconception nutrient deficiencies are perceived neither as a serious threat to health, nor as a relevant concern for most women.

Implications for future programs

Adherence among study participants is high, as may be reasonably expected from an efficacy trial with individual support and incentives for compliance. However, as the intervention moves from efficacy to effectiveness, initiation of supplement use will increasingly hinge on individual decision-making, which is strongly influenced by perceived threats and the valuation of supplements. Most interviewed participants did not plan to continue taking supplements after the study ended, with the exception of vitamin C and B vitamins on a curative basis, and iron during pregnancy.

Future efforts should prioritize increasing the valuation of 1) preventive supplementation and 2) supplementation of nutrients other than iron. Particular attention should go to increasing awareness of the importance of ensuring adequate folate, vitamin A, and B12 status before pregnancy. Awareness must also be raised regarding the importance of entering pregnancy with sufficient iron stores rather than relying solely on supplementation during pregnancy.

Health worker support will be critical to this effort. The widespread valuation of prenatal

iron supplementation is largely a result of anemia counseling and awareness-raising by CHC staff and Village Health Workers. Most women who had previous experience taking prenatal supplements did so on the recommendation of their doctor or VHW, and many said that they would take supplements in the future if they were advised to do so. Increasing knowledge of the importance of preconception micronutrient status among CHC staff and VHWs would improve the effectiveness of their consultations with WRA, and contribute to increased valuation of preconception MM supplementation.

Reducing barriers to adherence

Once supplement use is initiated, consistent adherence will require minimization of identified barriers. Many of the barriers identified by Galloway et al. do not appear to be relevant in this setting. Ninety percent of PRECONCEPT participants attended antenatal care during their last pregnancy, and 78 percent reported taking some prenatal IFA or MM supplements (P. Nguyen et al., 2012), which suggests that coverage and access issues were not significant barriers to adherence as found in in the countries included in the Galloway et al. study. There was no mention of the fear of delivering a large baby; to the contrary, a few women spoke positively about prenatal supplements helping to ensure strong, "chubby" babies.

As in the Galloway study, side effects were common, though not universal, and led a minority of women to discontinue supplement use. Evidence from previous supplementation interventions in Viet Nam and other countries suggests that some amount of attrition due to side effects is likely to be unavoidable. However, this can be minimized through support and reassurance from health workers. Most women are willing to tolerate side effects if they are temporary and relatively mild, and if they feel that the discomfort is outweighed by the benefits

of the supplements for themselves and their child.

The other significant barrier to adherence was forgetting. Many women found the weekly schedule difficult to remember, particularly if they had been advised that they must take the supplement at a specific time. Women who believed they must take the supplement within a strict window of time were likely to skip that week's tablet if they forgot.

Research on adherence to intermittent versus daily supplementation schedules among adult women has focused on prenatal iron supplementation. Most studies have found no significant difference in adherence between the two dosing schedules (Casanueva et al., 2006; Pena-Rosas et al., 2004); however, these studies are fairly short-term. The impact of a flexible dosing schedule on adherence may be greater for long-term supplementation regimens among non-pregnant women.

In addition, a defined cue to action should be established for weekly supplementation. Some PRECONCEPT participants developed their own individual-level cues, such as setting a weekly reminder alarm on their phone, or enlisting family members to remind them. Other suggested cues from participants and VHWs included automated mobile phone SMS reminders and announcements on community public address systems. To minimize the problem of forgetting, future programs should consider a flexible dosing schedule and supporting women to develop reminder strategies.

Social support

Support and counseling from VHWs and CHC staff had a positive influence on adherence among PRECONCEPT participants. However, most health workers are overburdened with work and limited in the time they can dedicate to counseling about supplementation.

Expansion of the supplementation program will therefore require alternative sources of support.

One alternative would be to establish social support mechanisms such as support groups for women of reproductive age. Such groups would give women the opportunity to share experiences, concerns, and advice, including strategies for managing side effects and effective cues for remembering the supplement schedule. Women could turn to each other for support and reassurance, rather than relying exclusively on their health workers. This approach also has the potential to increase initiation of supplementation, particularly among women who value experiential knowledge over scientific information received from health workers.

Micronutrient powders as an alternative to tablet supplements

One potential alternative to traditional tablet supplementation may be home fortification with multiple micronutrient powders (MNPs), which have been shown to be effective in reducing anemia and other deficiencies in children. The iron in MNPs is lipid-encapsulated, which aids digestion and reduces gastrointestinal side effects when prepared correctly (Suchdev, De-Regil Luz, Walleser, Vist, & Peña-Rosas, 2011). This reduction in side effects should have a positive effect on adherence.

Most of the research on multiple micronutrient powders has focused on children under 5 (Salam, Macphail, Das, & Bhutta, 2013). There have been several interventions promoting MNPs as a supplement among pregnant women, but to date, there are no published studies evaluating their impact on either maternal or child health outcomes (Suchdev et al., 2011). Due to this lack of evidence, the WHO does not currently recommend the use of MNPs as an alternative to traditional IFA supplementation during pregnancy (World Health Organization, 2011).

There is mixed evidence about whether current formulations of MNPs are sufficient to meet nutrient requirements during pregnancy. One small randomized trial among pregnant women observed lower iron absorption from a powdered iron-folate supplement compared to traditional IFA tablets (Hartman-Craven, Christofides, O'Connor, & Zlotkin, 2009). More recently, Choudhury et al. found that MNPs had a similar effect on hemoglobin status in pregnant women compared to IFA tablets (Choudhury, Aimone, Hyder, & Zlotkin, 2012). The authors suggested that iron absorption may be affected by the form of iron used in the MNPs, as well as the woman's hemoglobin status when initiating use.

There has been little research on adherence to MNPs among adult women. A randomized trial in Mexico found that pregnant women preferred IFA tablets to MNPs. Similar numbers of women from both treatment groups reported positive health effects as a result of the supplements, but women in the MNP group also citied unpleasant taste and gastrointestinal side effects, both of which may be due to incorrect preparation (Young, Blanco, Hernandez-Cordero, Pelto, & Neufeld, 2010).

However, an appropriately formulated MNP could be a viable alternative to tablet supplements among pre-pregnant women in Viet Nam. Furthermore, because MNPs are added to food, they may have higher acceptability among women who view tablet supplements as medicine and thus taken only on a curative basis. As discussed earlier, fortified "pregnancy milk" does not fall within the medicinal view of supplements, but is instead considered a way to increase dietary intake of nutrients. Promotion of MNPs in Viet Nam could emphasize the dietary angle, marketing them as a healthful and inexpensive way to improve the nutrients in food and nutritional status before pregnancy.

Strengths and limitations

This study is the first to examine influences on micronutrient supplement adherence among non-pregnant women of reproductive age in a developing country. As a sub-study of a long-term trial operating in multiple sites, the researchers had the opportunity to assess influences on adherence at various stages of participation, and across a range of demographics and nutritional statuses.

Certain characteristics of the PRECONCEPT participants may limit transferability of these results to the broader population. Their agreement to participate in the study may indicate a greater concern for their health or the health of their child, greater family support, or greater trust in the VHWs who recruited them. Conversely, the study only accepted women who had not recently taken IFA or MM supplements, so these results may not reflect the opinions of women who place greater value on supplementation outside of pregnancy.

Furthermore, PRECONCEPT is an efficacy trial with relatively high individual support, monitoring, and incentives for compliance. The in-depth interviews attempted to assess influences on past and hypothetical future use as well as participation in PRECONCEPT; however, there may still be some dissimilarity between the factors influencing adherence among study participants and the priorities of the general population.

Conclusions and recommendations for research and programming

The results from this study suggest that supplement adherence among WRA in Viet Nam is double-pronged. Initiation of supplement use requires recognition of the health consequences of micronutrient deficiencies and perceived personal susceptibility to those deficiencies, while maintaining consistent use requires a defined cue to action and minimization of attrition due to

side effects. Increased awareness of micronutrient deficiencies among CHC staff and Village Health Workers may improve women's valuation of micronutrient supplements. Once supplement use is initiated, functional support from health workers and the cultivation of social support mechanisms can maximize adherence.

To date, there has been little research on supplement acceptability and adherence among non-pregnant women of reproductive age. Themes from the present study indicate multiple areas for future research. Alternative supplementation strategies such as flexible dosing or micronutrient powders merit further investigation, as they may have the potential to improve acceptability and adherence among non-pregnant women. Research should investigate not only the efficacy of these treatment methods, but also acceptability and influence on adherence among non-pregnant women. In addition, peer support systems warrant further evaluation as a method of encouraging adherence while minimizing the burden on health workers.

The results of this study also yield concrete lessons to be applied to future supplementation programs. Prenatal iron supplementation is an established and relatively well-accepted practice in Thai Nguyen, with most women recognizing some health benefit to themselves and their children. However, women place little value on supplementation outside of pregnancy, aside from limited use of iron and certain vitamins on a curative basis. Future programs must prioritize increasing demand for supplements among non-pregnant women. Accomplishing this will require two components. First, awareness should be raised around the health consequences of micronutrient deficiencies other than iron, particularly "invisible" deficiencies which may not have a conspicuous effect on a woman's health, as well as the benefits of using a multiple micronutrient supplement in place of iron alone. Second, preventive supplementation should be promoted among women who are considering having children in the

near future, with an emphasis on the importance of entering pregnancy with adequate nutrient status. Commune Health Center staff and Village Health Workers should be primary targets of this campaign, as their advice is highly valued by women in their communities. Increasing demand for supplements will improve the effectiveness of future programs, and maximize health gains among mothers and children in northern Viet Nam.

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