Preventive Weekly Iron-Folic Acid Supplementation Can Improve Iron Status of Reproductive Age Women: Experience in Cambodia, the Philippines, and Vietnam

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Kanal, Koum; Busch-Hallen, Jennifer; Cavalli-Sforza, Tommaso; Crape, Byron; Smitasiri, Suttilak; The Cambodian Weekly Iron-Folic Acid Program Team,
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Foreword

Iron deficiency and its consequent anemia have plagued mankind for centuries and remain a public health problem of immense magnitude even today. The causes and consequences are well studied. Theoretically, treatment and prevention are straightforward: increase the absorbable iron available, either in the diet through eating iron-rich and/or iron-fortified foods or in the form of iron supplements. Within the medical system, a daily iron supplement, usually dispensed together with folic acid, is the common route for relieving deficiency in women of reproductive age, particularly when pregnant. Adherence to the daily regime, however, is frequently poor for a variety of reasons, including the unpleasant symptoms of nausea, black feces, and a medicinal iron aftertaste, as well as defects in delivery through the health system, especially in less-developed countries. Over a decade ago, Dr. Fernando E. Viteri of the Department of Nutritional Sciences at the University of California, Berkeley, suggested that weekly dosing with iron in synchrony with turnover of intestinal mucosal cells might be a more efficacious preventive approach in public health programs, result in fewer side effects, and be operationally easier to manage at the community level.

The first master protocol to conduct efficacy studies on weekly iron-folic acid supplementation was prepared by Dr. Viteri along with Drs. K. Bailey and N.S. Scrimshaw. The protocol was shared by Dr. Scrimshaw at the Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO) International Conference on Nutrition in Rome in December 1992. Its aim was to determine the efficacy of the weekly approach for the prevention of anemia under supervised conditions. If possible, the studies would compare the efficacy of weekly supplements with that of daily supplements. This led to investigators undertaking comparable projects in several countries among preschoolers, primary and secondary school children, and pregnant women.

In May 1996, the findings of several weekly iron-folic acid supplementation efficacy studies were reviewed at a meeting of researchers on weekly iron supplementation organized by Dr. Viteri, where the available finished and ongoing studies were presented. The evidence presented and available at that time was suggestive, but inconclusive, in the direction of similar efficacy between weekly and daily iron and iron-folic acid supplementation schemes, with some advantages of the former shown in terms of operation, adherence, and lower side effects. The key conclusion of that meeting was that more efficacy and effectiveness trials were needed to provide solid evidence of the value of long-term weekly supplementation in preventing iron deficiency and anemia in vulnerable groups.

In 1999, Beaton and McCabe at the University of Toronto, Canada reviewed available data on the efficacy of weekly and daily iron supplementation and, in a report to their supporters (Micronutrient Initiative and International Development Research Canada), concluded that: 1) both weekly and daily iron are efficacious; 2) supervision is important to ensure effectiveness of both delivery schemes; 3) improving compliance is essential to increase effectiveness of all iron supplementation programs in developing countries; 4) weekly iron may be disadvantageous during pregnancy and when the prevalence of anemia is very high; and 5) other causes of anemia not related to iron deficiency should be addressed, as they can represent a very substantial portion of causes of anemia in some countries.

Subsequently, additional positive results were reported from efficacy studies using weekly supplements of iron or iron-folic acid that were conducted in school-age children, adolescents, and pregnant women. Based on these encouraging results, the WHO Regional Office for the Western Pacific (WPRO) supported pilot projects in the Philippines and Vietnam initially (and later in Cambodia) to determine the effectiveness of the new weekly iron-folic acid supplementation approach under unsupervised program conditions. This supplement of Nutrition Reviews reports the results of these studies, as well as background information on the rationale for weekly supplementation and on essential elements to consider in the design of sustainable iron intervention programs.

The paper by Viteri and Berger (page S65) reviews the rationale for the weekly iron-folic acid regime and its application in the maintenance of iron status and preven-
tion of gestational anemia, describes some of the early efficacy studies, and reviews the implications for prevention of anemia throughout the reproductive years of a woman by establishing and maintaining adequate body stores.

The studies in the three Asian countries reviewed in this supplement, Vietnam, the Philippines, and Cambodia, are among the first to evaluate the effectiveness of the weekly ingestion of an iron-folic acid tablet by women of reproductive age sold and dispensed in community settings by community workers and accompanied by an intensive social marketing program. The paper by Cavalli-Sforza (page S77) details the master protocol and implementation plan for these studies. The principles of the social marketing program to guide these studies are described in the paper by Smitasiri and Solon (page S81). The cultural adaptations made and the results of knowledge, attitudes, and practices resulting from the social marketing/community mobilization effort in the Vietnam, Philippines, and Cambodia projects are described in the individual papers by Khan et al. (page S87), Paulino et al. (page S109), and Kanal et al. (page S126), respectively. In all three country’s projects, there was an impact on reducing anemia or improving iron status. The magnitude of the impact among women of reproductive age in different settings is described in the papers by Berger et al. conducted in rural Vietnam (page S95), Angeles-Agdeppa et al. in semi-urban areas of the Philippines (page S116), and Crape et al. in the factories, schools, and rural areas of Cambodia (page S134). The synergistic effect of including multiple public health interventions, in addition to weekly iron-folic acid supplements, on anemia control and health is reported in the paper by Longfils et al. (page S139), which was carried out among primary school children in Cambodia. Garcia et al. (page S146) provide industry’s perspective on the promotion and marketing of iron-folic acid supplements for weekly consumption, and lessons learned to guide the development of advocacy programs to be implemented on a national scale in the future.

Lastly, Dr. Cavalli-Sforza et al. (page S147) provide a summary of the main conclusions and lessons learned from the three studies, future plans for the expansion of the weekly iron-folic acid supplementation program in each country, and how the project contributes to achievement of the UN’s Millennium Development Goals.

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Importance of Pre-Pregnancy and Pregnancy Iron Status: Can Long-Term Weekly Preventive Iron and Folic Acid Supplementation Achieve Desirable and Safe Status?

Fernando E. Viteri and Jacques Berger

Most women worldwide enter pregnancy without adequate iron reserves or are already iron deficient. Estimates of iron needs during pregnancy are markedly reduced when iron reserves are available. The needs of absorbed iron to correct mild to moderate anemia in the last two trimesters are estimated. Pre-pregnancy and prenatal weekly supplementation can improve iron reserves effectively and safely, preventing excess iron and favoring better pregnancy outcomes. We explain how the weekly supplementation idea was developed, why current hemoglobin norms may be inadequately high (especially in pregnancy), and why excess iron as recommended by many agencies for developing populations can be undesirable.

Key words: anemia, iron status, women of reproductive age, iron deficiency.

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IRON STATUS OF WOMEN OF REPRODUCTIVE AGE

Women of reproductive age (WRA) are at risk of developing iron deficiency, which if continued for several months can progress to anemia. The World Health Organization (WHO) estimates that 43% of all non-pregnant women 15 to 59 years of age who live in the developing world have anemia; during pregnancy, this prevalence increases to 56%. These percentages translate to 535 and 54 million women, respectively, 41% of whom reside in southeast Asia. Mason et al. gave prevalence percentages for women 15 to 49 years of age for the year 1990 as 26.5% for non-pregnant women and 32.2% for pregnant women; for 2000, the numbers were 31% for non-pregnant women and 30.5% for pregnant women.

WRA and pregnant women are also at risk of anemia in many industrialized countries. Representative data from the United States indicate that 5% of non-pregnant women are anemic, that the prevalence of anemia increases to 17% among pregnant women, and that the prevalence is as high as 33% among pregnant women of low socioeconomic groups. Furthermore, iron deficiency among white, non-pregnant women in the United States is reported to be 10%, while it is 19% among African Americans and 22% among Mexican Americans. It is distressing that prevalence rates have increased by 2% to 4% from the period 1984–1988 to the period 1999–2000, despite fortification of flour with iron.

In their study at the University of California at Berkeley, Viteri et al. reported that 9% of non-pregnant female students presented with anemia and responded to iron administration, while 20% presented with depleted iron stores as defined by serum ferritin under 15 μg/L. The proportion of iron deficiency to anemia in the student population was 2.2 to 1, indicating that for each woman with iron deficiency anemia, there were between 2 and 2.5 who did not fit the criteria for being classified as anemic. A similar ratio of iron deficiency to iron deficiency anemia has been reported in many studies accepted by WHO and the US Centers for Disease Control and Prevention (CDC). Unfortunately, data about women in the developing world that would allow estimates of the magnitude of iron deficiency anemia independent from anemia due to other causes are lacking. However, most studies that have looked into these conditions confirm that more than 80% of cases of anemia in women, especially during pregnancy, are associated with or have an important iron deficiency component.

Ideally, to meet iron needs during gestation, women should have 300 mg or more of iron reserves prior to conception. Based on the information available, many
women, even in the industrial world, enter pregnancy with little or no iron to mobilize during the second half of pregnancy, when the requirement for that essential mineral increases significantly.\textsuperscript{11} Fifty-six percent of non-pregnant US WRA surveyed in the National Health and Nutrition Examination Survey in 1988–1994 (NHANES III) had less than 300 mg of iron reserves based on the serum transferrin receptor (TfR)/serum ferritin ratio for determining iron stores\textsuperscript{12} (Table 1). A longitudinal study of non-anemic Mexican women (who received prenatal care but no iron supplementation unless they developed anemia) followed through pregnancy starting at gestational week 10 showed that the incidence of anemia as pregnancy progressed became higher (nearly five times greater near term) among those with serum ferritin levels under 20 \(\mu g/L\) compared with those over 20 \(\mu g/L\) prior to conception.\textsuperscript{13}

In China, birth weight and preconceptional hemoglobin (Hb) were shown to be directly correlated.\textsuperscript{14} There are few accurate data on the distribution of estimated iron reserves in women in developing countries. In a study comparing serum ferritin levels in rural and urban Guatemalan non-pregnant women,\textsuperscript{15} the effects of location and hookworm infestation were very evident in relationship to iron reserves (Table 1).

Most women throughout the world enter pregnancy with less than desirable iron reserves, many with depleted iron stores, and, by current criteria, with iron deficiency even when they are not anemic.

PRE-PREGNANCY IRON STATUS CAN BE IMPROVED WHERE IDEAL DIETS ARE UNAVAILABLE

Iron Fortification

Iron stores estimated by a proposed algorithm that considers several indicators of iron status\textsuperscript{11} were obtained during a 3-year iron fortification study in the total population of non-pregnant women living in two coastal (tropical) and two highland Guatemalan towns.\textsuperscript{16} The two coastal populations and one of the highland populations received iron-fortified sugar (mean intake 4 mg/d of iron) from NaFeEDTA, while the remaining highland community received unfortified sugar and served as a control. Table 2 presents the distributions of iron stores for the women in each community before and after 3 years of fortification. The effectiveness in improving iron status above 300 mg in the communities receiving iron-fortified sugar with NaFeEDTA is evident. Even though the increase occurred mostly in the first year, by the third year, iron reserves were still slowly increasing (by about 40 mg/year).

A recent randomized, controlled study\textsuperscript{17} from Vietnam among moderately anemic women reported changes in iron stores and correction of iron-deficiency anemia after 6 months of consuming fish sauce fortified with NaFeEDTA providing 10 mg of iron daily. At baseline, 70% of the anemic women were iron deficient and had mean iron stores of about 15 mg. At the end of the study, mean iron stores were about 186 mg, the highest value attained being about 250 mg.

Another study in Vietnam evaluated the impact of uncontrolled consumption of NaFeEDTA-fortified fish sauce (providing 0.5 mL iron/mL fish sauce) provided free of charge in a sample of Vietnamese women, 25% of whom were anemic. After 12 months of intervention, less than 5.5% of the women had iron deficiency based on ferritin concentrations. This indicator of iron reserves had increased an average of 70 \(\mu g/L\), translating to median iron stores of 350 mg.\textsuperscript{18}

These studies demonstrate the effectiveness of food fortification by the addition of iron in a safe compound with good iron bioavailability when added to diets that do not favor iron absorption, even in women with mild hookworm infestation.

Preventive Supplementation

Centralized industrial production of fortified foods may not reach all populations, particularly the target populations most vulnerable to iron deficiency: infants, chil-

\begin{table}[h]
\centering
\begin{tabular}{lcccccc}
\hline
Iron Stores & \multicolumn{6}{c}{mg} \\
\hline
Population & \(\leq0\) & \(50\) & \(51-100\) & \(101-150\) & \(151-200\) & \(201-300\) & \(\geq300\) \\
\hline
United States & 12% & 2% & 8% & 9% & 8% & 17% & 44% \\
Guatemala urban highlands (no hookworm) & 39% & 19% & 15% & 12% & 4% & 11% & 0% \\
Guatemala rural highlands (no hookworm) & 55% & 17% & 14% & 7% & 6% & 1% & 0% \\
Guatemala rural lowlands (hookworm positive) & 67% & 5% & 4% & 10% & 6% & 8% & 0% \\
\hline
\end{tabular}
\caption{Percent Distribution of Women of Reproductive Age by Iron Stores in the United States\textsuperscript{13} and in Different Locations in Guatemala\textsuperscript{14a}}
\end{table}

\textsuperscript{1}Iron stores in the Guatemalan population were calculated only on the basis of serum ferritin values considering no reserves if plasma ferritin fell below 15 \(\mu g/L\) (11) and 8 mg of iron stores/\(\mu g/L\) of ferritin if above 15 \(\mu g/L\). Subjects were healthy, nulliparous women not using any fertility control methods and having normal serum folates.

\textsuperscript{2}Reserves lower than 0 mean iron deficiency.
dren, and WRA, especially those who are pregnant or prone to become pregnant. Several alternative approaches have demonstrated effectiveness: preventive weekly iron and folic acid supplementation, food complements such as Sprinkles, which contain iron and other essential nutrients and are added to foods at home; and supplements taken independently of food, such as foodlets. To our knowledge, these last approaches have been evaluated only in infants and children and should not be considered here. However, we look forward to future studies with these same approaches directed at WRA. Among female college students in the United States, anemia was corrected in less than 3 months and iron stores improved after 7 months of weekly supplementation with 60 mg of iron and 250 μg of folic acid.

Several studies based on weekly iron-folic acid supplementation in non-pregnant women, as well as other studies presented in this supplement, have indicated that iron reserves can be improved and anemia can be markedly reduced or totally corrected by this approach, particularly if the intervention is long term. Moreover, the superiority of weekly supplementation has been demonstrated in terms of efficiency and safety compared with administering daily iron supplements for 2 to 4 months per year, as has been suggested previously. The objective of preventive weekly supplementation to improve iron reserves, reduce anemia, and reduce the risk of neural tube defects from folate deficiency is lost if iron-folic acid supplements are only administered in periodic courses of 4 months duration aimed at reducing anemia; this approach then becomes therapeutic rather than preventive.

The importance of adequate iron nutrition throughout life for optimal function is well known, but the possible benefits of pre-pregnancy iron reserves on the course of pregnancy and its outcome is documented by only a few studies. A study by Scholl et al. illustrates the importance of taking multivitamin/mineral supplements containing iron prior to pregnancy and in the first trimester, which results in the reduction of low birth weight and very preterm deliveries and confirms the preventive effect on those outcomes by eliminating iron deficiency anemia early in pregnancy.

### Table 2. Percent Distribution of Women of Reproductive Age by Iron Stores in Guatemala Before and After 3 Years of Consuming Iron-Fortified Sugar

<table>
<thead>
<tr>
<th>Population</th>
<th>Iron Stores (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤0*</td>
</tr>
<tr>
<td>Rural (severe hookworm infection)</td>
<td>61%/46%</td>
</tr>
<tr>
<td>Rural (mild hookworm infection)</td>
<td>51%/40%</td>
</tr>
<tr>
<td>Rural (no hookworm infection)</td>
<td>48%/38%</td>
</tr>
<tr>
<td>Rural (no hookworm infection) controls</td>
<td>43%/47%</td>
</tr>
</tbody>
</table>

*Stores lower than 0 mean iron deficiency.
†Mean iron stores (mg) before/after 3 years.

### BRIEF HISTORY OF WEEKLY SUPPLEMENTATION WITH IRON AND FOLIC ACID

The idea of weekly iron supplementation was conceived as a preventive rather than a therapeutic measure for iron deficiency and its progression to anemia. More than 40 years of iron supplementation programs aimed at controlling gestational anemia have been ineffective. Therefore, the opportunity was ripe for exploring new possibilities for iron supplementation with a preventive approach. This approach considers the capacity of fresh intestinal cells to absorb iron and deliver it to transferrin in response to internal signals reflecting total body iron status and homeostatic need. Questions arose on the logic of daily oral administration of iron doses that far exceed the capacity of an individual to assimilate (absorb, utilize, and metabolize) iron safely. Is it inconsequential to maintain the intestinal mucosa and intestinal lumen with large amounts of unabsorbed “reactive” iron? For many years, national and international agencies have proposed high daily doses of iron (60, 120, 240, and even 300 mg) for populations in whom the prevalence of gestational iron deficiency anemia is above 40%. Estimates of the level of iron assimilated when supplemental iron doses above requirements are ingested for several days or weeks vary widely, from 2 to 3 mg/d to as high as 20 mg/d or even higher, depending on the dose and the total body iron status. In general, a sustained percentage of assimilated iron is less than 10% and bone marrow activity rarely increases more than three times the normal turnover.

Studies in rats administered daily the equivalent of 120 mg of iron given to humans demonstrated that supplemental iron absorption by iron-deficient rats declined very rapidly, from 20% to 5%–6%, resulting in their intestinal contents and mucosa becoming overloaded with iron. Daily supplemented iron-deficient rats also appeared to have impaired regulation of iron metabolism, causing significantly higher liver iron than normal, possibly by mass-effect-induced iron overload. This undesirable condition was associated with severe oxidative stress, which was most evident in previously iron-deficient rats, but also manifested...
in previously iron-normal, iron-supplemented rats. In humans, elevation of “free” reactive iron in plasma and high ethane production occurred after ingestion of daily iron at recommended supplementary doses. The apparent impaired regulation of iron metabolism and increased oxidative stress in previously iron-deficient rats strengthens the importance of preventing iron deficiency rather than correcting it once present.

The non-physiological conditions that occur when the recommended doses of daily iron supplements are given to already iron-deficient or even to normal animals and humans should be avoided. One option is to reduce the daily dose to levels that would be mostly absorbed and thus prevent the constant physiological disruption of the intestinal mucosa and metabolism. Another option could be to administer iron only in synchrony with the intestinal mucosal turnover that occurs every 3 days in the rat and every 5 to 6 days in the human.

The second option, that of presenting iron only to new mucosal cells, seemed most attractive for the reasons stated above, particularly if the objective was to prevent iron deficiency. The model tested in rats demonstrated that iron assimilation declined more slowly and was more than 2.5 times more efficient than when the same dose was administered daily. Thus, the concept of weekly iron-folic acid supplementation as a public health approach to prevent iron deficiency and anemia was presented at the 1993 World Health Organization (WHO)/UNICEF/United Nations University (UNU) meeting, the report of which was published in 2001. If effective, weekly supplementation would also have additional operational advantages, including the need to distribute one-seventh the number of iron tablets, making the program easier for communities to manage. Furthermore, if side effects occurred at similar rates as after taking each daily dose, they would only occur once weekly rather than daily.

In the last decade, many studies in different populations have confirmed that a weekly dose of iron could be effectively used for the prevention of iron deficiency in populations at risk, including during gestation. Even in short-term studies, this approach improves iron reserves and corrects mild to moderate anemia. Unfortunately, in many cases, the therapeutic concept of correction of anemia has prevailed in the experimental designs comparing daily and weekly iron supplementation. However, even under these “unfavorable” conditions, the overwhelming majority of studies in different parts of the world with populations of different ages and sex have shown that the weekly approach is efficacious and effective. The main reason that iron absorption studies in humans are conflicting is because they have been short term and conducted in essentially iron-normal populations. Longer-term absorption in iron-deficient populations demonstrates a more efficient, sustained absorption than from weekly supplementation.

### Table 3. Iron Needs (mg) during Pregnancy in the Absence and Presence of Pre-Pregnancy Iron Reserves and Gestational Anemia

<table>
<thead>
<tr>
<th></th>
<th>NO</th>
<th>YES (60 mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron Supplemented</td>
<td>Basal body loss</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>Fetal accumulation</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td>Placenta</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Maternal Hb and tissue increments</td>
<td>322</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>888</td>
</tr>
<tr>
<td></td>
<td>Dietary Contribution†</td>
<td>342</td>
</tr>
<tr>
<td>Iron Deficit (mostly in the last two trimesters)‖</td>
<td>No Iron Reserves</td>
<td>546 (888 – 322)</td>
</tr>
<tr>
<td></td>
<td>Using 300 mg Iron Reserves</td>
<td>246 (888 – 324 – 300)</td>
</tr>
</tbody>
</table>

*Iron supplemented increment in hemoglobin (Hb)†Delivery blood loss not considered
‡Assuming 0.8 mg and 1.5 mg of absorbed iron in first and last two trimesters, respectively
§Assuming a conservative 40% reduction in food iron absorption in the supplemented group
¶60 mg of iron daily should not allow an iron deficit, and only 7% of the 60 mg supplement needs to be absorbed (966 mg – 205 mg) = 761 mg/(60 mg × 180 days = 10,800 mg) = 0.07, or 7%, under the above assumptions
¶Note that if more food iron is absorbed late in pregnancy, less iron absorbed from the supplements is needed

### THE POSSIBLE IMPACT OF PRE-PREGNANCY IRON NUTRITION ON IRON STATUS DURING PREGNANCY

To illustrate the possible impact of two variables (pre-pregnancy iron reserves and iron supplementation) on the needs for absorbed iron to prevent iron deficiency during pregnancy, we constructed estimates of iron demands (in total milligrams) for well-nourished, non-
anemic women (Table 3). These estimates assume an absorption of 0.8 mg of dietary iron in the first trimester of pregnancy and 1.5 mg in the last two trimesters,\textsuperscript{42} either utilizing no iron from stores or using all of 300 mg of pre-pregnancy iron reserves. The milligrams of iron needed to be utilized, in the absence of anemia, from the intake of 60 mg of iron daily as a supplement during the last two gestational trimesters is also estimated. Table 4 expresses the estimates of iron deficits if mild to moderate anemia were present near term, as well as the amounts of iron needed to be absorbed during the last two trimesters of pregnancy to bring Hb concentrations to a non-anemic condition (110 g/L).

An adequate response to absorbed iron produces an Hb increment of 10 g/L per month. Therefore, for an Hb of 100 g/L, it would take 1 month to bring the Hb level to 110 g/L and 2 months to bring the Hb of 90 g/L to the desired 110 g/L level. This amounts to 7.1 mg/d for 30 days, for an initial Hb of 100 g/L and 7.0 mg/d for 60 days for an initial Hb of 90 g/L. The amounts of iron needed to be absorbed in the last 180 days (two trimesters) under these assumptions is:

- For an Hb of 100 g/L: 7.1 mg/d + 3.0 mg/d = 10.1 mg/d for 1 month (to replenish Hb deficit and satisfy basal needs) and 3.0 mg/d for 1 month (to satisfy basal needs), for a total of 483 mg.
- For an Hb of 90 g/L: 7.0 mg/d + 3.0 mg/d = 10.0 mg/d for 2 months (to replenish Hb deficit and satisfy basal needs), for a total of 690 mg.

These amounts of iron needed to be absorbed in the “anemia recovery” period constitute 16.8% of a 60 mg daily supplement for 1 month if Hb was 100 g/L, or 2 months if Hb was 90 g/L, respectively, under the assumed conditions. The times for recovery would vary if iron absorption from food and supplements were higher or lower.

Weekly supplementation with 120 mg of iron would cover the daily 3 mg deficit during the second and third trimesters (in the absence of iron reserves) if 17.4% of it were absorbed. It would take longer than 1 or 2 months to replenish the deficit in the case of anemia with Hb deficits of 10 and 20 g/L (Hb of 100 and 90 g/L, respectively), even if food iron absorption increased above the levels of 0.8 and 1.5 mg assumed in the calculations shown in Tables 3 and 4 and if the supplemental iron absorption values were also higher.

These calculations reveal the following:

1. Adequate pre-pregnancy iron reserves can be achieved by an adequate diet, food fortification, or preventive iron supplementation (low daily doses or weekly doses). Ideally, the last two types of intervention would include folate and, if needed, other nutrients such as vitamin A and zinc.

2. Correction of anemia during pregnancy is difficult and should therefore be prevented.

### Table 4. Hematologic Parameters for a 60-kg Woman Pre-Pregnancy and Near Term when Non-Anemic and Near Term with Mild to Moderate Anemic Conditions (90 or 100 g Hb/L)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-Pregnancy Non-Anemic</th>
<th>Ideal Conditions</th>
<th>Minimal Non-Anemic</th>
<th>Mild to Moderate Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total blood volume (TBV)</td>
<td>3645 mL ‡</td>
<td>4964 mL</td>
<td>4,964 mL</td>
<td></td>
</tr>
<tr>
<td>Total erythrocyte mass (TEM)</td>
<td>1677 mL ‡</td>
<td>2012 mL §</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total plasma volume (TPV)</td>
<td>1968 mL ‡</td>
<td>2952 mL §</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hemoglobin mass (THbM)</td>
<td>466 g ‡</td>
<td>559 g</td>
<td>499 g</td>
<td>453 g</td>
</tr>
<tr>
<td>Hemoglobin (Hb)</td>
<td>140 g/L</td>
<td>123 g/L</td>
<td>110 g/L</td>
<td>1540 mg</td>
</tr>
<tr>
<td>Total Hb iron*</td>
<td>1584 mg</td>
<td>1901 mg</td>
<td>1697 mg</td>
<td>1389 mg</td>
</tr>
<tr>
<td>Iron deficit</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>157 mg</td>
</tr>
<tr>
<td>Absorbed iron needed to correct deficit\textsuperscript{†}</td>
<td>196 mg</td>
<td>385 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[THbM \times 3.4 \text{ mg iron/g}\]

\[\text{‡TBV} = 60.75 \text{ mL/g}^{47}; \text{TEM} = \text{TBV} \times 46\% \text{ (packed cell volume); TPV} = 54\% \times \text{TBV}; \text{THbM} = \text{TEM} \times 27.8 \text{ (mean corpuscular hemoglobin concentration)}\]

\[\text{§TEM is increased 20% from pre-pregnancy and TPV is increased by 50% from pre-pregnancy}^{48}\]

\[\text{†Assume 80% incorporation of absorbed iron into Hb}^{45}\]
3. Weekly iron supplementation and its possible anemia-corrective capacity is valuable if sustained and started early in pregnancy. One caveat to the calculations in Tables 3 and 4 may be the need to correct “anemia” of the magnitude considered in those tables, based on studies indicating that very adequate pregnancy outcomes occur when Hb is above 90 to 100 g/L. Therefore, there is concern that the cutoff levels for gestational anemia proposed by the CDC and adopted by WHO might be too high, as discussed below.

DEFINITIONS OF ANEMIA AND IRON DEFICIENCY AND THEIR CONSEQUENCES

Anemia can have two definitions: one from a public health perspective and the other from a functional perspective. The public health definition of anemia has been based on cutoff points derived from the mean and standard deviations of Hb values determined from four studies (three of them with less than 25 women) in healthy, iron-sufficient, northern-European pregnant women receiving between 100 and 200 mg of iron as a daily supplement. CDC suggests the cutoff point at the fifth centile. WHO adopted the CDC Hb values and defined anemia as “when individual Hb levels are below two standard deviations of the distribution mean for Hb in an otherwise normal population of the same gender and age who are living at the same altitude.” This means that about 5% and 2.5% of a “normal” population would be expected to be classified as anemic depending on the cutoff chosen.

The biological and laboratory variability of Hb level adds to the uncertainty of cutoff points that misclassify more in the “anemic” category than in the “normal” category, because there are usually more subjects just above the cutoff point than just below it. Under field conditions, the standard deviation between Hb determinations must be even higher than in laboratory studies. This misclassification must also be taken into consideration in evaluating the effect of any intervention based on cutoff points. Therefore, the best method for evaluating the effectiveness of interventions is the change in Hb concentrations. In the case of pregnancy outcomes, a few detailed studies on the impact of iron deficiency and anemia show that the best outcomes in terms of the characteristics of newborns occur in women who are classified as “anemic” in the third trimester or at term by accepted cutoff levels.

The suggested CDC/WHO norms for Hb levels in pregnancy need revision. A careful analysis of the basis for such norms, based on only four studies with a small number of women of special characteristics, brings out the possibility that the cutoff points for the diagnosis of anemia are too high. A serious attempt to review such norms in a large sample of normal pregnant women must be undertaken. The bases for the derivation of the current norms are rather tenuous for the following reasons:

- Of the four studies mentioned, two from Sweden and one each from the UK and Finland, the first three included only 16, 21, and 24 cases, and one that consisted of three different sub-studies, each including 91, 103, and 106 women. The four studies have the virtue of being longitudinal.
- All of the women in these studies received at least 147 daily iron supplements containing from 113 to 200 mg (a total of 16,611 to 29,400 mg!), even though they were well-nourished. There is ample evidence of the development of hemoconcentration with more than 45 daily doses of 60 mg of iron (a total of 2700 mg), as discussed below.
- No analyses of the risk of hemoconcentration were described in the studies selected for derivation of the norms. Based on the mean and standard deviation of the published data, Hb concentration exceeded 130 g/L as early as in the 32nd gestational week and by the 36th week in every study. High Hb carries maternal and perinatal risks, as discussed below.
- The best outcome conditions (birth weight, delivery time, and maternal health) have been reported by other studies to occur when Hb at term is between 95 and 125 g/L. Only one of the studies from which the norms were derived gave means and standard deviations of newborn weights. Interestingly, the birth weight in the iron-supplemented group tended to be lower than in the “no therapy” group.

The implications of a norm with a fictitiously iron-induced high Hb can be serious when establishing the diagnosis of anemia and its prevalence in populations and in suggesting control measures for gestational iron deficiency and anemia.

The functional definition of anemia, as its concept implies, is based on impairment of functions due to low Hb concentrations. In the case of pregnancy outcomes, a few detailed studies on the impact of iron deficiency and anemia show that the best outcomes in terms of the characteristics of newborns occur in women who are classified as “anemic” in the third trimester or at term by accepted cutoff levels.

The diagnosis of anemia during the second and third trimester of pregnancy is the object of continuous debate because of the normal hemodilution taking place during gestation, and because pregnancy outcomes appear not to be related to Hb levels in the mild to moderate anemia range. A more consistent finding is the association of low Hb values during the first half of pregnancy with low birth weight and preterm delivery, while anemia in the third trimester does not influence the perinatal events unless it is severe. Scholl et al. clarified that the
association between anemia in general and iron deficiency anemia with preterm delivery was due predominantly to the latter.

An obstacle to many of the studies on gestational iron deficiency is that techniques available for diagnosing iron deficiency are imprecise, given that: a) serum ferritin and transferrin saturation, and even bone-marrow iron, decrease over the course of pregnancy even among women receiving high daily iron doses\(^55\); b) free erythrocyte protoporphyrins and serum ferritin increase with any inflammatory process such as vaginosis and chorioamnionitis, which are common in pregnancy; and c) reports of levels of serum transferrin receptors vary: some indicate a progressive increase in the course of pregnancy even in the absence of iron deficiency\(^74\) and others report them as stable\(^25\) with increased erythropoietic activity. The proposed method for estimating body iron based on the ratio of transferrin receptors to ferritin\(^12\) that appears to work well in discriminating iron-deficient women from non-iron-deficient women in non-pregnant adult populations and in evaluating the impact of interventions in these population groups may not be discriminating in pregnancy. Results of the TfR/serum ferritin ratio in the non-pregnant woman population from NHANES III reflect two distributions of body iron: one for non-iron-deficient women and one for iron-deficient women. These populations overlap, strengthening the preference of a probabilistic approach based on mixed-distribution analysis over cutoff points.\(^12,67\)

When the TfR/serum ferritin ratio method is applied to pregnant women (as exemplified by an analysis of data from Jamaica\(^12\)), the cumulative frequency distribution represents a single Gaussian-distributed population, with half the women with tissue iron deficiency and a range of body iron stores for women weighing 55 kg of 715 mg (from 275 mg to ~ 440 mg). In the range of body iron deficit (negative iron stores), Hb could be as low as 37 g/L below the mean of 118 g/L for week 29 of pregnancy (118 - 37 = Hb 81 g/L). Does the single Gaussian distribution indicate that an Hb of 81 g/L is normal in pregnancy? This seems improbable. Does this mean that "iron-deficient" pregnant women do not constitute a different population from "iron-sufficient" pregnant women? Obviously, more research based on functional outcomes is needed.

In summary, the diagnosis of iron deficiency in pregnancy, even by new methods, is not totally reliable. A retrospective view of iron status 4 or more weeks in the postpartum period does not provide data on iron status during the different stages of pregnancy and is affected by blood loss during delivery. The diagnosis of "true" anemia and of iron deficiency in pregnancy thus poses serious problems except when they are severe, which is rare in nutritional iron deficiency. Severe cases are usually complicated by a combination of causes (blood loss, infections, malaria, genetic disorders, etc.).

ARE THERE BENEFITS OF IRON SUPPLEMENTATION DURING PREGNANCY?

Iron supplementation or treatment of mild to moderately anemic pregnant women has proven beneficial in terms of iron status of infants at 3, 6, and 12 months of age, even when supplementation was begun late in pregnancy.\(^76-78\)

Maternal and perinatal outcomes due to iron supplementation are less clear. A comprehensive review\(^79\) on the effect of anemia and iron supplementation on pregnancy outcomes indicates that most studies have design flaws. Nonetheless, grouping studies by critical variables (with some leniency on flaws) in order to determine group tendencies on birth weight and preterm delivery in relation to anemia and iron supplementation shows that in developed countries: a) only non-anemic women entered the study; b) most received over 60 mg of iron/d for a variable time during pregnancy; and c) there were no benefits in terms of birth weight or on duration of pregnancy (except in two studies: one in which 30 mg of iron daily was administered to normal women for 8 weeks from gestational week 20\(^4\) and another in which anemic women were supplemented early\(^80\)). Iron nutrition was better in infants born from supplemented women, as indicated above. One study\(^81\) reported higher infant mortality among a group of women receiving universal iron supplementation compared with selectively supplemented anemic women. In contrast, in less-developed countries, most women entering studies were anemic, overall received less iron than women in developed countries, and half (three of six studies in Rasmussen's review\(^79\)) reported some benefit in reducing the incidence of low birth weights. Again, iron nutrition was better in infants born from supplemented women. One study reported that the lengths of newborns of supplemented women were longer, even though their weight was similar to newborns of unsupplemented women.\(^78\)

Rasmussen\(^79\) determined relative and attributable risks of low birth weight and preterm delivery in a few studies; a summary of the results is presented in Table 5. These results show that, in general, moderate gestational anemia carries little risk in developed countries, but that severe anemia carries an overall greater risk, especially for low birth weight over that for preterm delivery, suggesting increased risk of small for gestational age babies. A attributable risk is high for both outcome variables regardless of anemia severity, again being greater for low birth weight than for preterm delivery. The same pattern is observed in pregnant women from less-developed countries. Unfortunately, the number of studies is
very limited for drawing firm conclusions and preterm delivery is reported only if the newborn is of low birth weight, thus reducing its true prevalence. However, from the public health point of view, the importance of preventing anemia is clearly demonstrated.

The general picture emerging from available data suggests the following:

1. Iron deficiency anemia, particularly early in pregnancy, and anemia in general (moderate or severe) have negative effects on pregnancy outcomes that are reduced by iron supplementation.

2. The effect of universal iron supplementation on birth weight and preterm delivery are variable in less-developed countries (different study designs and flaws) and void in women from developed countries who are not anemic early in pregnancy.

3. In populations where iron deficiency is prevalent, the intake of small iron doses plus vitamins early in pregnancy (especially if combined with pre-pregnancy supplement intakes) reduces low birth weight and preterm delivery (the Vietnam study also showed a positive effect).

4. Even among women who appear to be non-anemic and iron sufficient by mid-pregnancy, the intake of small daily doses of iron compared with placebo starting at or before week 20 has a positive effect on both outcome variables, and these positive effects occur even when ferritin levels indicate the absence of iron stores and when Hb levels are suggestive of mild to moderate anemia by current norms.

In summary, adequate iron status and no anemia before the third trimester, preferably as early in pregnancy as possible, are highly desirable.

**IS INGESTING MORE IRON THAN WHAT IS NEEDED TO PREVENT IRON DEFICIENCY ANEMIA DESIRABLE AND/OR SAFE?**

To our knowledge, there are no studies reporting negative health effects of preconceptional iron-folic acid supplementation, with the exception of gastrointestinal discomfort and the possibility of accidental ingestion of large iron doses, producing iron intoxication, especially in children. However, elevations of plasma “free iron” and of breath ethane excretion rate after daily iron supplement intakes at recommended doses have been reported, indicating the presence of body-reactive iron and oxygen species and elevated lipid peroxidation. Lachili et al. also reported increased lipid peroxidation in pregnant women receiving iron and vitamin C supplementation.

A few studies indicate undesirable perinatal and infant developmental outcomes from iron supplementation. A study from Finland among healthy pregnant women found increased infant mortality, and studies from Aberdeen, Scotland and from other groups including the CDC, suggest that excessive iron supplementation can be dangerous because it increases total Hb concentration above desirable levels and inhibits the normal decline of Hb concentration that reaches a nadir by gestational week 34. There is renewed interest in determining whether there are negative effects of high Hb concentrations and ferritin levels during pregnancy. In a retrospective study, Murphy et al. showed that both low and high Hb levels increased the rates of premature delivery and low birth weights. In a prospective study, Zhou et al. confirmed that the relationship between Hb levels and risk of poor pregnancy outcome formed a U-shaped curve. In a large,

### Table 5. Relative* and Attributable† Risks for Low Birth Weight and Preterm Delivery by Study Location and Anemia Severity

<table>
<thead>
<tr>
<th>Location</th>
<th>Relative Risk Low Birth Weight</th>
<th>Relative Risk Preterm Delivery</th>
<th>Attributable Risk Low Birth Weight</th>
<th>Attributable Risk Preterm Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed Countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate anemia</td>
<td>1.4 (N = 2)</td>
<td>1.5 (N = 8)</td>
<td>53.0% (N = 1)</td>
<td>45.7% (N = 3)</td>
</tr>
<tr>
<td></td>
<td>(range 0.8-2.1)</td>
<td>(range 0.6-1.9)</td>
<td>(range 23-67)</td>
<td>(range 9-59)</td>
</tr>
<tr>
<td>Severe anemia</td>
<td>4.6 (N = 3)</td>
<td>1.7 (N = 3)</td>
<td>71.5% (N = 2)</td>
<td>32.7% (N = 3)</td>
</tr>
<tr>
<td></td>
<td>(range 2.4-6.3)</td>
<td>(range 1.1-2.6)</td>
<td>(range 59-84)</td>
<td>(range 9-59)</td>
</tr>
<tr>
<td>Less-Developed Countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate anemia</td>
<td>1.5 (N = 8)</td>
<td>1.8 (N = 4)</td>
<td>6.3% (N = 1)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(range 0.8-3.0)</td>
<td>(range 0.6-2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe anemia</td>
<td>2.6 (N = 9)</td>
<td>2.5 (N = 2)</td>
<td>52.9% (N = 4)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(range 1.4-5.0)</td>
<td>(range 1.0-4.0)</td>
<td>(range 42-83)</td>
<td></td>
</tr>
</tbody>
</table>

*Relative risk is “the probability of an event occurring in the active group divided by the probability of the event occurring in the control group.”

†Attributable risk is “the proportion of the events (in a specified time) in the whole population that may be preventable if a cause of the event were totally eliminated.”
A retrospective analysis of the relationship between Hb, low birth weight, and premature delivery, Steer59 showed that these undesirable effects increased slowly, with mild to moderate anemia considered to be when Hb was above 115 g/L, and dramatically when Hb levels increased above 130 g/L at any time in pregnancy. These same effects were also observed in other large studies.60,85 Animal studies also strongly suggest that administering daily iron at the current recommended doses may not be desirable or innocuous.36,37

According to recent studies addressing daily and weekly supplementation schemes as proposed by different investigators, the risk of developing hemoconcentration (Hb > 130 g/L) is significantly higher among anemic and non-anemic pregnant women (some iron deficient) ingesting daily iron supplementation at recommended levels than among women ingesting weekly iron.85 Eckstrom et al.65 found that 20 doses of 60 mg of iron administered either daily or weekly to anemic Bangladeshi women during gestational weeks 18 to 24 were enough to elevate Hb to desirable levels. An analysis of data from the same study shows that among women receiving 12 weeks of two tablets of 60 mg of iron once weekly, for a total of 24 doses, only two of 72 women (3%) had Hb levels above 130 g/L, while 18 of 66 women (27%) receiving daily doses of 60 mg of iron for 12 weeks had elevated Hb levels. Anemic women appear more prone to overshoot safe Hb levels that carry perinatal risk.

Casanueva and Viteri87 and Casanueva et al.88 found that 17.5% of non-anemic Mexican women receiving 60 mg of iron daily for 16 weeks starting at week 20 and 6.7% of non-anemic women receiving two tablets of 60 mg of iron once weekly developed Hb values (adjusted for altitude) greater than 134 g/L. In this study, women developing these high Hb values by weeks 24 to 28 had a significantly higher relative risk of having lower-birth weight infants and preterm deliveries. The negative effect of high Hb in the second trimester was also reported in a large retrospective study.85 Dr. J.S. Robinson graciously allowed us to analyze data from two unpublished supplementation trials performed in the Maluku province of Indonesia (these same data were used by Beaton and McCabe in their report to the Micronutrient Initiative89). This analysis revealed that among 188 pregnant women receiving supervised daily iron (60 mg) and 183 pregnant women receiving weekly iron (two tablets of 60 mg once weekly), there were no women with Hb levels below 90 g/L after the ingestion of 30 tablets containing 60 mg of iron in 24 weeks. The proportion of women developing Hb levels greater than 134 g/L (hemoconcentration) increased exponentially from 6% after 45 tablets to 40% after ingesting 127 of the 60 mg tablets.

The studies in Bangladesh65 and in Mexico71 and the data from Maluku suggest that excessive daily iron intake increases the risk of hemoconcentration. In the Mexican study, hemoconcentration was associated with perinatal risk, supporting the suggestion of the Aberdeen43,56,83 and CDC85,86 groups. Unfortunately, neither the Bangladesh nor the Maluku studies recorded pregnancy outcomes. A recent Cochrane review of iron and iron folic acid supplementation reinforces these findings.62 High gestational Hb concentration in response to excessive iron administration appears to be a unique phenomenon during gestation that warrants further in-depth investigations.

Additional studies in Mexican pregnant women receiving 60 mg of iron and 250 μg of folic acid daily for 8 weeks starting either at week 20 or at week 28 showed marked increases in plasma thiosulfuric-acid reacting substances (TBARS). In contrast, women receiving a weekly supplement of 120 mg of iron and 500 μg of folic acid from week 20 to week 28 did not show an increase in TBARS measured 6 days after the previous dose. Moreover, if women with high TBARS at week 28 transferred to the weekly supplementation regimen, TBARS at weeks 32 and 36 fell to levels similar to those prior to iron supplementation (gestational week 20).89

Similar to the debate on how to diagnose iron deficiency and anemia in pregnancy is the debate on the benefits of routine daily iron supplementation during pregnancy at levels currently recommended by different agencies.51,32,63 It appears that small daily doses as recommended by the US Food and Nutrition Board90 and the US Institute of Medicine,91 as well as weekly dosing starting early in pregnancy, are safer and essentially as efficacious as daily iron in preventing iron deficiency and improving iron nutrition when adherence is satisfactory.

**CONCLUSION**

Field research to further validate the “preventive supplementation” approach with intermittent iron-folic acid supplementation is needed. The studies should address women’s needs during pregnancy and during their life-times as long as they are a group particularly at risk of iron deficiency and anemia. Long-term weekly supplementation with iron and folic acid to non-pregnant women can also bring benefits in terms of the prevention of neural tube defects and hyperhomocysteinemia.92,93 Further supplementation with vitamin A and possibly with multiple minerals and vitamins may bring further health benefits.94,95 Weekly dosing is more economical and more manageable in community settings given its greater safety, and can be managed under the supervision of health establishments and given to community organizations, schools, religious groups, markets, factories, etc., thus increasing coverage of vulnerable groups.
ACKNOWLEDGMENTS

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REFERENCES


28. DeMaeyer EM, ed. Preventing and Controlling Iron...


Effectiveness of Weekly Iron-Folic Acid Supplementation to Prevent and Control Anemia among Women of Reproductive Age in Three Asian Countries: Development of the Master Protocol and Implementation Plan

Tommaso Cavalli-Sforza

The master protocol for studying the impact and process of implementation of weekly iron-folic acid supplementation under program conditions is described. Pilot projects guided by the protocol were carried out in the Philippines, Vietnam, and Cambodia, where anemia rates are high and different socio-economic and cultural conditions exist. Each country utilized the same supplement but adapted implementation processes to their specific conditions. Social marketing and community mobilization were considered to be essential tools for sustainability.

Key words: anemia, folic acid, iron, supplementation, women of reproductive age

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Until 1999, all studies comparing the efficacy of intermittent iron supplementation (with or without folic acid) using daily and/or weekly regimes were conducted only during pregnancy, usually with supplementation supervised to investigate maximum achievable effect under ideal research conditions. Weekly iron-folic acid supplementation, however, was conceived as a preventive approach aimed at ensuring satisfactory iron and folic acid status throughout the reproductive life of a woman, enabling her to start pregnancy with optimal iron reserves and to avoid iron deficiency during pregnancy.1

Although not the focus of the weekly iron-folic acid supplementation studies reported herein, an additional benefit of including folic acid in the supplement taken before conception is the reduced risk of neural tube defects due to folic acid deficiency. Epidemiological studies suggest that 70% or more of neural tube defects can be prevented by increasing the intake of folic acid.2,3 Norsworthy et al.4 in a randomized, controlled trial of a once-weekly 2.8 mg folic acid supplement taken for 12 weeks, reported increased red blood cell folate to concentrations associated with a low risk of bearing a child with a neural tube defect. Other investigators5,6 reported that 5 mg of folic acid taken weekly achieved the desired effects of reducing neural tube defects and hyperhomocysteinemia.7 A combined iron-folic acid supplement, therefore, may reduce the risks of adverse pregnancy outcomes from deficient intake of both nutrients and may also have additional health benefits.

THE MASTER PROTOCOL

Considering the positive results reported up to 1998 from supervised weekly iron or weekly iron-folic acid studies in a number of different settings and age groups,8-18 the World Health Organization (WHO) Regional Office for the Western Pacific (WPRO) decided to support pilot effectiveness projects from 1998 to 2002. A master protocol was prepared in collaboration with Prof. Silvano Milani of the Institute of Statistics, Faculty of Medicine, University of Milano, Italy, and Prof. Fernando Viteri of the University of California, Berkeley, California, USA, for pilot projects to be conducted in more than one country to study the impact and processes of implementing the weekly supplementation approach under program conditions in countries with similarly high anemia rates and different socioeconomic systems and cultures. The Philippines and Vietnam were selected initially (and Cambodia was added later) to determine the effectiveness of weekly iron-folic acid supplementation under unsupervised program conditions. Program strategies included:

1. Promoting the regular intake of weekly iron-folic
acid supplements in combination with a diet rich in iron and other micronutrients by training health workers, counseling pregnant and non-pregnant women, providing social marketing with information, education, and communication (IEC) materials and events (but not radio and television, because the pilot was limited to certain geographical areas), and mobilizing community leaders (e.g., mayors, village captains, councilmen, commune leaders, etc.);

2. Producing attractive supplements that women would consider “worth buying”;

3. Selling the supplements to non-pregnant women and secondary school girls through local drugstores and village health workers; and

4. Providing the supplements free of charge to pregnant women through health services.

The weekly supplement contained the same dose of folic acid for non-pregnant and pregnant women: 3.5 mg—a dose well below the tolerable upper intake level of 1 mg/d\textsuperscript{19} and considered more than sufficient to maintain satisfactory folic acid levels in blood and red blood cells.\textsuperscript{4–7} The supplement also contained 60 mg of elemental iron (187 mg of ferrous sulfate) for non-pregnant women and twice this amount, 120 mg (374 mg of ferrous sulfate), for pregnant women to take into account the greater iron requirements in pregnancy, as has been done in previous efficacy studies. The supplements were film-coated to avoid any unpleasant smell and taste and to reduce the risk of gastric reactions, small in size to facilitate swallowing, and color-coated to distinguish the pill with lower iron content for non-pregnant women (light pink) from the pill with higher iron content for pregnant women (red). For stability and protection, pills were packaged in flexible aluminum foil (in Cambodia, the pills were blister packed). Each package contained a 1-month supply (four pills).

The foil package was contained within a colorful cover meant to catch the woman’s attention, as well as provide instructions for use, information about the product, and guidance for a healthy diet. Women were asked to take the supplement before going to bed to reduce side effects and to favor greater iron absorption in the absence of possible inhibitors found in meals. The supplements used for non-pregnant women in the three countries are shown in Figure 1.

Because governments are usually unable or unwilling to pay for supplies in long-term preventive programs, supplements were to be sold to women at a price found to be affordable through local consultations. The exception was in Cambodian factories, where the supplements

![Figure 1. Weekly iron/folic acid supplements used in the Philippines, Cambodia, and Vietnam.](image-url)
were provided free of charge, as the law requires factory owners to provide for the health of their staff.

The aim in each of the three countries was to reach about 30,000 women of reproductive age. These women would be encouraged to buy and take the supplements regularly while not pregnant and to continue taking them (free of charge dispensed from health centers) if they became pregnant. Based on known fertility rates, it was expected that at least 600 to 1000 women would become pregnant during the proposed project duration of 1 year; a large number of these women would take the supplements for several months before pregnancy, and part of them would deliver within 12 months of the start of the project.

The main challenge was to ensure that the supplements would be purchased and taken regularly for periods of months and even years to take full advantage of the greater efficiency of weekly intake of iron compared with daily intake. The protocol, therefore, was designed to mobilize the community to participate and to provide intensive social marketing, both approaches being considered essential tools in promoting the use of the supplements and to sustain their sale. A WHO social marketing expert was contracted to support the planning, monitoring, and evaluation of the social marketing component of the three programs.

The master protocol prepared for the Philippines and Vietnam projects envisaged that by the end of the intervention, the cohort of women in the weekly group would be subdivided for data analysis into four subgroups: 1) women who remained non-pregnant during the study period, 2) women who became pregnant in the first 3 months after baseline, 3) women who became pregnant between 4 and 6 months after baseline, and 4) women who became pregnant 6 months after baseline. This last group of women would be evaluated during the first months of pregnancy (at most up to the second trimester), which is the most important period in terms of perinatal outcomes. All of the women in these four groups would receive weekly iron-folic acid supplementation for the 12 months of the project. In addition, there would be women already pregnant who would be given the usual daily iron-folic acid supplements throughout the rest of their pregnancy, and their outcomes would then be compared with the four groups of women in the study.

IMPLEMENTATION CONSIDERATIONS

In each country, a national government institution was to be responsible for planning, managing, monitoring, and evaluating the program in collaboration with local government, civil organizations such as the Women’s Union in Vietnam, and community organizations in Cambodia. United Laboratories (UNILAB), the largest pharmaceutical company in the Philippines, would produce the supplements for all three countries and would also provide essential input into planning, conducting, monitoring, and evaluating the social marketing component of the Philippines program.

In the Philippines and Vietnam, the project design aimed to study the effect on hemoglobin and iron status (assessed by serum ferritin and transferrin receptors) of taking weekly supplements started before pregnancy or in the first 20 weeks of pregnancy, and compare this with the effect of daily supplements taken for a few months, as often happens in antenatal care programs, usually starting in the second half of pregnancy (if supplements are taken at all). The plan was to assess anemia and iron stores in up to 1000 women per country. Since the availability of and access to daily supplements are often part of the limited success of supplementation programs, project staff in the Philippines and Vietnam were to ensure that both types of supplements would be available locally.

The projects also aimed to define the duration of preventive iron-folic acid supplementation needed to prevent anemia and improve iron stores under non-supervised program conditions. In addition, although not initially planned, birth weight was determined on a number of the infants born to women taking both daily and weekly supplementation in Vietnam.

In the Philippines and Vietnam, both non-pregnant and pregnant women were enrolled in the projects. Also, in the Philippines and Vietnam the baseline survey was to include a “high fertility subset” of married women planning to have a child as soon as possible and willing to participate in the impact evaluation. In Cambodia, only non-pregnant women working in factories or living in rural villages and secondary school girls living in rural areas were included. Women with severe anemia (<70 g/L) and chronic infectious or metabolic disorders were excluded at baseline and referred for treatment. A WHO consultant set up the impact evaluation in each country.

Blood tests to assess the impact of the intervention were performed by national institutions in the Philippines (the Bureau of Research and Laboratories) and in Vietnam (the National Institute of Nutrition). Blood tests were done at baseline and after 4.5, 9, and 12 months of implementation. In addition, a questionnaire was administered on the same four occasions to assess changes in knowledge, attitudes, and practices (KAP) in the same women who provided blood samples. Additional support was provided in Vietnam by Dr. Jacques Berger, senior researcher of the research unit “Nutrition, Food, Societies” of the Institute of Research for Development in Montpellier, France (a WHO collaborating center), who
has worked at the National Institute of Nutrition for several years, and by WHO staff in all three countries.

In Cambodia, a team assembled and directed by a WHO consultant was responsible for data collection, including the KAP questionnaire and hemoglobin measurements to evaluate program impact, but not iron status, as it was not feasible to perform more complex laboratory procedures in the settings where the program was carried out.

Community mobilization and social marketing were considered essential tools in promoting the use of the supplements and to sustain their sale. Since social marketing principles were new to many of the professional and local implementation staff, particularly in Vietnam and Cambodia, orientation and training sessions were conducted in each country. The paper that follows by Smitasiri and Solon describes the governing principles of social marketing that were adapted to the context of each country setting.

REFERENCES

Implementing Preventive Iron-Folic Acid Supplementation Among Women of Reproductive Age in Some Western Pacific Countries: Possibilities and Challenges

Suttilak Smitasiri and Florentino S. Solon

Lack of effective implementation mechanisms is identified as a major obstacle in the prevention and control of iron-deficiency anemia. This paper discusses experiences gained from implementing iron-folic acid supplementation in the Philippines, Vietnam, and Cambodia. The understanding of contextual elements is proposed as a foundation for planning interventions. Moreover, it is suggested that a social marketing framework should provide a way of thinking about how to influence related behaviors. The application of a social marketing framework applied using a “5 P’s” approach: public relations and collaboration, product, price, place, and promotion, is described, as well as enabling factors (possibilities) and inhibiting factors (challenges) of this approach. Although a program to improve iron nutrition among women of reproductive age may not be simple to implement, it is essential to enhancing health, human development, and economic advancement in developing countries.

Key words: iron nutrition, preventive supplementation, weekly iron-folic acid supplements, social marketing, western Pacific region

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INTRODUCTION

The adverse effect of iron-deficiency anemia on health and human development is now beyond question. Basic and applied sciences have made major contributions in recent decades to understanding the effects of iron-deficiency anemia, and have made recommendations for remedial and preventive actions. Nevertheless, overall progress in the prevention and control of iron-deficiency anemia is still limited. Lack of effective implementation mechanisms, rather than lack of knowledge, is said to be a major impediment to progress.1 However, scientific progress alone may not be sufficient. Collaborative efforts and active participation of stakeholders at all levels are essential and need to be in place to bring about effective interventions.2

Based on existing knowledge, the most desirable preventive strategy for iron interventions is a food-based, dietary approach within a public health context (the sustained ingestion of bioavailable iron in food in adequate amounts and reducing iron losses throughout the life cycle).3 In the environment of developing countries, however, dietary iron interventions are often impractical to implement. Two main reasons are: 1) dietary iron solutions, e.g., changing food habits and preparation practices, may be too complex for the target populations to comprehend; and 2) iron-rich foods are relatively costly for poor populations (who are at the highest risk). Therefore, many perceive iron fortification of staple foods and commonly used condiments and/or iron supplementation as more promising solutions for developing countries.

There have been a number of successful large-scale iron fortification interventions, but there is still a need to determine the cost and access to the fortified products for target populations. Iron supplementation is a strategy widely used in developing countries, especially for pregnant women, but these programs generally have not been effective due mainly to logistical and compliance problems.3,4

This paper relates experiences and results from implementing preventive iron-folic acid supplementation to women of reproductive age (WRA) in three western Pacific countries: the Philippines, Vietnam, and Cambodia. In this paper, the program’s foundation and the overall framework and principles used to design the
interventions are described and the possibilities and challenges of this preventive approach discussed.

**PREVENTIVE SUPPLEMENTATION: AN IMPLEMENTATION PERSPECTIVE**

For the control of iron deficiency, the World Health Organization (WHO) currently recommends treatment of those already anemic by periodic repeated administration of daily iron supplements among populations that exhibit a high prevalence of anemia. This therapeutic approach uses daily iron doses with the aim of correcting anemia quickly. On the other hand, the newer preventive weekly iron-folic acid supplementation approach, as proposed by Viteri, recommends intermittent iron doses taken over a prolonged period of time with the aim of sustained improved iron nutrition.

From an implementation perspective, a strategy for improving nutrition rather than correcting an illness makes it possible to communicate positive messages, for example, that the supplements are to enhance health and nutritional well-being. This is in contrast to practices that often focused on women being sick, thus bombarding them with negative messages. Positive messages motivate audiences better for long-term change; furthermore, fewer side effects from lower iron doses is appealing because side effects are a known impediment to compliance.

WRA in developing countries usually suffer from all of the consequences of iron deficiency and iron-deficiency anemia, whether or not they are pregnant. Therefore, prolonged supplementation beginning before a woman becomes pregnant is a better strategy to benefit the majority of the population. If this strategy can be implemented, people should be convinced by the combined benefits of improved women’s health, enhanced cognitive performance (learning ability), and increased productivity, together with ensuring healthy motherhood. From an implementation perspective, it is therefore important to know whether the concept of preventive iron-folic acid supplementation among WRA before pregnancy can be implemented in developing countries.

Viteri proposed preventive supplementation based on a community-centered regimen of weekly iron doses to populations or groups within populations at risk of developing iron deficiency. He noted that the key to success, like many other public health interventions, is the active involvement of stakeholders at all levels. A UNICEF/United Nations University/WHO/Micronutrient Initiative technical workshop in 1999 noted that, although evidence is growing that in some situations preventive supplementation can be efficacious when compliance is achieved, there is still a need to further assess its effectiveness under program conditions.

**APPLICATION OF A SOCIAL MARKETING FRAMEWORK TO FORGING WEEKLY IRON-FOLIC ACID SUPPLEMENTATION**

The WHO Regional Office for the Western Pacific (WPRO) identified “social marketing” as a framework to be applied for introducing preventive supplementation under program conditions in the Philippines, Vietnam, and Cambodia. Contextual elements of each participating country, which were the foundation of the program designs, are as follows:

**The Philippines**

The Philippines had provided daily iron supplementation for pregnant women at a national level for nearly three decades, but with limited success. Existing obstacles, as identified by the authorities, were supply irregularities, logistics problems, and compliance issues. After several discussions with important stakeholders, a strong partnership between the government and the private sector in health development was identified as a foundation for intervention planning in this country.

**Vietnam**

The national health system in Vietnam was rapidly developing when this preventive iron-folic acid supplementation program was initiated. Daily iron supplementation for pregnant women had been implemented, but only in some targeted areas of the country. The National Institute of Nutrition of the Ministry of Health previously had outstanding success at the national level in implementing a vitamin A supplementation program. This success was achieved through strong community involvement in health and development and skilled social mobilization of grassroots organizations from the national to the community level (e.g., the Women’s Union and Youth Union were identified as important implementation elements).

**Cambodia**

After a long period of civil war, the Cambodian government was working hard to develop the nation’s health infrastructure with assistance from many external agencies. There was clearly a need for international agencies (the United Nations and bilateral and non-governmental organizations, or NGOs) to work with the government in the development process. Among the three countries selected by WPRO for the program, Cambodia was the most challenging for implementing a preventive supplementation approach because there were already many priority health issues in this population.
THE SOCIAL MARKETING FRAMEWORK

A social marketing framework was applied to formulate intervention strategies for each country based on these contextual elements and as additional rapid situation assessments with the program teams. “Social marketing” originally was defined as the design, implementation, and control of programs calculated to influence the acceptability of social ideas and involving considerations of product planning, pricing, communication, distribution, and market research. The level of funds in each country for investment in preventive iron programs, however, did not permit full application of this framework.

Instead, in the three programs, social marketing was adopted as a way of determining how to influence related behaviors necessary to promote preventive iron-folic acid supplementation in the identified populations. In other words, the concept was used in designing processes whereby the programs were put into place and implemented. These processes, discussed herein only in principle, were founded on the five elements of social marketing (the “5 P’s approach”): public relations and collaboration, product, price, place, and promotion. Process papers in this supplement discuss intervention strategies in more detail, while impact papers highlight outcomes of the programs.

THE FIVE ELEMENTS OF SOCIAL MARKETING

Public Relations and Collaboration

As indicated by Viteri, involvement and active participation are success elements of preventive supplementation. Program teams, therefore, arranged meetings and visits, as well as other creative activities, to ensure that the most important stakeholders in the programs understood the importance of iron-folic acid supplementation. One important assumption in these programs was that success came from people and their actions.

In the Philippines, leaders established a program team that was able to work closely with private sector partners from the beginning. In addition, municipal mayors, medical doctors, nurses, health care workers, and school teachers were also important in discussions of the program to elicit their direct participation. Workshops and training exercises and local activities followed to generate added understanding and participation.

In Vietnam, a meeting with important government representatives was organized at the beginning of the program to discuss the benefits for the country. Scientific review sessions were also arranged to ensure that scientists, nutritionists, and medical doctors could see the benefit of a social marketing framework. At the time, the concept of “social marketing” was new to the Vietnamese nutrition science community. Visits to national leaders of the Women’s Union were critical in ensuring collaboration between this important grassroots organization and the National Institute of Nutrition. Meetings with local leaders were also essential, not only so that they understood the importance of the program, but also to ensure their active involvement.

A national steering committee for the program was created in Cambodia. The first steering committee meeting discussed the importance of improved iron nutrition and correcting iron-deficiency anemia, informed about available iron intervention strategies, and presented the strategies and plans for the proposed preventive program. This meeting, together with several individual follow-up visits, brought together the Ministries of Health, Social Affairs, Labor, Vocational Training, and Youth Rehabilitation and Education and the Ministry of Youth and Sport with WHO and UNICEF as national and international participating organizations for the program. This collaboration made it possible to conduct the interventions in a workplace (factory) setting, as well as in schools and communities.

Product

Results of the rapid assessments revealed that women who had received iron supplements did not generally view the product favorably. Thus, the social marketing program had to reposition thinking of the target audience about iron supplementation. Weekly iron-folic acid supplements were therefore designed to be perceived by WRA as a lifelong habit that they could depend on to enhance their physical and emotional well-being as they progressed through the different stages of womanhood. A concept statement for the product was:

All women experience physical, mental and emotional changes as they go through life stages, especially during their reproductive years. All women at this lifecycle stage need weekly iron-folic acid supplements (60 mg elemental iron and 3.5 mg of folic acid) to enhance their well being and prevent iron deficiency. Moreover, when women are pregnant and for three months after their delivery, they need weekly iron-folic acid supplements (120 mg elemental iron and 3.5 mg of folic acid) not only for their health but also for their babies’ health.

Resilient, confident, dependable, and caring were suggested as promotional characteristics of the new supplements.

Together with United Laboratories (UNILAB), a wholly Filipino-owned private drug industry based in the Philippines, two preparations of iron-folic acid supplements were designed and produced for the program. The...
design of the product was described previously in this supplement.

In the Philippines, “Femina” was chosen as the product name to enhance the concept of womanhood. Images of beautiful WRA to represent the target groups were used in covers and advertisement designs. In Vietnam, “Bo Huyet Hoa Hong” related the supplements with the traditional concept of “tonic for women health” and “a beautiful flower,” which represents a woman’s beauty.

“Kolap Krahom” or “red rose” was the name of the product in Cambodia. Images of beautiful WRA and a beautiful flower were used in both Vietnam and Cambodia. Covers in all three countries also included educational information and listings of recommended locally available iron-rich foods.

**Price**

A paradigm shift in thinking about iron supplementation is necessary for preventive supplementation of WRA before and after pregnancy to fully achieve its potential for reducing iron deficiency in developing countries. To expect menstruating women in populations at risk to adopt taking iron-folic acid supplements weekly for a large part of their lives as normative behavior presents a social marketing challenge. Simply providing the supplements is unlikely to be sufficient. A process needs to be put in place that is capable of motivating women to both adopt and maintain the behavior for a long period of time.

It is also unlikely that the governments of developing countries will continuously provide weekly iron-folic acid supplements as they would provide daily iron supplements to pregnant women. Governments can facilitate establishing the system, but the communities, and most importantly the women themselves, must actively participate in the process. For the programs discussed here, it was decided that investments would be allocated to set up and facilitate the process, but that the women (only non-pregnant WRA) would share the cost by purchasing the supplements during the programs. Therefore, the three programs were developed to determine whether women in developing countries were willing to adopt the proposed behavior. Pregnant women participating in the programs, on the other hand, received their iron-folic acid supplements free of charge through health services.

Based on unique contextual characteristics of the three countries, the rationale for pricing for the supplements varied. In the Philippines, strong partnership between the government and the private sector made it possible to set the product price based on the market system (with the assistance of UNILAB). Subsidized prices were set for the programs in Vietnam and Cambodia. In summary, non-pregnant WRA participating in the programs purchased their supplements, with the exception of non-pregnant WRA in factories in Cambodia (the program team decided that it was necessary for this group to receive free supplements as required by government policy). Product prices were discussed at great length among program stakeholders before decisions were made to ensure that prices, in principle, would be affordable to all target women in the programs.

Local change agents were informed by program teams to locate disadvantaged, non-pregnant WRA in the intervention areas who could not afford the supplements and to provide them free of charge to these women. In practice, none of the three programs found this to be a notable issue. Only after the Cambodian program ended at the community level did cost become an issue.

Funds generated from supplement sales to non-pregnant women went into the market system in the Philippines; in the case of sales by health workers, a small monetary incentive was provided out of the funds from selling each package. In Vietnam, the money remaining after deducting a small financial compensation for women selling the supplements and some funds for additional social marketing activities, 50% of the sale price went to a revolving fund under the supervision of the local program steering committee. In Cambodia, money earned (minus local operation costs) from WRA in participating schools went to each school’s revolving fund, while money earned (minus local operation costs) from WRA in communities went to each village fund (the intervention communities were UNICEF-integrated development communities with a strong component of village fund management).

**Place**

All three programs set up mechanisms to ensure that the target populations could easily have access to the products. In the Philippines, the supplements for non-pregnant women were available from local drug stores, schools, and local health workers in the intervention area. In Vietnam, direct sales by Women’s Union collaborators were key to the success of the program (the program provided bicycles to women collaborators for supplement distribution). Teachers and student change agents conducted direct sales to student WRA in participating schools, female change agents promoted sales in communities, while company nurses or doctors on duty provided supplements to non-pregnant WRA in Cambodian factories.

Participating pregnant women in the Philippines and Vietnam received weekly iron-folic acid supplements at health centers. Pregnant women in the intervention areas of Cambodia relied on the supply from the existing system, since weekly supplements were not provided from the program.
Promotion

The promotion components of program were designed in principle to: 1) promote active involvement of important stakeholders including the target women; 2) increase effectiveness of counseling, group, and/or individual education in the existing health system; 3) introduce “women’s supplements” through culturally appropriate channels; and 4) provide generic education on issues related to the programs. The fundamental assumption was that when a new approach was first introduced, promotion needed to be comprehensive, going well beyond posters and their accompanied printed materials regardless of how well they were designed and developed.

IMPROVING IRON NUTRITION AMONG WRA: POSSIBILITIES

One important lesson learned from efforts discussed here is that a significant number of stakeholders in the three developing countries were interested in improving women’s health using a positive outlook, since they knew that disease-oriented approaches adopted previously had not been effective. Therefore, they were open to new practical ideas. With adequate facilitation processes, positive results could be reasonably achieved through iron-folic acid preventive supplementation.

Policy and decision makers need to become more familiar with the concept of preventive supplementation for a sustainable shift from the current therapeutic paradigm to occur in developing countries. International agencies and scientific communities can contribute greatly to the process. Investments in operation-oriented research to help countries define intervention strategies appropriate to their particular context are clearly essential, since top-down, quick-fix ("one size fits all") strategies are incompatible with a sustainable preventive approach. Good understanding of the contexts and trends of overall development and strategic positioning of the change process are important prerequisites to successful interventions.

Preventive supplementation is possible if well-informed women and/or communities (large and small) accept it along with promotion of improved nutrition and health. The current mindset of many stakeholders needs to change from one of thinking that women in developing countries will only take action to improve their health when they are ill. Similarly, to say that no government in developing countries will only take action to improve their health is definitely not sufficient; a process to convince other related stakeholders to take positive actions toward adoption of the program is also necessary. With appropriate support and facilitation at the global, national, and community levels, preventive iron-folic acid supplementation should be reasonably accomplished under program conditions in the 21st century.

IMPROVING IRON NUTRITION AMONG WRA: CHALLENGES

Generally speaking, any action taken thus far to reduce iron-deficiency anemia in developing countries has been a challenge. Recent qualitative research reveals that people directly involved in iron supplementation programs express pessimism. Some of their statements were: “iron is messy”; “iron is the most studied micronutrient but we have the least consensus on it”; and “iron has been neglected due to a lack of good, simple programs to implement.” Perhaps it is time for all stakeholders to admit that iron nutrition is a complex problem that needs a complex solution. However, if the preventive iron supplementation program is to be well managed, a successful and sustainable outcome will be achieved.

The idea of “preventive supplementation” itself is also a true challenge. One paradox in the iron community is that everyone wants to reduce the burden of anemia among poor populations, while it is also recognized that a long-term approach such as promoting better iron nutrition might be a better way to get and sustain the result. As a consequence of this paradox, successful iron intervention is often determined by the most cost-effective way to reduce anemia prevalence in a population. With this line of thinking, a paradigm shift from a therapeutic approach (curative supplementation) is less likely.

Preventive supplementation focuses on increasing the number of WRA with better iron nutrition and on the number of women entering pregnancy with good iron stores. Putting this approach into practice is indeed a practical challenge, since success indicators are often based on thinking in the old paradigm. For this reason, weekly iron-folic acid supplementation (preventive supplementation) is easily mistaken and sometimes promoted as a cure for iron-deficiency anemia (again, the same disease-oriented mindset).

Traditionally, a major effort in an iron supplementation program in a developing country is to provide enough supplements to pregnant women through a health care system (a provider approach). The new preventive approach, however, requires much more than a sufficient supply of supplements. It requires dynamic processes to influence WRA’s adoption in populations at risk. Therefore, consumer demand is not a small part of the program, but it has become a fundamental program element.
With this thinking, working only within a health care system will no longer be sufficient. An intersectoral approach with the health care system as a core (a facilitator approach) will be crucial.

An intersectoral approach in health and nutrition development is a sound and rather old concept. For many, this concept has remained impractical. This fact is indeed a challenge for a preventive iron-folic acid supplementation approach, since sustained participation of intersectoral stakeholders seems critical. For example, strong government and private sector collaboration was a key success factor for the program in the Philippines. After the program, the private sector took the lead and invested in marketing the supplements as a company’s product at the national level. The collaboration during this later phase was not as strong, which indicated a need for careful development of implementation mechanism to scale up the program.

A community-centered regimen has been suggested for preventive supplementation. In this way, a community (large or small) should be the center of attention. Members of the community, including the WRA themselves, should be key actors in this operation; an empowerment or facilitation approach is thus necessary. For international agencies, non-governmental organizations, governments, and those in the private sector in developing countries to play the role of facilitators in the change process is another challenge. In other words, the implementation mechanism necessary for preventive supplementation is not yet the norm in “the way we work.”

CONCLUSION

Policy makers, program managers, technical experts, community (large or small) leaders, and donors are urged to consider these possibilities and challenges carefully. They need to decide how they would like to address the prevention and control of iron deficiency and iron-deficiency anemia, for which potential benefits are said to be great for health and human development, as well as having implications for national economic development. Preventive supplementation as discussed here may not be a simple program to implement, but it can be very beneficial in improving health among many women. Women in developing countries are often on the frontlines in family, community, and national development processes. Better health will not only have an impact on productivity and quality of life in these women, but also on the overall health of families, communities, and the development of nations.

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REFERENCES

2. Underwood BA. Scientific research: essential, but is it enough to combat world food insecurities? J Nutr. 2003;133(5 suppl 1):1434S–1437S.
Community Mobilization and Social Marketing to Promote Weekly Iron-Folic Acid Supplementation: A New Approach Toward Controlling Anemia Among Women of Reproductive Age in Vietnam

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Community-based social marketing and mobilization increased knowledge and participation in preventive weekly iron-folic acid supplementation among women of reproductive age in Vietnam. Rates of buying and taking the weekly supplement containing 60 mg elemental iron and 3.5 mg folic acid among non-pregnant women of reproductive age was between 55% and 92%. Free distribution to pregnant women of the weekly supplement containing 120 mg iron and 3.5 mg folic acid covered almost all pregnant women during the project. In developing countries where community women’s groups and health networks are strong, preventive supplementation can be successfully promoted to encourage active participation in the prevention and control of iron-deficiency anemia.

Key words: anemia, weekly iron-folic acid supplementation, women of reproductive age, social mobilization, Vietnam

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INTRODUCTION

Vietnam, located in southeast Asia, has a population of more than 80 million, of whom about 20 million are women of reproductive age (WRA). Among them, the prevalence of anemia is estimated at 30% to 45%. A primary cause of the problem is iron deficiency. To reduce iron-deficiency anemia, a national program was formulated in 1993, which gradually expanded to 130 of the 600 districts in the country. The program’s core activity was to provide daily iron-folic acid tablets to pregnant women in their last trimester of gestation. This intervention approach, however, does not correct iron deficiency existing in early pregnancy. Moreover, daily administration of iron tablets frequently produces side effects that usually result in poor motivation for regular intake. In addition, even though women receive iron tablets free of charge, mainly through health services (nutrition and primary health care programs), they do not understand their value, resulting in a low compliance rate. The challenge for the Vietnam national program was to find appropriate ways to improve compliance and sustain the supplementation program through a community-based approach.

In recent years, preventive supplementation with iron-folic acid tablets provided weekly has been considered by many developing countries as a new approach toward controlling anemia in WRA. In addition, social marketing and mobilization have been suggested as an effective way to implement several health and nutrition promotion programs. With the support of the World Health Organization (WHO) Regional Office for the Western Pacific (WPRO), a study was carried out between 1999 and 2000 to introduce weekly iron-folic acid supplementation to WRA in Vietnam. The two specific objectives of the project were: 1) to promote a new preventive supplementation of iron-folic acid to WRA through social marketing and mobilization activities, and 2) to assess the effectiveness of such a combined approach in improving knowledge, attitudes, and
practices (KAP) in the prevention and control of iron-deficiency anemia.

STUDY DESCRIPTION AND DESIGN

The study was planned based on the assumption that preventive iron-folic acid supplementation accompanied by social marketing and community mobilization would improve program effectiveness and result in greater biological impact on the prevention of iron-deficiency anemia in WRA. In early 1998, the National Institute of Nutrition (NIN) and the Institute of Research for Development (IRD) designed the study protocol with technical assistance from WPRO. The study was launched in March 1999.

The intervention was implemented in Thanh Mien District, which is in the Hai Duong Province located in the Red River Delta. The district is situated about 70 km southeast of Hanoi and is composed of 19 rural communes with a population of nearly 133,000, about one-fourth of which are WRA. Rice production provides the main source of income. The poverty rate is estimated to be between 15% and 25%. In 1994, the prevalence of malnutrition among children under 5 years of age was about 50%, and about 36% of WRA suffered from chronic energy deficit. According to a 1999 survey, the prevalence of anemia among pregnant women in this district was over 50%.13 Both curative and preventive health activities are the responsibility of district health centers. Each commune has a health center that is staffed, on average, by four to six health workers. In addition, each village has one village health worker or collaborator.

There are several community organizations in the district; for example, the Youth's Union, Women's Union, Farmer's Association, and Veteran's Association. The Women's Union is very strong, with a well-organized network reaching from the district out to communes and villages. Members of the Women's Union are a known for their active participation in several primary health care programs. They are also noted for their creative community social mobilization activities.

KEY INTERVENTION STRATEGIES

The iron-folic acid supplements used in this study were produced by United Laboratories (UNILAB), Philippines, in accordance with a formula recommended by the WHO. The supplements were described previously in this issue.14

In Vietnam, iron supplements have long been perceived as medicine, and this conveys a negative image. To counter this, a marketing strategy to create a new image was developed following a rapid formative assessment. The iron-folic acid supplement was given a new name, “bo huyet hoa hong.” Bo huyet means “nutrition supplement for healthy blood” and hoa hong means “rose,” a flower attractive to young girls. The cover of each package depicted a beautiful young girl with a rose. To differentiate the two formulations, light pink packs contained supplements for non-pregnant women and carried the message “take one bo huyet hoa hong (BHHH) only once a week and you will be assured of welfare.” Red packs were for pregnant and lactating women and carried the message: “take BHHH once a week during pregnancy and for three months after being delivered to ensure your and your baby’s welfare and strength.” Pictures and messages appeared on both the packs and boxes containing the supplements. For a photograph of the packages, please see page S78 in this issue.

All WRA, whether or not they were pregnant, in all 19 communes of Thanh Mien District were eligible for the study. Women identified as pregnant at baseline were assigned to receive free of charge a different iron-folic acid supplement supplied through UNICEF (60 mg elemental iron and 0.25 mg folic acid) from a health station in their commune. They were advised to take one tablet per day based on the existing national iron supplementation program.

WRA who were not pregnant at the baseline survey were motivated to buy and take weekly doses of the BHHH. When pregnancies were detected by the women themselves or by health personnel during the course of the project, the women received free of charge the project weekly dose of 120 mg elemental iron and 3.5 mg folic acid at the health station.

The existing national program distributed supplements to pregnant women exclusively at the commune health station. Village health workers or health collaborators were only used to inform and encourage women to come to the station to receive the tablets. This distribution system was inconvenient, especially for distribution of a preventive supplement to non-pregnant study subjects. To overcome this constraint, a collaborative arrangement was made with the Women’s Union network, which was capable of distributing supplements to non-pregnant women in their own communities.

Since the local Women’s Union collaborators usually knew their village colleagues, it was not difficult for them to be in contact with non-pregnant women, thus expanding opportunities for communication and education beyond that possible by the health personnel. Furthermore, this arrangement allowed workers at commune health stations to focus on distributing the supplements for pregnant women, which started as soon as pregnancy was detected and continued until 3 months after delivery.

For a preventive iron-folic acid supplementation program to be sustainable, non-pregnant women should
perceive the supplement to be of sufficient value to purchase it themselves, making them more likely to use it. The price, therefore, needs to be suitable to the economic condition of communities and acceptable to women for purchase over a long period of time. After conducting in-depth interviews with women and family members in the intervention area, a subsidized price of 1000 Vietnamese dong (VDN) ($0.08 US) was set for one package containing four tablets, sufficient for 1 month. Over a year, a woman would spend 12,000 VDN ($0.96 US), which was acceptable for rural women in Vietnam.

Money from the sales financed an incentive for collaborators (20%) and management costs and regular communication activities within communes (30%). The remaining 50% was held in a local bank under the supervision of a district steering committee. Commune leaders agreed that this revolving fund would be used to sustain this approach by buying the supplements after the project period ended.

**SOCIAL MOBILIZATION ACTIVITIES**

Strengthening organizational support for nutrition and health activities at the district and commune levels was critical in ensuring a supportive policy environment for implementing the project.

A representative of the District People’s Committee (local government) was invited to chair a district steering committee that included representatives from the district health office, the Women’s Union, the Committee for Protection and Care of Children (CPCC), and the education, information, and cultural sectors. A similar structure was established for the commune steering committees. The steering committees’ function was to give policy guidance for project implementation. This created a supportive environment for integrating existing health care and social mobilization activities.

The project began with two consultative meetings. At the first meeting, representatives from the Ministries of Health, Planning and Investment, and Finance and representatives from the intervention district and the project team reviewed the project’s goal and objectives, the intervention plan, and management issues. At the second meeting, the project team and key actors from the intervention district and commune levels developed operational plans and signed a commitment document, which clearly defined roles and responsibilities of related parties, including an appeal for support from local authorities.

Commune health workers (midwives, nurses, and paramedics), medical doctors from the obstetric department of the district hospital, and members of the district steering committee received training to ensure the effectiveness of the existing service system. Training included: 1) how to improve pre- and postnatal care services, 2) cause and recommended actions for management of anemia, 3) nutrition and dietary recommendations, and 4) an introduction to preventive weekly iron-folic acid supplementation. Training sessions emphasized a participatory approach, including formal presentations, discussions, and role playing. Participants were provided with a practical manual on women’s health and the prevention of iron-deficiency anemia, posters, leaflets, and educational videos.

Billboards, banners, promotional cars, and loudspeakers were used to communicate the project’s messages during campaigns carried out in May 1999 (right after the baseline data collection) and during the project period in October 1999 and February 2000. These campaigns were aimed at informing the target populations about project activities, promoting the participation of all those involved in the prevention of anemia.

About 20,000 leaflets were distributed to WRA in the intervention area. The key content of the leaflet was how to prevent iron-deficiency anemia through diet and weekly iron-folic acid supplementation. In addition, 5000 leaflets were distributed with messages specifically for pregnant women to motivate them to improve their food intakes and take BHHH if possible before pregnancy, throughout pregnancy, and for 3 months after delivery. Billboards were placed in front of the Commune People’s Committee Buildings and the health stations in each of the 19 communes, and banners were hung on the main roads during the campaign periods. The product logo was shown on promotional bags and bicycles of collaborators who distributed BHHH to the women. A handbook containing messages on the health consequences of anemia, how to prevent anemia, iron-rich foods, and BHHH was prepared for use by local loudspeaker announcers.

About 570 participants from the Women’s Union network, including the district, communes, and villages, attended six training workshops at the beginning of the intervention. The importance of women’s health, iron-deficiency anemia, and the importance of iron nutrition for women were discussed. Participants were also trained on how to monitor the sale and usage of iron-folic acid supplements, how to collect and manage the fund from sale of the products, and how to improve communication skills in order to motivate women through counseling and group discussions. The training workshops were conducted through role-playing and composing folk songs, poems, and dramas. The participants subsequently conducted education and communication sessions for WRA in their communes and villages.

Although all 19 communes in the intervention district had women’s clubs, only five were active 3 months...
after the project implementation started. After the sixth month, the number doubled, and all 19 communes had active club activities after 9 months of intervention. Project communication activities were on the monthly agenda in these clubs. WRA were persuaded to come to these sessions to discuss and share experiences on the prevention of anemia and the importance of taking BH HH weekly. Women composed poems, dramas, and folk songs on usage of BH HH to prevent anemia and shared their compositions at club sessions. These activities were very popular and effective for improving KAP. A total of 85 poems, 15 dramas, and 11 folk songs on project contents were composed.

In Vietnam, teachers play an important role in education and communication to the WRA who are still in school. Therefore, a training workshop for 63 high school teachers was organized to inform them about the importance of preventive iron-folic acid supplementation for adolescent girls, how to use BH HH, and how to communicate effectively to the WRA in schools. BH HH was available to high school WRA through their mothers or sisters in project villages.

During the intervention, the project’s messages were also communicated through meetings of Elderly Clubs (people who have prestige in a commune), the War Veteran Organizations, and the Youth Unions. Members of these organizations were asked to assist in further communicating the project’s messages in their communities.

Continuous and impromptu communication between the project team and the commune/village leaders was key to success in maintaining their interest and support. Such organized regular visits and impromptu workshops with community leaders and the Women’s Union collaborators were arranged when necessary. For example, when the sale of BH HH was observed to have dropped, six workshops were organized to discuss the problem and how to communicate effectively with WRA. A campaign in all intervention communes was also conducted to clarify any issues that had arisen, and confirmed the necessity of continued adoption of the supplement.

KAP of pregnant and non-pregnant women were evaluated through a questionnaire developed by the Nutrition Information Education Center of the NIN. The Nutrition Community Department of the NIN implemented these surveys by interviewing randomly selected WRA. Before intervention, 863 WRA were interviewed; after 4.5 months of intervention, 860 were interviewed; and after one year, 856 were interviewed. The WRA interviewed at baseline and after 4.5 and 12 months of intervention were the same women.

RESULTS

KAP changes occurred during the course of the project, even though a high percentage of WRA were informed about anemia from the outset of the study. Table 1 shows that 90.8% of the WRA knew about anemia before the intervention, and this improved to 95.5% after the intervention. However, specific knowledge about causes of anemia and prevention strategies was limited at baseline. After 1 year of the social marketing and mobilization intervention, the percentage of women who knew that poor nutrition led to anemia, that weekly iron-folic acid supplementation could help to

<table>
<thead>
<tr>
<th>KAP</th>
<th>Before ($n = 863$)</th>
<th>After 4.5 Months ($n = 860$)</th>
<th>After 12 Months ($n = 856$)</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia in general</td>
<td>784 90.8</td>
<td>788 91.6</td>
<td>814 95.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Poor nutrition leads to anemia</td>
<td>195 22.6</td>
<td>286 33.3</td>
<td>794 92.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Higher iron requirement of reproductive women when becoming pregnant can lead to anemia</td>
<td>82 9.5</td>
<td>426 49.5</td>
<td>738 86.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Monthly menstruation can contribute to anemia</td>
<td>75 8.7</td>
<td>282 32.8</td>
<td>724 84.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hookworm infection contributes to anemia</td>
<td>36 4.2</td>
<td>424 49.3</td>
<td>654 76.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Iron-folic acid supplements can help prevent anemia</td>
<td>248 28.7</td>
<td>552 64.2</td>
<td>704 82.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anemia affects health seriously</td>
<td>133 15.4</td>
<td>268 31.2</td>
<td>550 64.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Taking iron-folic acid tablets weekly can prevent anemia</td>
<td>176 20.4</td>
<td>368 42.8</td>
<td>623 72.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Before and after 12 months.
prevent anemia, that women needed more iron during pregnancy, and that hookworm infection played an important role in iron-deficiency anemia had remarkably increased. Furthermore, the percentage of women who recognized the health effects of anemia and the health benefits of taking BHHH had increased significantly.

KAP improved substantially from the first months of the project, as shown by the survey conducted after 4.5 months. This indicates that the social marketing campaign was effective within a short period of time.

As shown in Table 2, regularly taking BHHH improved certain aspects of WRA’s perceptions. After 1 year of taking BHHH, the percentage of WRA who felt stronger, were less tired, and slept better had increased. Buying practices also changed, as sales of BHHH to non-pregnant women rose from 54.5% to 92% in the first 6 months of the project (Figure 1). The decline in purchases 9 months after the intervention began was partially reversed by increasing the social mobilization activities in the remaining 3 months of the project. All women who bought the supplements reportedly used them regularly.

Among pregnant women, health station records in the intervention district indicated that the percentage of pregnant women who received daily and weekly supplements was relatively high.

**PROJECT EXPANSION**

Based on the results of the first phase in the Thanh Mien District, the project was expanded to a new district in the same province (Binh Giang District). Funds raised from sales of BHHH in Thanh Mien District were used to buy a domestically produced iron-folic acid supplement to be distributed to WRA in both schools and communities in Thanh Mien District and Binh Giang District. The local supplement was provided in a blister package containing 30 tablets, with 240 packages per box. In both districts, non-pregnant women were motivated to buy and take a weekly dose of the local iron-folic acid supplement that contained 60 mg elemental iron and 0.4 mg folic acid (one tablet per week). The folic acid composition of the locally produced tablet (0.4 mg) conformed to that authorized by the Vietnamese government and was comparable to the UNICEF formulation. The price of one package containing 30 tablets (a 7-month supply) was 2500 VDN ($0.20 US). This price was acceptable for rural women in Vietnam. Pregnant women received iron-folic acid free of charge from health collaborators with weekly doses (two tablets per week) of 120 mg elemental iron and 0.8 mg folic acid. The social marketing and mobilization approach was also applied in the Binh Giang District.

Table 3 shows the sales and usage of the locally produced iron-folic acid supplement in phase II (expansion phase) carried out in the Thanh Mien and Binh Giang Districts in 2003. The rate of sales and usage of iron-folic acid supplements by WRA in the two districts varied from 42% to 65%, which is considerably lower than the usage achieved with the UNILAB supplement. Funds raised from the sales of the local product were used to buy the supplements for continuous availability to WRA in the two intervention districts.

**DISCUSSION**

Strong support and commitment of local authorities and active community participation are crucial for community-based health and nutrition programs to be successful and sustainable. In Vietnam, several successful primary health care programs have effectively used a social mobilization approach. For example, the successful national expanded program on immunization was launched in the early 1990s by two national campaigns involving the participation of many local people and authorities. Also, the vitamin A supplementation program that began in 1993 with vitamin A capsules provided twice yearly free of charge by UNICEF to children under the age of 5, but with no special financial support for the campaigns, was successful because of people’s participation and a high commitment by authorities from different levels of government and community. Vietnam’s market system generally, and particularly in the area of health services, is still not well developed compared with some other Asian countries such as the Philippines. Due to this fact and past experiences, social marketing and mobilization within communities was likely to be a critical activity to a self-sustainable, weekly

**Table 2. Perception of Women after Taking Iron-Folic Acid Supplements**

<table>
<thead>
<tr>
<th>Perception of Women</th>
<th>At 4.5 Months of Intervention</th>
<th>At 9 Months of Intervention</th>
<th>At 12 Months of Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-Pregnant</td>
<td>Pregnant</td>
<td>Non-Pregnant</td>
</tr>
<tr>
<td>Stronger</td>
<td>53.5%</td>
<td>49.6%</td>
<td>77.7%</td>
</tr>
<tr>
<td>Less tired</td>
<td>33.1%</td>
<td>26.4%</td>
<td>39.7%</td>
</tr>
<tr>
<td>Sleep better</td>
<td>40.8%</td>
<td>27.9%</td>
<td>50.0%</td>
</tr>
<tr>
<td>Better appetite</td>
<td>38.1%</td>
<td>31.0%</td>
<td>32.0%</td>
</tr>
</tbody>
</table>
iron-folic acid supplementation program for the prevention of iron-deficiency anemia.

The social marketing and mobilization strategy emphasized the “5 P’s” approach: public relations and collaboration, product, price, place, and promotion. The supplements used during phase one of the project were produced and packaged in the Philippines in a foil package containing four tablets, sufficient for 1 month. Although the product was suitable for Vietnam, Vietnam currently does not have the capacity to produce the same product locally. A product development study is needed to assess the local feasibility and means to provide an affordable, acceptable product for use in a national program.

A convenient distribution channel was also a critical issue for success of the project. Distribution of the iron-folic acid tablets for WRA in this project involved two systems: 1) the health station staff distributing the supplement to pregnant women from a central location, and 2) the Women’s Union collaborators distributing to non-pregnant women in their communities. The local Women’s Union network is a reliable, respected community organization whose members are highly esteemed. The positive attributes of distribution through the Women’s Union network included the important motivational role that these women collaborators played by sharing understanding and problems about anemia with WRA, since they understood well the local situation. They were able to help local residents to view the supplement not as a curative medicine, but as a preventive measure purchased through local market channels.

The compensation paid to the women collaborators was small compared with their contribution to the success of the project. This was due to the fixed price subsidized to suit the economic conditions of the community, which allowed only a small margin for compensation. The price of the tablet, 1000 VDN ($0.08 US) for one pack of four tablets, was underpriced compared with production costs; however, the low socioeconomic status

Table 3. Reported Buying and Using Iron-Folic Acid Supplements by Non-Pregnant Women in the Two Intervention Districts in Vietnam in 2003 (Project Expansion Phase)

<table>
<thead>
<tr>
<th>Month</th>
<th>Thanh Mien</th>
<th>Binh Giang</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2003</td>
<td>13,845</td>
<td>10,054</td>
</tr>
<tr>
<td>April 2003</td>
<td>15,535</td>
<td>10,486</td>
</tr>
<tr>
<td>May 2003</td>
<td>17,119</td>
<td>11,142</td>
</tr>
<tr>
<td>June 2003</td>
<td>17,524</td>
<td>11,284</td>
</tr>
<tr>
<td>July 2003</td>
<td>19,443</td>
<td>12,308</td>
</tr>
<tr>
<td>August 2003</td>
<td>21,462</td>
<td>12,642</td>
</tr>
<tr>
<td>September</td>
<td>20,045</td>
<td>10,685</td>
</tr>
<tr>
<td>October</td>
<td>18,939</td>
<td>10,404</td>
</tr>
<tr>
<td>November</td>
<td>18,642</td>
<td>10,243</td>
</tr>
</tbody>
</table>
of the populations in the 19 rural project communes required this subsidy. It is expected that as the project expands, the larger market demand will increase the size of the revolving fund available to compensate collaborators.

Promotional activities contributed significantly to changing and sustaining behaviors of WRA in the community. WRA were knowledgable about the existence of nutritional anemia from the beginning of the project. However, they were less knowledgable about ways to prevent it, such as taking BHHH weekly. This situation changed during the project as a result of promotional activities. Thus, promotional reinforcement activities are important and need to be sustained to build and strengthen the knowledge base and participation.

The need for continuous educational and promotional activities was obvious from observing the rate of buying and using BHHH by WRA. Although high through the first 9 months of the project, sales suddenly dropped after 9 months. Our investigation revealed that this occurred because of a rumor that taking BHHH would cause interruption of pregnancy and certain diseases. Regular communication and educational activities were needed to counteract unanticipated negative influences, especially among women who travel outside their communes, where they might be exposed to inaccurate information. Moreover, WRA were very busy in the harvest season and often forgot to take the supplement regularly; therefore, they need reminders during this time.

Some WRA complained of side effects from weekly iron-folic acid supplements in the first months, such as vomiting, constipation, itchiness, indigestion, etc. After that period, however, these complaints decreased. These side effects noted above appeared to be more common in subjects taking daily supplementation compared with weekly supplementation. Nevertheless, due to lack of a placebo control, no definitive conclusion is possible from this study. An earlier study in Indonesia indicated that the daily supplement caused greater side effects than the weekly supplement.

The savings generated in the revolving fund from selling BHHH was used to finance the purchase of a domestically produced iron-folic acid supplement in order to maintain and expand the program. However, the form of the domestic supplement was less attractive than BHHH and the content of folic acid was higher (0.4 mg). The Women’s Union collaborators had to exert greater efforts to encourage and motivate the WRA to regularly buy and use the domestic product without receiving extra benefits. The funds generated from selling project BHHH were small ($10,000 US), sufficient only to buy enough domestic supplements to expand and maintain the project in two districts. The Women’s Union collaborators did not receive benefits from other health care programs under the management of the district and commune steering committees. These constraints need careful consideration to ensure that an expanded project would continue to be effective.

Consideration should be given to providing all adolescent girls with the iron-folic acid supplement, since they have higher requirements than can be met through the common diet. Furthermore, their iron status needs to be improved in preparation for motherhood. Preventive iron-folic acid supplementation for adolescent girls through the educational system deserves consideration. In phase one of this project, high school girls received BHHH through their mothers or sisters. Since then, the strategy was changed and BHHH tablets were provided to adolescent girls through the school system. Preliminary results indicate a higher compliance rate in these girls in phase two than in phase one.

CONCLUSION

The new approach introduced by the present project created a significant impact on changing KAP of WRA toward the prevention and control of nutritional anemia, especially by weekly iron-folic acid supplementation. This model revealed that the systematic application of the social marketing and mobilization approach was feasible and accomplishable in promoting preventive supplementation in the Vietnamese context, particularly in a rural community setting. The approach merits further development to generate a sustainable prevention and control program for iron-deficiency anemia in Vietnam at the national level.

ACKNOWLEDGEMENT

WHO funded this project. The project implementing team would like to gratefully acknowledge the participation and support of the leaders and WRA in the two intervention districts, Thanh Mien and Binh Giang, in the Hai Duong Province.

REFERENCES


Community Mobilization and Social Marketing to Promote Weekly Iron-Folic Acid Supplementation in Women of Reproductive Age in Vietnam: Impact on Anemia and Iron Status

Jacques Berger, Hoang Thi Kim Thanh, Tommaso Cavalli-Sforza, Suttilak Smitasiri, Nguyen Cong Khan, Silvano Milani, Pham Thuy Hoa, Nguyen Dinh Quang, and Fernando Viteri

The community mobilization and social marketing program promoting a preventive approach of weekly iron-folic acid supplementation in women of reproductive age improved iron status of non-pregnant women in Vietnam. Three to six months of weekly pre-pregnancy supplementation and regular weekly intake of supplements during pregnancy allowed women to achieve good iron and hemoglobin status during the two first trimesters of pregnancy. In the third trimester, iron deficiency and anemia were notably present but low birth weight prevalence was low. This demonstrates the effectiveness and safety of the preventive approach as implemented here to prevent and control iron deficiency and anemia in women of reproductive age before and during pregnancy.

Key words: anemia, weekly iron-folic acid supplementation, community mobilization, reproductive age women, social marketing

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INTRODUCTION

Iron deficiency, which in its most severe form results in anemia, is a major health problem in developing countries, where it affects about 3.5 billion people throughout the world, mainly women of reproductive age (WRA), infants, and young children. In Vietnam, the National Nutrition Risk Factor Survey in 1995 reported a high prevalence of anemia: about 40% to 50% in young children and in adult women, both pregnant and non-pregnant. Insufficient iron intake and/or low iron bioavailability were identified as important factors in the etiology of anemia, although other important contributing factors (such as hookworm infection) that increase iron losses were also highlighted. A more recent Nutrition Risk Factor Survey, based on data collected in the year 2000, showed that the mean prevalence of anemia had decreased to about 34% in young children and 25% in women. However, anemia remains a significant public health problem in Vietnam (Khoi HH, Khan NC, Mai LB, unpublished data).

The consequences of anemia and iron deficiency are multiple and serious, affecting not only the health of individuals, but also the development of societies and countries. In the adult, anemia and iron deficiency result in a reduction of physical capacity and productivity. In pregnant women, severe anemia is responsible for 20% of maternal deaths related to childbirth and also increases the risk of fetal and neonatal morbidity and mortality, prematurity, and low birth weight.

The prevention and control of iron deficiency and anemia require that different interventions, such as dietary improvement, food fortification, supplementation, treatment of anemia, and several other public health actions, are integrated. However, at some periods of life, especially during pregnancy and in infants and young children, iron requirements are high and fortification of...
staple foods and/or supplementation should be considered.

Current recommendations are for daily supplementation of pregnant women with iron-folic acid tablets continuing up to 2 months postpartum. When the prevalence of anemia is high, the recommendation is that iron supplementation should be extended to all WRA and young children. However, only daily antenatal iron-folic acid supplementation is usually applied, generally with a therapeutic orientation. In most situations, this supplementation schedule, delivered through the health services, does not have a significant public health impact because of: 1) insufficient coverage of the at-risk populations, 2) the absence of political commitment and financial support, 3) deficiencies in supply and distribution of the supplements to health centers, 4) beliefs and cultural practices of the providers and recipients, 5) inadequate training of health workers, 6) inadequate information among recipients, 7) undesirable side effects, 8) and the presentation and characteristics of the supplements.

To date, nearly all studies evaluating the efficacy or effectiveness of intermittent iron supplementation to pregnant women were conducted during the course of pregnancy and often compared to daily supplementation. However, weekly iron-folic acid supplementation starting before pregnancy and continuing throughout is preventive and ensures a satisfactory iron and hemoglobin (Hb) status throughout the reproductive life of the woman. Preventive supplementation would enable women to begin pregnancy with optimal iron reserves in order to avoid iron deficiency during pregnancy. Moreover, most previous studies evaluated the effect of supervised distribution of supplements. What is needed are studies to assess the effectiveness of the weekly iron-folic acid supplementation approach under usual program conditions accompanied by community-based social mobilization and social marketing initiatives. Such a plan was developed in Vietnam, as presented in a previous paper, and had a positive impact on knowledge, attitudes, and practices (KAP) of women and on the use of weekly iron-folic acid pills.

This paper presents the impact of this program on iron status in WRA through the evaluation of the effectiveness of weekly iron-folic acid supplementation (60 mg iron and 3.5 mg folic acid) before pregnancy, followed by weekly iron-folic acid supplementation during pregnancy (120 mg iron and 3.5 mg folic acid), in preventing and controlling anemia and iron deficiency in WRA. This approach was compared with the usual practice in Vietnam and elsewhere of giving daily iron-folic acid pills from the first antenatal visit onward. In addition, the project aimed to define the duration of pre-pregnancy preventive iron-folic acid supplementation needed to have the desirable impact on Hb and iron stores under non-supervised program conditions.

**SUBJECTS AND METHODS**

The study was implemented from April 1999 to December 2000 in all 19 communes of the Thanh Mien district in the Hai Duong province located in the Red River Delta 70 km southeast of Hanoi. Selection criteria for the study site included lack of interventions to control iron deficiency anemia in non-pregnant women and approval of the study by local health authorities. This rural district had a population of 135,000 living in 32,865 households and about 33,000 WRA. All WRA of the 19 communes of Thanh Mien district had the opportunity to participate in the program. All women included in the study were informed by the social marketing campaign about the benefits of taking preventive iron-folic acid supplementation before and during pregnancy, combined with improved diets.

Women recruited for the study were married, willing to participate in the evaluation, nulliparous, and planning to have a child as soon as possible or pregnant for the first time. A brief medical examination was included at baseline to exclude women with gastrointestinal or metabolic disorders. Participating women were allocated to two treatments according to their pregnancy status at baseline:

1. **Daily treatment**: women who were pregnant at baseline. These women were directed to a health center to receive free of charge UNICEF tablets (60 mg iron and 0.25 mg folic acid) and instructed to take one tablet per day. Health centers were provided with the UNICEF tablets.

2. **Weekly treatment**: women who were non-pregnant at baseline who could buy the weekly pink tablets made by United Laboratories (UNILAB), Manila, Philippines, and sold in each village by collaborators from the Women’s Union. When pregnancy was detected, the pregnant women received weekly the red tablets free of charge from the same collaborators of the Women’s Union (for a description of the red and pink UNILAB tablets, please see Khan et al.). After delivery, women were given weekly pink tablets for 3 months free of charge. At the end of this period, these women were expected to purchase the iron tablets the same way as other non-pregnant WRA.

The protocol of the study stated that at the end of the intervention, the cohort of non-pregnant women of the weekly group would be divided into three groups: 1) those women who remained non-pregnant during the study period; 2) those women who became pregnant.
within the first 3 months after baseline; and 3) those women who became pregnant between the first day of the fourth month and the last day of sixth month after baseline. The outcomes in the women who took daily supplements would then be compared with the corresponding group of women who took weekly supplements.

The sample size was estimated to be 120 subjects per group based on a difference of 5 g/L Hb concentration between any two groups or between any two times of blood sampling, with a confidence interval of 95% (two-sides test, SD = 12 g/L) and a power of 90%. Assuming a dropout rate of about 20%, the initial sample size required was estimated to be 150 subjects per group.

The probability that a WRA, married, nulliparous, and planning to have a child as soon as possible would become pregnant within 1 year was estimated to be about 60%. Then 1000 non-pregnant women were needed at the beginning of the study to obtain about 600 pregnancies per trimester.

The iron-folic acid tablets were produced especially for this project by UNILAB and packed according to the criteria defined by the social marketing approach in Vietnam. The tablets were packaged in foil to ensure stability and protection, each package containing four supplements (a 1-month supply). Tablets were available immediately after baseline at the time when the social marketing campaign started.

Blood samples were collected at baseline (visit 1), i.e., before the supplements were available, and after 4.5 months (visit 2), 9 months (visit 3), and 12 months (visit 4). At each sampling, 4 mL of venous blood was drawn into EDTA-containing tubes. Tubes were kept cool and transported to the laboratory at the National Institute of Nutrition (NIN) in Hanoi within 8 h. Hb concentration, serum ferritin and serum transferrin receptors (TfR) were measured at each of the four visits. TfR levels were measured on a subsample of subjects. Hb was determined in whole blood by the cyanmethemoglobin method within 12 h. Serum was separated by centrifugation at 5000 \( \times \) g for 10 min at 4°C. A aliquots of serum were stored at -20°C until analysis of serum ferritin and TfR at the end of the study. Serum ferritin was measured by a two-site enzyme-linked immunosorbent assay using monoclonal reagents for both the capture and indicator antibodies. TfR were measured with a similar assay using double-monoclonal antibodies against intact TfR purified from human placenta.

Anemia in non-pregnant women was defined as Hb < 120 g/L and in pregnant women as Hb < 110 g/L. However, as a cutoff of Hb < 105 g/L had been suggested during the second trimester of pregnancy, prevalence of anemia was also measured using this cutoff.

Low iron stores were defined by serum ferritin less than 12 \( \mu \)g/L \(^{17}\) and tissue iron deficiency by TfR higher than 8.5 mg/L. \(^{18}\) Iron deficiency was defined by low serum ferritin value or elevated TfR value and iron deficiency anemia by the simultaneous presence of iron deficiency and anemia.

**STATISTICAL ANALYSIS**

Analysis of variance was applied for quantitative response variables and logistic regression for binary response variables. The models were fitted with Proc GLM and Proc Genmod (SAS release 8.2 for Windows, SAS institute, Cary, NC). When data were not normally distributed, statistical analysis was carried out after log transformation. For continuous response variables (Hb, serum ferritin, TfR), results are presented as means and standard deviation or geometric means for log-transformed data. Prevalence data are given for binary indicators (anemia, iron deficiency indicators).

For non-pregnant women, to take into account the repeated measurement structure in the data, repeated measure models were used. After choosing a suitable model for the covariance structure of the error terms, models featuring visits (one to four), group (pregnancy status of women taking daily treatment or weekly treatment), and interaction group as fixed effects were fitted using maximum likelihood estimation. The effect of treatment on the evolution of the response variables was assessed by the test of group (null hypothesis of no differential evolution between two groups). Contrasts were computed to assess differential evolution between groups for specific visits, difference between groups at each visit, and/or difference between visits within groups. The models were fitted with Proc Mixed and Proc Genmod. At each analysis, points in the distribution of Hb and serum ferritin were plotted to gather further information on the prevalence of low and high values that have been associated with risks of poor pregnancy outcomes.

The Scientific Committees of NIN, Hanoi, and of the Ministry of Health reviewed and approved the study protocol. All women were informed orally and in writing about the aims and procedures of the study, and informed written consent was obtained from all women before enrollment in the study.

**RESULTS**

The study profile is presented in Figure 1. According to the protocol, 1000 non-pregnant women and 150 women pregnant at baseline should have been included in the study. However, only 912 women agreed to participate and were included in the study. Forty-eight
women did not come at baseline. Thus, 864 women participated in the study, 163 in the daily group, and 701 in the weekly group.

At the end of study period, 87 women were excluded from data analysis for the following reasons: 31 women had miscarried, 12 in the daily group (7.4%) and 19 in the weekly group (7.5%); 24 women indicated two or more different delivery dates, 12 in the daily group and 12 in the weekly group; 18 women took both the UNICEF and UNILAB tablets during their pregnancy (9 in daily group and 9 in weekly group); and 14 women had no indication of their pregnancy status (13 in daily group and 1 in weekly group). Moreover, data analysis of weeks of gestation at each visit indicated that 45 women of the weekly group were in fact already pregnant at baseline (because most of the women knew of their pregnancy only during the second trimester of pregnancy). Data of these women were excluded from statistical analysis. Thus, 732 women were included in the data analysis, 117 in the daily group (71.8% of those who participated in the data collection) and 615 in the weekly group (87.7%).

Considering women included in data analysis, 7 women (6.0 %) dropped out in the daily group and 187 (30.4 %) in the weekly group between baseline and the end of the intervention period. Dropouts occurred mainly between baseline and visit number 2. Reasons for most of the dropouts were refusal by members of the family, especially mothers-in-law and husbands, to allow the women to participate. Body weight and hematological values at inclusion in the study were not significantly different between dropouts and women who completed the study, either in the daily or in the weekly group.

**Impact on Anemia and Iron Status in Non-Pregnant Women**

Table 1 presents the changes in hematological values at the four evaluation periods for women of the weekly group who were not pregnant at each evaluation period. The Hb concentration increased significantly from visit 1 to visit 2, again from visit 2 to visit 3, and decreased significantly from visit 3 to visit 4 (P < 0.0001). However, at visits 3 and 4, Hb was significantly higher than at visit 1. Figure 2 shows that from visit 2 on, Hb distributions were shifted to higher concentrations.
compared with visit 1, and the tail of low Hb was almost eliminated (Hb \( \leq 110 \) g/L dropped from 14.2% at baseline to 3.6% at visit 3). Serum ferritin values lower than 12 \( \mu g/L \) decreased at each visit during the study (\( P < 0.02 \)). TfR were measured only at visit 1 and visit 4 and only on a subsample of subjects (\( N = 230 \) at visit 1 and \( N = 147 \) at visit 4). TfR concentration did not change significantly between these visits.

Anemia, iron deficiency, and iron-deficiency anemia decreased from baseline to visit 3. As indicated above, these statistical analyses included at each time all women who were not pregnant at that time. Statistical analysis of

**Table 1.** Hemoglobin (Hb), Serum Ferritin (SF), and Transferrin Receptor (TfR) Concentrations, and Anemia (Hb \( \leq 120 \) g/L), Iron Deficiency (ID), and Iron-Deficiency Anemia (IDA) Prevalence at Each Visit in Non-Pregnant Women

<table>
<thead>
<tr>
<th>Visit*</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>( p^i )</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>615</td>
<td>352</td>
<td>265</td>
<td>238</td>
<td></td>
</tr>
<tr>
<td>Hb (g/L)$^a$</td>
<td>121.2 (12.0)$^a$</td>
<td>124.3 (14.3)$^b$</td>
<td>129.0 (10.7)$^c$</td>
<td>126.9 (10.1)$^d$</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SF (( \mu g/L ))^§</td>
<td>40.7$^a$</td>
<td>44.7$^a$</td>
<td>50.6$^b$</td>
<td>40.9$^a$</td>
<td>0.0016</td>
</tr>
<tr>
<td>(38.3–43.4)</td>
<td>(41.0–48.6)</td>
<td>(45.9–55.8)</td>
<td>(37.0–45.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TfR (mg/L)$^§$</td>
<td>4.9</td>
<td>5.0</td>
<td>0.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4.7–5.2)</td>
<td>(4.7–5.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>45.6$^a$</td>
<td>29.0$^b$</td>
<td>19.7$^c$</td>
<td>19.1$^c$</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ID (%)</td>
<td>8.9$^a$</td>
<td>5.5$^a,b$</td>
<td>4.0$^b$</td>
<td>5.1$^a,b$</td>
<td>0.02</td>
</tr>
<tr>
<td>IDA (%)</td>
<td>8.6$^a$</td>
<td>3.0$^{a,b}$</td>
<td>1.4$^b$</td>
<td>1.0$^b$</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Visit 1 = baseline; visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.

†Group times visit interaction term: Repeated measure ANOVA for Hb, SF, and TfR (carried out on log-transformed values for SF and TfR) and logistic regression for binary variables (prevalence): different letters indicate significant differences between visits (after Bonferroni correction for group vs. group comparison at same time).

§Mean (SD).

TfR were measured in 230 and 147 women, respectively, for the daily group and the weekly group at visit 2.

**Figures 2.** Hemoglobin distributions in non-pregnant women at each of four visits: baseline (visit 1); 4.5 months (visit 2); 9 months (visit 3); and 12 months (visit 4) after baseline.
data of women who were never pregnant during the study period led to similar results.

The number of UNILAB tablets bought by the non-pregnant women per month was 3.0 ± 1.6 (mean ± SD) between baseline and visit 2; 2.5 ± 1.9 between visits 2 and 3; and 2.0 ± 1.9 between visits 3 and 4.

Impact on Anemia and Iron Status during Pregnancy

The design of the study and the low sample size of women who became pregnant during the study led us to analyze iron status variables according to trimester of pregnancy of women who took weekly and daily supplements. Table 2 presents the sample size and pregnancy/lactation status expressed by the range of weeks and number of days (mean ± SD) of pregnancy and lactation at each visit.

Table 3 indicates the mean and range of UNICEF and UNILAB tablets ingested by the women. In the weekly group, these were calculated from the theoretical number of pink and red UNILAB tablets that they were expected to ingest according to their pregnancy status, and to the mean number of tablets bought by pregnant women each month. The mean number of UNILAB tablets bought per month by non-pregnant women during the study period was 3.5 tablets, but decreased to an average of about 2.7 tablets between visits 3 and 4. For the weekly group, the total number of UNILAB tablets bought at visits 2, 3, and 4 was 17, 34, and 44, respectively. This table also shows the number of pink UNILAB tablets used by women before the start of pregnancy for each trimester of pregnancy. This number increased with each visit. For example, women in the first trimester of pregnancy had consumed, prior to pregnancy, on average, 11 pink UNILAB tablets by the time of visit 2; 29 tablets by visit 3; and 36 tablets by visit 4; whereas the number of red UNILAB tablets consumed was about the same for all visits (mean range 5–8).

Considering women in their first trimester of pregnancy, data were available at baseline for 70 women in the daily group and for 58, 40, and 23 women, respectively, at visits 2, 3, and 4 for the weekly group for a total of 121 women (Table 4). In the weekly group, mean Hb was significantly higher at visits 3 and 4 compared with weekly visit 2 and daily visit 1, and the Hb distribution showed no women with values lower than 100 g/L, while 10.5% had levels above 135 g/L at visit 3 (not shown). Mean serum ferritin was not significantly different between the weekly and daily groups. The prevalence of anemia was significantly lower in the weekly group at visits 3 and 4 compared with visit 2, and also lower compared with the daily group. By then none of the women had iron-deficiency anemia in the weekly group.

For women in the daily group in the second trimester of pregnancy, data were available from 46 women who had been evaluated at visit 1 and from 8 women at visit 2 (Table 2). As women in the daily group received the UNICEF tablets daily since pregnancy was detected, data from both visits were pooled (Table 5). Hb was not

Table 2. Sample Size, Number of Weeks (Range), and Days (Mean ± SD) of Pregnancy and Lactation of Women at Each Visit According to their Pregnancy/Lactation Status at Every Visit

<table>
<thead>
<tr>
<th>Visit*</th>
<th>Non-Pregnant</th>
<th>Trimester 1</th>
<th>Trimester 2</th>
<th>Trimester 3</th>
<th>Lactating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daily Group</td>
<td>Weekly Group</td>
<td>Daily Group</td>
<td>Weekly Group</td>
<td>Daily Group</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>— — — —</td>
<td>615 352 265 238</td>
<td>— — — —</td>
<td>— — — —</td>
<td>— — — —</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>70 — — —</td>
<td>— 58 40 23</td>
<td>— 1-13 1-13 6-13</td>
<td>— 47 (25) 41 (24) 67 (19)</td>
<td>— — — —</td>
</tr>
<tr>
<td>Days of pregnancy</td>
<td>120 (23) 177 (10) — —</td>
<td>— 128 (16) 145 (30) 140 (26)</td>
<td>— 128 (16) 145 (30) 140 (26)</td>
<td>— — — —</td>
<td>— — — —</td>
</tr>
<tr>
<td>Days of pregnancy</td>
<td>191 233 (22) — —</td>
<td>— 232 (24) 235 (25)</td>
<td>— 67 52 (31)</td>
<td>— — — —</td>
<td>— — — —</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>— 9 107 110 — —</td>
<td>— 2 — 67</td>
<td>— 2 — 67</td>
<td>— — — —</td>
<td>— — — —</td>
</tr>
<tr>
<td>Days of lactation</td>
<td>— 32 (27) 104 (33) 190 (34) — —</td>
<td>— 2 — 67</td>
<td>— 2 — 67</td>
<td>— — — —</td>
<td>— — — —</td>
</tr>
<tr>
<td>Total no. of subjects</td>
<td>117 102 107 110</td>
<td>615 443 411 428</td>
<td>615 443 411 428</td>
<td>615 443 411 428</td>
<td>615 443 411 428</td>
</tr>
</tbody>
</table>

*Visit 1 = baseline; visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.
significantly different between the three visits in the weekly group, but the mean Hb in the weekly group was significantly higher at visits 3 and 4 compared with the daily group. As in trimester 1, there was a reduction of lower Hb values at visits 3 and 4 with weekly supplementation compared with visit 2 and with the daily group: 13.0% of women in the daily group and 16.1% in the weekly group at visit 2 had Hb values under 95 g/L compared with 1.7% and 7.3%, respectively, at visits 3 and 4 in the weekly group (Figure 3). At the same time, with a cutoff at 110 g/L, large increments in anemia in both supplementation groups occurred: 25% in the daily group and 12%, 26%, and 31%, respectively, at visits 2, 3, and 4 of weekly groups. However, the prevalence of anemia was significantly lower in the weekly group at visits 3 and 4 compared with the daily group, and the prevalence of anemia in the weekly group at visit 2 was intermediate.

Similar results were obtained when the prevalence of anemia was calculated with the cutoff of 105 g/L with a cutoff at 110 g/L, large increments in anemia in both supplementation groups occurred: 25% in the daily group and 12%, 26%, and 31%, respectively, at visits 2, 3, and 4 of weekly groups. However, the prevalence of anemia was significantly lower in the weekly group at visits 3 and 4 compared with the daily group, and the prevalence of anemia in the weekly group at visit 2 was intermediate.

### Table 3. Estimated Number of UNICEF (Daily Group) and UNILAB Tablets (Weekly Group) Used by Women at Each Visit According to their Pregnancy Status*

<table>
<thead>
<tr>
<th>Group</th>
<th>Daily UNICEF Tablets</th>
<th>Weekly UNILAB Tablets†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visit 2‡</td>
<td>Visit 3</td>
</tr>
<tr>
<td>Non-pregnant</td>
<td>—</td>
<td>14</td>
</tr>
<tr>
<td>Trimester 1</td>
<td>10 (0-31)</td>
<td>25</td>
</tr>
<tr>
<td>Pink§</td>
<td>6 (1-11)</td>
<td>5 (1-11)</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>Trimester 2</td>
<td>68 (38-129)</td>
<td>2 (0-5)</td>
</tr>
<tr>
<td>Pink§</td>
<td>15 (12-17)</td>
<td>18 (13-24)</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>Trimester 3</td>
<td>171 (143-220)</td>
<td>—</td>
</tr>
<tr>
<td>Pink§</td>
<td>—</td>
<td>30 (24-33)</td>
</tr>
<tr>
<td>Total</td>
<td>—</td>
<td>33</td>
</tr>
</tbody>
</table>

*Means (range).
†Mean number of tablets used by women in the weekly group was calculated based on the theoretical number of pink and red tablets they were expected to use according to their pregnancy status and to the mean number of tablets bought by non-pregnant women each month.
‡Visit 1 = baseline (not shown); visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.
§Containing 60 mg iron and 3.5 mg folic acid.
<table>
<thead>
<tr>
<th>Group</th>
<th>Daily Group</th>
<th>Weekly Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>70</td>
<td>58</td>
</tr>
<tr>
<td>Hb (g/L)§</td>
<td>111.3 (14.6)a</td>
<td>115.2 (14.9)a</td>
</tr>
<tr>
<td>SF (ug/L)§</td>
<td>57.5 (48.7-67.9)</td>
<td>52.5 (43.4-63.5)</td>
</tr>
<tr>
<td>TfR (mg/L)§</td>
<td>4.1 (3.5-4.7)</td>
<td>3.4 (2.6-4.4)</td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>40.0a</td>
<td>33.3a</td>
</tr>
<tr>
<td>ID (%)</td>
<td>8.6</td>
<td>7.3</td>
</tr>
<tr>
<td>IDA (%)</td>
<td>6.7</td>
<td>0</td>
</tr>
</tbody>
</table>

*Visit 1 = baseline; visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.
†ANOVA for Hb and SF values (carried out on log-transformed values for SF) and logistic regression for binary variables (prevalence): different letters indicate significant differences between visits.
‡M ean (SD).
§Geometric mean (confidence interval).
||TfR were measured in 60 and 44 women, respectively, for the daily group and the weekly group at visit 2.

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prevalence of 53.7% for the daily group and 35.5%, 17.2%, and 14.6% (P < 0.0001), respectively, for the weekly groups at visits 2, 3, and 4. Serum ferritin was not significantly different between visit and groups, whereas TfR were significantly lower in the weekly group at visits 2 and 3 compared with the daily group. Prevalence of iron deficiency was lower at visits 3 and 4 compared with visit 2 in the weekly group and with the daily group. Iron-deficiency anemia had disappeared at visits 3 and 4 in the weekly group.

In women in the third trimester of pregnancy, data were available only at visit 2 for the daily group and at visits 3 and 4 for the weekly group (Table 6). In the weekly group, Hb was significantly higher at visit 3 than

Table 5. Hemoglobin (Hb), Serum Ferritin (SF), and Tranferrin Receptor (TfR) Concentrations, and Anemia (Hb < 110 G/L), Iron Deficiency (ID), and Iron-Deficiency Anemia (IDA) Prevalence at Each Visit in Pregnant Women in their Second Trimester of Pregnancy

<table>
<thead>
<tr>
<th>Visit*</th>
<th>Daily Group</th>
<th>Weekly Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 and 2</td>
<td>2</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>54</td>
<td>33</td>
</tr>
<tr>
<td>Hb (g/L)‡</td>
<td>105.9 (13.9)a</td>
<td>110.5 (13.6)a,b</td>
</tr>
<tr>
<td>SF (ug/L)§</td>
<td>44.7</td>
<td>34.6</td>
</tr>
<tr>
<td>(35.8-55.7)</td>
<td></td>
<td>(26.6-45.0)</td>
</tr>
<tr>
<td>TfR (mg/L)§</td>
<td></td>
<td>4.3</td>
</tr>
<tr>
<td>(3.8-4.8)a</td>
<td></td>
<td>(2.4-3.5)b</td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>64.8a</td>
<td>45.2a,b</td>
</tr>
<tr>
<td>ID (%)</td>
<td>11.1a</td>
<td>12.5a</td>
</tr>
<tr>
<td>IDA (%)</td>
<td>13.8</td>
<td>4.8</td>
</tr>
</tbody>
</table>

*Visit 1 = baseline; visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.
†ANOVA for Hb and SF values (carried out on log-transformed values for SF) and logistic regression for binary variables (prevalence): different letters indicate significant differences between visits.
‡Mean (SD).
§Geometric mean (confidence interval).
||TfR were measured in 44, 22, and 38 women, respectively, for the daily group and the weekly group at visits 2 and 3.
}

Figure 3. Hemoglobin distributions among pregnant women in their second trimester of pregnancy while taking a daily iron-folic acid supplement compared with a weekly supplement at 4.5 months (visit 2), 9 months (visit 3), and 12 months (visit 4) after baseline.
Table 6. Hemoglobin (Hb), Serum Ferritin (SF), and Tranferrin Receptor (TfR) Concentrations, and Anemia (Hb < 110 g/L), Iron Deficiency (ID), and Iron-Deficiency Anemia (IDA) Prevalence at Each Visit in Pregnant Women in their Third Trimester of Pregnancy

<table>
<thead>
<tr>
<th>Visit*</th>
<th>Daily Group</th>
<th>Weekly Group</th>
<th>Daily Group</th>
<th>Weekly Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>85</td>
<td>45</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>110.4 (14.0)a</td>
<td>117.3 (9.7)b</td>
<td>111.8 (11.1)a</td>
<td>0.01</td>
</tr>
<tr>
<td>SF (ug/L)</td>
<td>21.0</td>
<td>19.5</td>
<td>18.9</td>
<td>0.75</td>
</tr>
<tr>
<td>(17.5–25.2)</td>
<td></td>
<td>(15.3–24.9)</td>
<td>(14.9–24.1)</td>
<td></td>
</tr>
<tr>
<td>TfR (mg/L)</td>
<td>5.0</td>
<td>4.3</td>
<td>5.2</td>
<td>0.12</td>
</tr>
<tr>
<td>(4.5–5.4)</td>
<td></td>
<td>(3.7–5.0)</td>
<td>(4.6–5.8)</td>
<td></td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>46.9 a</td>
<td>20.9b</td>
<td>40.0a</td>
<td>0.02</td>
</tr>
<tr>
<td>ID (%)</td>
<td>34.6</td>
<td>38.6</td>
<td>24.4</td>
<td>0.33</td>
</tr>
<tr>
<td>IDA (%)</td>
<td>30.6</td>
<td>15.0</td>
<td>12.9</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Visit 1 = baseline; visit 2 = 4.5 months after baseline; visit 3 = 9 months after baseline; visit 4 = 12 months after baseline.
†ANOVA for Hb and SF values (carried out on log-transformed values for SF) and logistic regression for binary variables (prevalence): different letters indicate significant differences between visits.
‡Mean (SD).
§Geometric mean (confidence interval).
||TfR were measured in 75, 35, and 25 women, respectively, for the daily group and the weekly group at visits 3 and 4.

at visit 4 and significantly higher in the weekly group at visit 3 than in the daily group at visit 2. Figure 4 shows that the Hb distribution of the weekly group at visit 3 was shifted to higher Hb concentrations compared with those of the weekly group at visit 4 and those of the daily group. Serum ferritin and TfR in the weekly group were not significantly different compared with the daily group or between visits in the weekly group. Serum ferritin distributions were strongly skewed to the left (not shown), which explains the higher prevalence of iron deficiency at this stage of pregnancy. The prevalence of anemia in the weekly group was significantly lower at visit 3 compared with visit 4 and with the daily group. No woman had an Hb concentration lower than 95 g/L at

Figure 4. Hemoglobin distributions among pregnant women in their third trimester of pregnancy while taking a daily supplement compared with a weekly supplement at 9 months (visit 3) and 12 months after baseline (visit 4).
visit 3 in the weekly group, whereas 8.9% in the weekly group at visit 4, and 12.3% in the daily group had Hb levels below 95 g/L. The prevalence of iron deficiency or iron-deficiency anemia was not significantly different between groups and between visits in the weekly group.

Considering lactating women, data were available at visits 2, 3, and 4 for the daily group and at visits 3 and 4 for the weekly group. Data in both groups were pooled independently of the visits (Table 7). There was no difference between groups or visits for any variable except serum ferritin, which was significantly lower in the daily group than in the weekly group. Several women in the daily group had high serum ferritin levels (14% had serum ferritin > 100 µg/L). Only 1.5% of the women in the weekly group and 0.5% in the daily group had Hb under 95 g/L and less than 4% had Hb under 105 g/L.

Birth weight data were available for 114 infants in the weekly group and 86 infants in the daily group. Mean (±SD) birth weight was 2989 ± 356 g in the weekly group and 2908 ± 443 g in the daily group (P = 0.15). Prevalence of low birth weight (<2500g) was 2.8% and 9.3% (P = 0.08), respectively, in the weekly and daily groups. Given the few number of cases, this difference did not reach significance, but the tendency for greater

| Table 7. Hemoglobin (Hb), Serum Ferritin (SF), and Tranferrin Receptor (TfR) Concentrations, and Anemia (Hb < 110 g/L), Iron Deficiency (ID), and Iron-Deficiency Anemia (IDA) Prevalence in Lactating Women* |
|---|---|---|---|
| **Group** | **Daily** | **Weekly** | P* |
| No. of subjects | 221 | 68 | 0.97 |
| Hb (g/L)† | 125.0 (10.4) | 125.1 (12.1) | 0.006 |
| SF (ug/L)§ | 45.9 (41.6–50.6) | 34.8 (29.9–40.6) | 0.74 |
| TFR (mg/L)¶ | 5.2 (4.9–5.5) | 5.1 (4.6–5.6) |
| Anemia (%) | 29.0 (23.6) | 34.2 (29.9–40.6) | 0.35 |
| ID (%) | 8.8 (7.1) | 13.2 (12.1) | 0.20 |
| IDA (%) | 6.5 (5.1) | 6.1 (5.1) | 0.61 |

*For lactating women, data were available at visits 2, 3, and 4 for the daily group and at visits 3 and 4 for the weekly group. Data in both groups were pooled independently of the visits.
†ANOVA for Hb and SF values (carried out on log-transformed values for SF) and logistic regression for binary variables (prevalence).
‡M ean (SD).
§Geometric mean (confidence interval).
¶TFR were measured in 126 and 56 women, respectively, for the daily group and the weekly group.

birth weight (a difference of 80 g) and lower prevalence of children with birth weight under 2500 g favored the weekly group.

**DISCUSSION**

Anemia was a public health problem in almost one-half of the non-pregnant WRA included in the study. This prevalence was similar to the national prevalence of anemia in WRA of the 1995 National Nutrition Risk Factor Survey. However, iron deficiency as measured by low serum ferritin values (less than 12 µg/L) or high TFR values (more than 8.5 mg/L) was detected only in approximately 9% of the women (18.4% of low serum ferritin values when the cutoff was 20 µg/L). A similar rate of iron deficiency, but a lower prevalence of anemia occurred in WRA in another district of the same province.

Serum ferritin is an acute-phase reactant protein that can increase dramatically with both acute and chronic infection or with B12 or folic acid deficiencies, thus masking iron deficiency. However, women with apparent infection were not included in the study, and a low prevalence of iron deficiency was confirmed by data from TFR, which are not influenced by inflammation. These results suggest that iron deficiency was not the only reason for anemia, which can also result from other micronutrient deficiencies, such as folic acid, vitamin B12, vitamin A, or riboflavin, or other causes not identified in the study, as demonstrated in Chinese and Vietnamese WRA.

Implementation of the weekly iron-folic acid preventive supplementation program improved significantly the iron status of non-pregnant WRA. The prevalence of anemia and of iron deficiency decreased significantly during the year-long study period. Comparison of the iron status of non-pregnant women at the different visits allowed for the evaluation of the effect of duration of weekly iron-folic acid supplementation: visit 2 corresponded to 4.5 months of intervention; visit 3 to 9 months; and visit 4 to 12 months. The Hb concentration had already significantly improved and the prevalence of anemia decreased after 4.5 months of weekly supplementation when women had taken, on average, 14 pink UNILAB tablets, as estimated from sales data. Mean Hb continued to increase and anemia was eliminated in the most anemic individuals when women had taken an average of 25 pink UNILAB tablets, and iron stores were significantly higher compared with baseline. These results indicate that 9 months of weekly iron-folic acid supplementation under program conditions reduces significantly the prevalence of anemia and iron deficiency to 19.7% and 4.0%, respectively. The higher prevalence of anemia after iron-folic acid supplementation compared

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with iron deficiency would point to causes of anemia other than iron or folate deficiency.

The mean Hb and serum ferritin concentrations decreased from visit 3 to visit 4, but the prevalence of anemia and iron deficiency did not change. A decrease in the compliance to treatment may account for this, as the purchase records of UNILAB tablets by all women showed a decrease in purchases from December 1999, just before visit 3; 92.5% of women bought UNILAB tablets in October 1999, 87% in December 1999, and 67.4% in January 2000. Data recorded in the non-pregnant women who participated in this study also indicated a decline in sales of the number of tablets per month between visit 3 and 4 (average of 2.0 UNILAB tablets/month between visits 3 and 4 compared with 2.5 UNILAB tablets/month between visits 2 and 3). The participation of women in sowing winter-spring crops between visits 3 and 4, with fewer opportunities for communication, contributed to this decline. Variability or defective laboratory analysis would not account for the differences between visits 3 and 4, as all serum ferritin and TfR assays were carried out at the same time at the end of the study on frozen serum, and Hb concentration was carried out with controls.

Women who became pregnant after baseline used a combination of weekly pink UNILAB tablets before pregnancy and weekly red UNILAB tablets when pregnancy was detected. Comparison of women in the same trimesters of pregnancy at the different visits allowed comparing women who received, on average, the same number of red tablets according to their trimester of pregnancy, but different numbers of pink UNILAB tablets before pregnancy (Table 3). For each trimester of pregnancy, length of supplementation before pregnancy increased with each visit.

The implementation of the pre-pregnancy part of the program had a positive effect on anemia in women in their first and second trimesters of pregnancy when weekly iron-folic acid supplements were used 3 to 6 months before the start of pregnancy and continued during pregnancy. Shorter pre-pregnancy supplementation periods were associated with lower Hb concentrations, but this was not significantly different from that of women taking daily supplementation.

In the first trimester of pregnancy, the Hb concentration was higher and the prevalence of anemia lower in the weekly group when women had used an estimated average of 29 pink UNILAB tablets (range 23–33) and an average of 5 red UNILAB tablets (range 1–11). In fact, because women were often aware of their pregnancy only after the first gestational month, they probably took more pink—and less red—UNILAB tablets than estimated here. Mean serum ferritin concentrations were not different between daily and weekly groups and between visits in the weekly group. Women who received daily supplements showed high serum ferritin values in a considerable number of cases (17.3% with values ≥ 100 μg/L). This would indicate that weekly iron supplementation performed as well as daily supplementation and at the same time prevented the excessive ferritin levels that may be associated with oxidative stress and inflammation.

In the weekly group, mean values of serum ferritin were slightly higher than in non-pregnant women at the same visits, whereas Hb concentrations were lower. This could be attributed to the normal physiological changes occurring during pregnancy, as there is evidence in the literature that serum ferritin rises modestly early in pregnancy (presumably because of reduced erythropoietic activity diverting iron to stores) and that Hb concentration decreases during the first half of pregnancy due to hemodilution. However, the prevalence of anemia in women in the first trimester of pregnancy was less than 9% at visits 3 and 4 and lower than in non-pregnant women at the same visits. None of the women had iron-deficiency anemia. These results are important in terms of public health, as low Hb values or anemia during the first half of pregnancy are associated with low birth weight and preterm delivery.

In the second trimester of pregnancy, iron requirements begin to increase and continue to do so throughout the remainder of pregnancy. The prevalence of anemia and iron deficiency were significantly lower when the length of the weekly supplementation was at least 9 months (i.e., 3 months before pregnancy started) compared with women who received the daily supplements. This corresponds to an estimated average of 34 UNILAB tablets; 16 pink tablets (range 10–21) and 18 red tablets (range 13–24). In the absence of iron reserves, the requirement for absorbed iron in second trimester of pregnancy is about 4 mg/d. Diets would have supplied some iron, but the amount of iron absorbed is low when the diet contains only small amounts of bioavailable iron in places such as in rural Vietnam.

In iron-deficient persons, dietary iron can provide as much as 1.5 mg/d even with poor availability diets. In Senegalese non-pregnant women, iron absorption from both daily and weekly iron supplements can be as high as 20% to 28%, and a weekly 120 mg dose can provide as much as 33 mg of absorbed iron (equivalent to 4.7 mg/d). The mean is 8.8% iron absorption (that is 10.5 mg/week or the equivalent of 1.5 mg/d). If 300 mg of reserves are used, 3 mg/d are available for Hb replenishment. In the absence of reserves, 60 mg/d of iron can provide as much as 3.9 mg/d, and with 300 mg of reserves available, as much as 5.2 mg/d can be available for Hb regeneration. In general, it is difficult to separate the contribution of diet and supplements and to assume a “mean” absorp-
The fact is that those women who had consumed preventive pre-pregnancy supplementation were better iron nourished throughout pregnancy consuming weekly iron than women receiving iron only during pregnancy.

Assuming 10% and 7% absorption, respectively, of the 60 mg and the 120 mg iron dose, the amount of absorbed iron from the tablets was about 6 to 9 mg per week, or about 1 mg/d (0.85 to 1.3 mg/d). This suggests that part of the iron stores were mobilized to meet the increased demands of pregnancy. The lower serum ferritin concentrations in the weekly group in the second trimester of pregnancy compared with non-pregnant women and women in the first trimester of pregnancy also suggests this process. During pregnancy, when iron needs increase, women utilize iron stores first and absorption increases markedly only after most of the storage iron has been used. However, mean values of serum ferritin concentration in women in the second trimester of pregnancy were in the range of serum ferritin concentrations among healthy women supplemented daily with 200 mg iron from the 10th week of pregnancy, and prevalence of iron deficiency was low when preventive weekly iron-folic acid supplementation started at least 3 months before pregnancy.

Assuming that each microgram of serum ferritin per liter corresponds to 8 mg of iron stores, iron stores before pregnancy of these women were on average 290 mg. About 10% of the women had no iron stores. Bothwell indicates that a pre-pregnancy iron store of 300 mg is probably sufficient to carry a woman through pregnancy if her diet is high in bioavailable iron, whereas a higher amount of stored iron is needed when the diet is less than optimal. This assumption is discussed by Lynch, who states that iron balance in pregnancy depends more on the adequacy of intake of bioavailable iron than on iron stores at conception, and that iron supplements are required during pregnancy by women consuming low amounts of absorbable dietary iron. Lynch concludes, as does Viteri, that preventive iron supplementation should be viewed as an additional strategy to supplementation during the second and third trimester. In our study, a weekly pre-pregnancy iron-folic acid supplementation for 6 months and continued during pregnancy protected women from low Hb levels (below 95 g/L) and iron deficiency.

The lower Hb concentration in women in the second trimester of pregnancy compared with non-pregnant women and women in the first trimester of pregnancy was probably mostly due to hemodilution. The longer the pre-pregnancy preventive supplementation, the better the iron nutrition during pregnancy. A shorter duration of weekly supplementation (i.e., when weekly supplementation started with pregnancy) was as efficient as the daily supplementation, but was less effective than longer preventive supplementation in protecting women against anemia. A recent study indicated that 20 doses of 60 mg of iron administered either daily or weekly to Bangladeshi anemic women in the second trimester of pregnancy increased the concentration of Hb. Unfortunately, serum ferritin levels decreased during pregnancy even when 100 mg/d of iron were administrated, reducing the diagnostic value of low serum ferritin values in pregnancy.

The third trimester of pregnancy corresponds to the period when iron needs are the highest. The dramatic decrease of iron stores and increase of iron deficiency that affected about one-third of the women in this study indicate that under the non-supervised conditions of this program, none of the treatments (daily or weekly iron-folic acid supplementation) provided enough iron to meet the needs in the third trimester of pregnancy. Low iron stores before conception must have played a role, as it seems impossible to normalize Hb concentrations during pregnancy regardless of iron dose or mode of administration unless substantial preconception iron stores exist. Hb at term correlates with initial Hb and serum ferritin concentrations. Women of the weekly group in the third trimester of pregnancy who had received no or less than 3 months of weekly supplements before pregnancy occurred probably received too little to increase iron stores to an optimum level. Indeed, as noted earlier, a period of at least 9 months of weekly supplementation, corresponding to a period of 3 to 6 months of preventive iron-folic acid supplementation before pregnancy, was required to significantly improve iron stores in non-pregnant women and induce a positive protective outcome.

Whereas the prevalence of anemia was notable, almost no women had an Hb concentration less than 95 g/L during the third trimester of pregnancy. Beaton suggested that a target mean at term for Hb of 110 g/L with a cutoff of 90 to 95 g/L of Hb that defines moderate anemia would be more relevant than the actual 110 g/L cutoff in estimating the success of a program. Perinatal risk for mother and newborns increases significantly as Hb levels fall below 90 to 100 g/L at term. In our study, less than 1.5% of women had an Hb concentration of less than 95 g/L in the third trimester. The prevalence of low birth weight was less than 3% in the weekly group and about 9% in the daily group.

**CONCLUSIONS**

Under the non-supervised conditions of the program implemented in the Than Mien district of Vietnam, weekly iron-folic acid supplementation improved the iron status of non-pregnant WRA after 12 doses based on Hb and serum ferritin, and improved more when about...
26 weekly supplements were taken (over a period of 9 months). However, improvement was fragile, which suggests that regular intake of weekly supplements in menstruating women is one of the key factors of the success of this approach, and should be recommended to insure that women begin their pregnancy with adequate iron stores and Hb concentrations.

Adequate iron stores before conception and regular intake of weekly iron-folic acid supplements during pregnancy allowed women in this study to achieve good iron and Hb status during the first and second trimesters of pregnancy. This was obtained, under non-supervised program conditions, when supplements (60 mg iron and 3.5 mg folic acid) were taken for 3 to 6 months before the beginning of pregnancy and continued weekly (120 mg iron and 3.5 mg folic acid) during pregnancy.

Due to the limited time of the study, women evaluated in their third trimester of pregnancy received only a few or no weekly iron-folic acid supplements before pregnancy, and iron stores were probably low in some of these women. Iron deficiency and anemia were notably present in women under both daily and weekly schemes, but only one woman suffered from moderate anemia. The prevalence of low birth weight was lowest among women supplemented weekly during pregnancy.

Under these non-supervised program conditions, daily iron-folic acid supplementation (UNICEF tablets containing 60 mg iron and 0.25 mg folic acid) during pregnancy was less efficient compared with the weekly approach, since the Hb concentration was lower and the prevalence of anemia higher in all trimesters of pregnancy. Still, high levels of serum ferritin were common in this group. This may not be safe for mothers and newborns.25,36

These findings demonstrate the effectiveness and safety of the preventive approach of weekly iron-folic acid supplementation, including social mobilization and social marketing components, to prevent and control iron deficiency and anemia in WRA before and during pregnancy.

ACKNOWLEDGMENTS

The authors are grateful to all women who participated in the study and to the field workers and other personnel at the National Institute of Nutrition (Hanoi), the Ministry of Health, and health authorities in Thanh Mien district for their collaboration. The technical assistance of Dr. Nguyen Xuan Ninh during blood analyses and Ms. V. Bianco during the statistical evaluation are gratefully acknowledged, as well as continued support from D. Bosch and N. Paliakara of WHO. WHO and IRD funded this study.

REFERENCES

Weekly Iron-Folic Acid Supplementation to Improve Iron Status and Prevent Pregnancy Anemia in Filipino Women of Reproductive Age: The Philippine Experience through Government and Private Partnership

Lourdes S. Paulino, Imelda Angeles-Agdeppa, Unita Mari M Etorma, Adelisa C. Ramos, and Tommaso Cavalli-Sforza

With the participation of the government and private sectors in the Philippines, weekly iron-folic acid supplementation introduced within a social marketing framework and a social mobilization campaign successfully improved knowledge and practice of buying and regularly taking supplements by women of reproductive age, both pregnant and non-pregnant. Adolescent girls in school were also active participants.

Key words: anemia, weekly iron-folic acid supplementation, reproductive age women, government/private partnerships

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INTRODUCTION

The Philippines is a tropical country in southeast Asia with an estimated population of about 80 million. About 38% of the population are under 15 years of age, and 6.5% are 65 years and older. Filipinos are almost equally divided between the sexes, with males comprising 50.4%. Women of reproductive age (WRA) comprise about 23% of the population.¹ The average life expectancy of Filipinos as projected in 1998 was 68.6 years: 71.3 years for females and 66.0 years for males.²

Iron deficiency is the most common form of micronutrient malnutrition and the most common cause of anemia in the Philippines. A national nutrition survey conducted in 1998 reported that the prevalence of anemia was 50.7% and 45.6% for pregnant and lactating women, respectively.³ Major causes of these problems were reportedly: 1) a low intake of iron-rich foods, accounting for only 64.7% of the recommended dietary allowance (RDA) for iron; 2) the presence of inhibitors such as phytates from rice, which is the main component of Filipino diets; 3) a low intake of enhancers of iron absorption such as vitamin C, which accounts for only 73% of the RDA; 4) intestinal parasites; 5) malaria and schistosomiasis, which are prevalent in some areas of the country; and 6) vitamin A deficiency.³–⁶

The Philippines’ Department of Health (DOH) implemented an iron supplementation program for pregnant and lactating women almost three decades ago. A circular issued in 1977 stated that, beginning at the fourth month of pregnancy and during lactation a supplement containing 60 mg elemental iron and 2 mg folic acid should be taken twice a day. A revised iron supplementation policy was issued in 2003 (Administrative Order No. 3-As. 2000: Guidelines on Micronutrient Supplementation), which stated that a dose containing 60 mg elemental iron and 2 mg folic acid should be taken twice a day. A revised iron supplementation policy was issued in 2003 (Administrative Order No. 3-As. 2000: Guidelines on Micronutrient Supplementation), which stated that a dose containing 60 mg elemental iron and 400 µg folic acid should be taken daily as soon as pregnancy is diagnosed, or for at least 6 months during the entire duration of pregnancy, and continued for 3 months after delivery.

In countries such as the Philippines, where supplementation programs historically have had limited success, the following constraints were identified: 1) late reporting of pregnant women to antenatal clinics; 2) low compliance to iron supplementation because of side effects; 3) inadequate awareness of health workers of the severity of the problem, who are therefore unable to
motivate and provide appropriate counseling; and 4) the erratic supply of the supplements due to financial and logistic constraints. Limited access to health care also complicates the situation.4-8

Weekly iron supplementation is a preventive approach, the objective of which is to improve and sustain the iron status of women before they become pregnant and therefore avoid their becoming anemic during the course of pregnancy.9-11 Folic acid, which usually is given with iron, combats the risk that folic acid deficiency contributes to anemia and also reduces the risk of neural tube defects.12,13 Various trials conducted using weekly iron supplementation have shown a number of advantages over daily dosing, including lower cost and better compliance to supplementation because of fewer side effects. In the 1998, the International Nutritional Anemia Consultative Group (INACG)/World Health Organization (WHO)/UNICEF14 program planners were urged to consider the feasibility and sustainability of implementing weekly supplementation within their local context.

The objectives of this weekly iron-folic acid supplementation project in the Philippines were:

- To introduce iron-folic acid supplements to WRA in the Philippines, starting with weekly doses of 60 mg elemental iron and 3.5 mg folic acid before pregnancy, continuing with a weekly dose of 120 mg elemental iron and 3.5 mg folic acid when pregnancy was detected, and for 3 months after delivery, using community-based social marketing and mobilization to promote the approach; and
- To assess the effectiveness of the approach in improving knowledge, attitudes, and practices (KAP) and the iron status of WRA in the Philippines.

This paper focuses on process, and therefore describes the project activities and results on the intervention process only. Results on the effectiveness of the approach are presented in the Philippines’ impact paper also in this publication.15

PROJECT DESCRIPTION AND DESIGN

The weekly iron-folic acid supplementation project was conducted in three selected municipalities in Pangasinan, one of the provinces in the Philippines located in northern Luzon. The study was conducted for 1 year between November 1998 and December 1999. All WRA in the three intervention municipalities, both non-pregnant and pregnant, were participants in the project.

This project was implemented by the DOH in collaboration with the United Laboratories (UNILAB) of the Philippines, the largest privately owned local pharmaceutical company in the country. To facilitate implementation, a project team was created from the DOH to involve the national coordinators with the participation of the provincial health office through its nutritionist-dietitians. In addition, technical working groups were created at the national and municipal levels. The national group served an advisory role and recommended solutions to problems identified or raised at the municipal level through monthly meetings.

Two iron preparations, both produced by UNILAB, were used and were the same supplements used in the Vietnam and Cambodia studies described elsewhere in this publication.16,17 “Femina,” which suggested femininity, was adopted as the common name for the products in the Philippines. Femina 60 was prepared for non-pregnant women, and contained 60 mg elemental iron and 3.5 mg folic acid per tablet; Femina OB was designed for pregnant women, and contained 120 mg elemental iron and 3.5 mg folic acid per tablet. Social marketing, which is the design, implementation, and control of programs seeking to increase the acceptability of a social idea or behavior in a target group, was used to promote the supplements. The goal of social marketing is social change.18 For this project, the ultimate goal was to convince WRA, including non-pregnant, pregnant, and lactating women in the Philippines, to take weekly iron-folic acid supplements regularly, as well as to improve their consumption of iron and vitamin C-rich foods. To do this effectively, project teams at the national, regional, and provincial levels were trained in social marketing and interpersonal communication skills. Rural health unit personnel and the village (“barangay”) health workers also were trained by the project team. Strategies for social marketing in the community and for the project were initiated and conducted jointly by DOH and UNILAB.

Social mobilization was an integral part of the project’s social marketing strategy. Mobilizing local officials such as the mayor, barangay captains, councilmen, and priests in the project areas was crucial to obtaining their leadership support. Strengthening municipal and barangay support for nutrition and health was adopted as a major strategy to ensure the participation and support of all sectors in the community, including local officials, health personnel, village health workers, and store owners, as well as community residents.

The social marketing strategy for this project was structured around the “4 P’s” of social marketing:

- Product: the target audiences were made aware about the importance of iron and its benefits to the body.
- Price: the target audience was informed of the cost of the iron tablets and their willingness to buy the product was encouraged.
- Place: the target audience was informed of the availability of the iron tablets at all times in places such
as drugstores, barangay health stations, rural health units, and secondary schools. The village health workers participated in the distribution system by selling Femina 60.

- Promotion: efforts were made to tell the target audience about the product, price, and place, including advertising, packaging, point-of-sale displays, and special events.

The project management team from the DOH at the national and regional levels, in close coordination with the provincial health office and the municipal health officers, conducted the following social marketing strategies:

- Advocacy to local officials, namely mayors, barangay captains and councilmen, and parish priests: The aim was to solicit commitment and support to ensure smooth implementation of the project.
- Development, production, distribution, and dissemination of information, education, and communication (IEC) materials to specific audiences: The IEC materials developed for the project by the DOH were in the form of posters, pamphlets, pocket calendars, and flyers made into fans. The materials were used in the interpersonal counseling activities conducted by the village health workers. The main message contained in the different IEC materials was “Your iron/my iron makes us healthy.” Guidelines for the health workers were developed to ensure that all IEC materials were effectively distributed and used.
- Project and product launching with UNILAB: A special event to create attention introduced the project and product to the target population in one single event at a certain place and time. This event consisted of a motorcade and a program participated in by local government officials and health workers. T-shirts imprinted with information about the project and the products were worn during the motorcade, streamers were suspended in strategic places in the community and on vehicles, balloons were available to create a fiesta-like atmosphere, and flyers formed into fans were distributed.
- Orientation/training of project implementers: Training of all staff at the rural health units, including village health workers and high school teachers, was conducted to increase their knowledge about iron deficiency and iron-deficiency anemia, orient them about the project, identify their roles and responsibilities in project implementation, orient them to social marketing strategies, and improve their skills in counseling.
- Improvement of service delivery through the existing health systems and pre/postnatal services: This was accomplished with the distribution of free weekly iron-folic acid supplements from the first antenatal visit to three months after delivery. The IEC materials, such as the pamphlet for pregnant women, served to reinforce what was learned from the interpersonal counseling. The back portion of the pamphlet reminded women to take the iron tablet every Tuesday at night and to eat foods rich in iron and vitamin C. Moreover, the municipal health officers organized monthly meetings to monitor project progress. Issues that could not be resolved during meetings were referred to the project technical group for solutions.
- Introducing the availability of the iron supplements for non-pregnant women into the market system: UNILAB assumed the lead role in making the iron supplements available in the market through local drugstores, and coordinated distribution with the DOH and the mayors and rural health physicians. In addition, the village health workers were tapped as direct sellers of the supplements. UNILAB also conducted intensive promotional activities for the target users both in the community and in schools. The promotional activities included sports activities, raffles, talent shows, and beauty contests with cash giveaways and the establishment of “Club Femina” among female high school students. During the first three-quarters of the year after Femina 60 was available on the market, every packet entitled both the buyer and the seller to a raffle coupon from which cash giveaways were awarded to the winners.
- General community educational/promotional programs: In addition to the program activities already mentioned, IEC materials were provided to increase the community’s level of awareness and knowledge about the importance of reproductive health and nutrition. These general community education/promotion activities further increased the effectiveness of interpersonal communication approaches made by the health workers.19

IMPLEMENTATION OF THE INTERVENTION

The standard protocol for taking Femina was as follows: Non-pregnant women 15 years old or who had started menstruating were instructed to take Femina 60 once a week on Tuesday nights before going to bed. Pregnant women were to take Femina OB once a week if seen for a prenatal checkup at the health center during their 20th week of gestation or less. They were to continue taking the tablets until delivery and for 3 months thereafter. They were also instructed to take the tablets on Tuesday nights before going to bed. Three months postpartum, they were to switch to Femina 60 and continue to take the weekly supplement. Pregnant women seen at the health
center for a prenatal checkup at more than 20 weeks gestation were instructed to take the daily dose of iron given free of charge by the DOH. This iron tablet contained 60 mg elemental iron with 0.4 mg folic acid.

For non-pregnant women, Femina 60 was available from main drugstores in the three study sites, and from village health workers and high schools at a cost of P14 (14 Philippine pesos) per package for a month’s supply or P3.50 (about 7 US cents per tablet) per week. Femina OB was given free to all pregnant and lactating women for 3 months after delivery in all health centers, including the barangay health stations in the three intervention sites. One package was given during the monthly checkup. To keep track of these pregnant women, the rural health midwife had an active list compiled with the help of the village health worker. Three months postpartum, women were encouraged to continue to take Femina 60 acquired through the market system.

RESULTS

Table 1 shows the distribution of the subjects according to reproductive status who participated in the KAP survey during each of the four survey periods.

Table 1. Distribution of Women According to Pregnancy Status at Each Survey Period

<table>
<thead>
<tr>
<th>Pregnancy Status</th>
<th>Survey Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>409</td>
</tr>
<tr>
<td>Pregnant</td>
<td>335</td>
</tr>
<tr>
<td>Total</td>
<td>744</td>
</tr>
</tbody>
</table>

The first specific objective of the project was to increase awareness in the community on the importance of iron and folic acid for WRA. To meet this objective, women were asked to respond to seven statements reflecting their beliefs on anemia and the importance of taking iron-folic acid tablets. The seven statements were:

1. I believe that anemia can be prevented by taking iron-folic acid tablets every day.
2. I believe that anemia can be prevented by taking iron-folic acid tablets weekly.
3. I believe that women should take iron-folic acid tablets at the start of menarche.
4. I believe that women should take iron-folic acid tablets weekly when they are pregnant.
5. I believe that women should take iron-folic acid tablets before pregnancy.
6. I believe that women should take iron-folic acid tablets weekly throughout their reproductive period.
7. I believe that I should give my daughter iron-folic acid tablets weekly from the time she starts menstruating.

Results from the KAP surveys are shown in Figures 1 and 2. The initial level of awareness on the role of daily iron-folic acid supplementation was high for both pregnant and non-pregnant women and remained unchanged throughout the four survey periods. In contrast, only half of the women initially were aware of the role of weekly supplementation in anemia prevention. As social marketing and social mobilization activities were implemented over the 12 months of intervention, awareness increased to over 80% for both pregnant and non-pregnant women. Notable changes were also observed in awareness of the need for women to take iron-folic acid supplements throughout their reproductive years.

All social marketing and mobilization activities were geared toward promoting the importance of taking weekly iron-folic acid supplements and adoption of this practice. Activities also encouraged the selling of Femina 60 by drugstores, village health workers, and high school teachers. Femina 60 was made available in the market in all three municipalities from December 1998 to December 1999. UNILAB sales records were monitored over this period as one indicator of adoption. During the first quarter of 1999, sales were increasing but declined briefly during the first month of the second quarter before again rising to the highest peak. The fourth quarter was best with regard to supply and demand (Figure 3). High school girls were the largest initial buyers of Femina 60. These records also indicated that 56% of the total Femina sales was from the drugstores, while about a third (31%) were from the village health workers. Sales at schools accounted for only 13% of the total.

The KAP survey was conducted four times during the course of the project to determine the level of knowledge about iron and iron-folic acid tablets. It also included questions on the benefits of taking iron-folic acid tablets, the target groups for supplementation, and the identification of iron-rich foods. Results of the survey are shown in Table 2. At baseline, there was a low level of knowledge on iron and iron-folic acid supplementation among the respondents. Pregnant women were the only recognized priority group for iron-folic acid supplementation. In the case of iron-rich foods, “malunggay” (horseradish) was identified as the known source of iron (31%) compared with the other possible sources of iron. With time, the level of knowledge on iron and iron-folic...
Acid supplementation increased. There was also a marked increase in knowledge of food sources of iron other than horseradish, such as eggs, meat, fish, liver, and jute (saluyot) leaves. Overall, the KAP survey showed positive attitudes of the respondents to iron-folic acid supplementation. Almost all respondents wanted more information about iron-folic acid tablets and felt that they needed to take the supplements.

Compliance is a recognized issue in iron supplementation programs, reportedly because of the side effects of iron. To estimate compliance to weekly supplementation, both pregnant and lactating women were asked if they were still taking the iron-folic acid supplements during each survey period. Table 3 shows that compliance to weekly iron-folic acid supplementation progressively improved with time into the project. Over 95% of respondents indicated that they were taking the supplements by the fourth survey.

The adverse side effects of iron supplementation include nausea, vomiting, constipation, diarrhea, headache, and black stools. However, the occurrence of these side effects is dose related. Adverse side effects of iron-folic acid supplements were reported in this study, but without a placebo group for comparison, it is not valid to draw conclusions regarding frequency or severity of side effects.

**DISCUSSION**

Iron supplementation is the most common strategy for the control of iron deficiency and iron-deficiency anemia. In the Philippines, an iron supplementation program through the DOH has been in effect for almost three decades, but has not been effective. For example, the prevalence of anemia increased between 1993 and 1998 according to the Food and Nutrition Research Institute National Nutrition Surveys. The erratic supply of iron supplements through the DOH and private market sources and compliance are considered major reasons for the low effectiveness of anemia control programs in the Philippines.

A number of field trials on the efficacy of iron supplements conducted in Indonesia and China have documented that weekly iron supplementation is just as effective as daily supplementation in improving hemoglobin in non-pregnant WRA if taken regularly for several months. This study demonstrated that women in a non-controlled setting are willing to buy iron supplements in the right environment. Such an environment was developed by providing adequate knowledge about iron deficiency and iron-deficiency anemia to health workers and the target population (WRA) and by making the supplements available at an affordable price. Because women in the country commonly attribute dizziness or even the general feeling of not being well to being “anemic,” persuading them through effective social marketing and mobilization to take an iron supplement was possible. Weekly iron-folic acid supplementation in the Philippines, therefore, is feasible as a preventive strategy for anemia control among fertile women, beginning with adolescence, to ensure sufficient iron reserves before pregnancy.

**CONCLUSIONS AND RECOMMENDATIONS**

This project demonstrated that weekly iron-folic acid supplementation can be an alternative to a daily approach...
in improving the iron status of Filipino WRA. Our study demonstrated that a social marketing/mobilization program for anemia control facilitated a willingness among non-pregnant women to purchase a weekly supplement from commercial and other local sources. The study also demonstrated that social marketing and mobilization improved compliance among pregnant women taking the supplement provided free through government services. An accompanying paper in this volume provides data that iron status improved among these women.15

For such a strategy to be successful, a strong public/private partnership is needed. For example, the pharmaceutical industry must produce and market iron-folic acid supplements that are safe, reasonably priced, and attractive. Accessibility through local private and public/government outlets is important to facilitate availability. Public/private partnerships are also needed to ensure consistent educational messages and facilitate promotional activities.

Given the results and conclusions derived from the project, the following recommendations are made: 1) a government-issued policy statement on the adoption of weekly iron-folic acid supplementation for all non-pregnant WRA will facilitate its implementation in any country; 2) social marketing and social mobilization play major roles in the promotion of weekly iron-folic acid supplementation and should be given priority consideration; and 3) a strong

<table>
<thead>
<tr>
<th>Table 2. Percentage of Respondents at Each Survey Period Who Agreed to Different Statements Reflecting Women’s Knowledge and Attitudes on Iron and Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STATEMENT</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>I know something about iron-folic acid tablets</td>
</tr>
<tr>
<td>The benefits of taking iron-folic acid tablets are:</td>
</tr>
<tr>
<td>It improves one’s nutritional status</td>
</tr>
<tr>
<td>It prevents anemia</td>
</tr>
<tr>
<td>It treats anemia</td>
</tr>
<tr>
<td>It makes me more healthy</td>
</tr>
<tr>
<td>It makes me more beautiful</td>
</tr>
<tr>
<td>It makes me have a healthy child</td>
</tr>
<tr>
<td>The following need to take iron-folic acid tablets:</td>
</tr>
<tr>
<td>Pregnant women</td>
</tr>
<tr>
<td>Married women</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Lactating women</td>
</tr>
<tr>
<td>Female students</td>
</tr>
<tr>
<td>Women in the reproductive age groups</td>
</tr>
<tr>
<td>The following are iron-rich foods:</td>
</tr>
<tr>
<td>Eggs</td>
</tr>
<tr>
<td>Meat</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Fish</td>
</tr>
<tr>
<td>Malunggay (horseradish)</td>
</tr>
<tr>
<td>Saluyot</td>
</tr>
<tr>
<td>Kangkong</td>
</tr>
<tr>
<td>Wishes to know more about iron-folic acid tablets</td>
</tr>
<tr>
<td>Feels that she needs to take iron-folic acid tablets</td>
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</table>

<table>
<thead>
<tr>
<th>Table 3. Percentage of Women Taking Weekly Iron-Folic Acid Supplementation by Pregnancy Status and Survey Period</th>
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<tbody>
<tr>
<td><strong>Pregnancy Status</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
</tr>
<tr>
<td>Not pregnant</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
collaboration should be established and sustained with medical associations to support and adopt a weekly iron-folic acid supplementation program (such a collaboration should be established with local pharmaceutical companies who could be of assistance in the promotional campaign).

ACKNOWLEDGEMENTS

We would like to thank all those who made this project successful: first and foremost for the support of the Regional Health Office headed by Dr. Juvenicio Ordone; Dr. Alyce Ochootorena, Provincial Health Officer of Pangasinan and the nutritionist-dietitians M.s. Marie Jacinto, M.s. Francisca Romatan, M.s. Milagros Gutierrez, and M.s. Mila Carrera; Nemesia Mejia, Chief of District Health Hospital, San Carlos City; Dr. Gil del Rosario, Medical Center Chief, Pangasinan Medical Center; the Honorable Mayors of Calasiao, Binmaley, and Santa Barbara and all its rural health unit staff headed by the municipal health officer; all of the barangay captains, councilmen, village health workers, the religious organizations, and the drugstore owners of the three municipalities; the medical technologists of the Bureau of Research and Laboratories (BRL) who were part of the central office team and who did the biochemical analysis; M.s. Nymphar Arcaida, M.s. Lydia Gatmaitan, M.s. Laura Roque, and M.s. Marites Go of the Nutrition Foundation of the Philippines, who provided administrative support; United Laboratories, Philippines for producing the Femina; M.s. Diane Bosch of WHO for providing technical inputs; Dr. Ophelia Mendoza for her statistical and technical inputs; Dr. Socorro Ignacio, who joined the DOH team for her thesis focused in schools; Dr. Suttiak Smitasiri, who provided input on social marketing and reviewed this paper; and to WHO for providing the project funds.

REFERENCES


Imelda Angeles-Agdeppa, Lourdes S. Paulino, Adelisa C. Ramos, Unita Marie Etorma, Tommaso Cavalli-Sforza, and Silvano Milani

The effectiveness of weekly iron-folic acid supplements promoted through a government-industry partnership was assessed in pregnant and non-pregnant women in the Philippines. Compliance to both weekly and daily supplementation increased during the year-long study period, but was highest with weekly supplementation. Serum ferritin and hematocrit increased significantly, whereas the hemoglobin level showed minimal change, probably because of lack of other heme-forming nutrients such as vitamin A. Serum ferritin increments were significantly higher in women taking the iron-folic acid supplements for more than 6 weeks. Weekly iron-folic acid supplementation should be recommended as a preventive strategy to control iron deficiency among reproductive-age women in the Philippines.

Key words: anemia, weekly iron-folic acid supplementation, reproductive age women, government-private partnerships

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INTRODUCTION

Almost three decades ago, the Department of Health (DOH) in the Philippines initiated a policy supportive of daily iron supplementation for pregnant and lactating women for control of the long-standing problems of iron deficiency and iron deficiency anemia. The policy, however, had limited effectiveness, as the prevalence of anemia across population groups remains high to the present day. A survey conducted in 1998 reported iron-deficiency anemia in 50.7% and 45.7% of pregnant and lactating women, respectively; 31.7% in non-pregnant women aged 20 to 39 years; and 33.2% in adolescent females. Ineffectiveness of daily iron supplementation programs in other developing countries, which might also be true in the Philippines, have been attributed to: 1) low compliance by subjects, particularly because of discomfort when taking daily iron tablets leading to non-adherence to treatment; 2) low motivation and ability of health workers to provide appropriate counseling; 3) lack of motivation of pregnant women to take iron pills due to lack of knowledge of the importance, advantages, and harmlessness of the practice; 4) limited availability of supplies due to insufficient funds and problems in the procurement and distribution of supplements; and 5) inaccessibility, i.e., problems with the time, cost, and efforts required to reach a health center where iron tablets are available.2-4 Other contributing factors to the high iron-deficiency anemia prevalence among Filipinos are low intake of iron from food (64.7% of RDA), and low bioavailability of dietary iron due either to the low intake of iron absorption enhancers such as vitamin C (73.2% of RDA) and/or the presence of iron absorption inhibitors, such as phytates found in the usual diet, which is a mixture of rice, fish, and vegetables.1

An alternative to daily dosing is weekly iron supplementation, which is proposed as a preventive strategy to reduce the prevalence of anemia in the Philippines. Trials on efficacy of weekly iron-folic acid supplements consumed under strict supervision show that they can be as efficacious as daily supplements if taken regularly for several consecutive months, and have a much lower rate of side effects.5-7 These findings support the so-called “mucosal block” hypothesis, wherein administering iron every 7 days allows time for the shedding of cells loaded...
with iron from a previous dose, thereby increasing iron absorption while avoiding a constant luminal and mucosal iron overload likely to provoke gastrointestinal symptoms.\textsuperscript{8-9} Thus, weekly iron-folic acid supplementation could be considered a new approach to improving iron stores and preventing anemia during pregnancy, thus lowering the risks of low-birth-weight infants and miscarriages. Iron-folic acid supplementation prior to or very early in pregnancy offers the additional advantage of reducing the risk of neural tube defects.\textsuperscript{10-11}

Although the efficacy of weekly iron-folic acid supplementation was demonstrated under strictly supervised conditions,\textsuperscript{5-7} effectiveness also needs to be demonstrated under usual program conditions before policy decisions are taken to launch a new preventive strategy. Therefore, a pilot project was launched as a government-industry partnership to promote the adoption of weekly iron-folic acid supplements among women of reproductive age (WRA). Project implementation emphasized community-based social mobilization and social marketing approaches in selected areas of the Philippines, as described in detail in an accompanying paper.\textsuperscript{12} This paper presents results of the impact of this project on the iron status of pregnant and non-pregnant women between the ages of 15 and 49 years in the Philippines.

**SUBJECTS AND STUDY DESIGN**

The study was a community-based longitudinal intervention in which weekly iron-folic acid supplements were provided to all WRA, both pregnant and non-pregnant, in selected sites. A strong social mobilization and social marketing effort accompanied the program. Three pilot municipalities of Pangasinan province were selected: Calasiao, Binmaley, and Santa Barbara. The three study municipalities were selected because of the strong support and cooperation of local leaders and health personnel, their close proximity to the medical centers in Dagupan and San Carlos City, where blood samples were analyzed, and easy access between project sites.

The three chosen sites were homogenous in socioeconomic and environmental-demographic profiles. Basic services are provided in government health facilities located at rural health units at the municipal level and at village (“barangay”) health stations at the village level. Staff in these facilities include physicians, nurses, and midwives assisted by volunteer barangay health workers. Government health and nutrition activities are complemented by services provided by existing active non-government organizations (NGOs).

All WRA, both pregnant and non-pregnant, between the ages of 15 and 49 years in the three municipalities were potential subjects. The intent was to include 1000 women, but only 744 who met eligibility criteria were identified in the baseline survey. Eligibility criteria were WRA who were considered most likely to become pregnant within the 12-month duration of the study, who were pregnant at the time, and who volunteered to participate. Excluded were pregnant and non-pregnant women already taking daily iron-folic acid supplements at baseline and women suffering from severe anemia, other blood disorders, acute/chronic diseases, or who had previously suffered from malaria. These women were referred to the nearest health facility.

Supplements were produced specifically for this study by United Laboratories (UNILAB), Manila, Philippines, the largest private pharmaceutical company in the country. Two preparations of iron-folic acid supplements (named “Femina” for use in The Philippines) were used. Femina 60 was for non-pregnant women, and contained 60 mg elemental Fe and 3.5 mg folic acid; Femina OB was for pregnant women, and contained 120 mg elemental Fe and 3.5 mg folic acid. Four capsules, a one-month supply, were placed in flexible foil packets to ensure greater stability and protection. Packets were attached to an attractive cover that contained information about the product, food sources of iron and folic acid, indication and product dosage.

Administration of weekly iron-folic acid supplements started immediately after the baseline survey, which was conducted in November and December 1998. The standard supplementation protocol was: 1) non-pregnant women at least 15 years of age were encouraged to take Femina 60 once a week; 2) pregnant women seen at health centers at \( \leq 20 \) weeks gestation were advised to take the free weekly dose of Femina OB until 3 months into lactation (after this period, these women were advised to buy and take Femina 60); 3) pregnant women seen at the health centers at \( \geq 20 \) weeks gestation were advised to take the usual daily dose of iron-folic acid tablets containing 60 mg elemental iron and 0.4 mg folic acid provided free by the DOH. The weekly groups were advised to take the supplement on Tuesdays before bedtime. This schedule permitted health workers to monitor and ask about adherence to supplementation the following day, as Wednesday was scheduled in all health stations as immunization day. In discussions with health workers, this level of commitment was considered sustainable in the long term.

Each pregnant woman was given a monthly dose of the supplement (one packet with four tablets) whenever they came for prenatal check-ups at the rural health units and barangay health stations. If pregnant women failed to go to the rural health units, the trained volunteer barangay health workers or midwife responsible in that catchment area visited the home and delivered the supplements specifically allotted for each woman. Each health
worker kept a master list of these women for follow-up to ensure continuity of supplementation.

Femina 60 was sold at local drugstores and by barangay health workers and rural health unit staff. Direct selling of the product to all WRA in their respective catchment areas made supplements more accessible and created the opportunity to conduct one-on-one counseling to motivate the women to buy and take the supplement (pregnant women received Femina OB free from the health system). The iron-folic acid supplement cost P14 (14 Filipino pesos) per packet, or P3.50 per tablet (i.e., about 7 US cents per week). Social mobilization and social marketing were key approaches to motivate and promote purchase and use of the Femina 60 supplement.13

Four surveys were conducted about every four months: at baseline and 4.5, 9, and 12 months later to evaluate the effects on hematologic parameters of weekly iron-folic acid supplementation. At each survey, blood samples were collected and analyzed for various hematological parameters.

METHODS

Experienced medical technologists extracted about 7 mL of blood from each subject. Blood samples were placed in an iced box and transported to the medical center in Dagupan City located 30 minutes travel time from the project sites. Analysis for hemoglobin (Hb), hematocrit (Hct), red cells (RBC), white cells (WBC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and differential count measuring monocytes, lymphocytes, granulocytes, eosinophils, and platelets were done using a MICROs (ABX Hematology, Montpellier, France). To ensure accuracy, a quality control procedure was performed before every series of measurements. Anemia in non-pregnant women was defined as Hb less than 120 g/L, while in pregnant women it was Hb < 110 g/L.14

Blood was allowed to clot for 30 minutes and centrifuged at 2000 to 2500 rpm for 20 to 30 minutes. The serum was transferred to labeled cryo-vials and stored frozen at −20°C at the Bureau of Research Laboratory, DOH, until analyzed. Serum ferritin was analyzed using a Spectro ferritin machine (RAMCO Laboratories, Houston, TX) employing an enzyme immunoassay procedure for the quantitative analysis. The normal value for serum ferritin with this kit is 20 ng/mL, so values below this cutoff were considered deficient in iron.15

Transferrin receptors (TfR) were analyzed using a TfR enzyme immunoassay (TFX-94, RAMCO Laboratories). Control sera were analyzed daily with each assay as a quality control. If controls were not within the expected ranges, the assay was considered invalid, as indicated in the assay kit instructions. The normal range for serum TfR in the kits used was 2.9 to 8.3 µg/mL.

A structured questionnaire was administered to determine compliance to supplementation during each of the four survey periods. Women were asked whether they were taking iron-folic acid supplements. Pill intake was also checked by counting empty packets that subjects turned in to become eligible for raffle prizes (raffle entries were an added indicator of supplement intake). At each survey, women were also asked if they experienced one or more side effects after taking the iron-folic acid tablets. Side effects were recorded as the point and interval estimates of the proportion of women who reported experiencing at least one adverse side effect after taking the tablet, categorized according to duration of supplementation. Among the self-reported adverse side effects considered were nausea, vomiting, constipation, diarrhea, epigastric pain, black feces, and headache.

STATISTICAL ANALYSIS

Data were rigorously scrutinized for errors and lack of consistency. All values exceeding the mean ± 3.3 SD were regarded as outliers. Data were analyzed using the Statistical Analysis System (SAS). Both Pearson’s and Spearman’s coefficients were employed to determine if WBC count and serum ferritin were correlated. Such a positive correlation would suggest infection-influenced high serum ferritin values. The same analysis was conducted between Hb or Htc and WBC.

Hematological records were classified according to “pregnancy status” (TRIM) and “previous supplementation” (SULN). These two variables were coded as shown in Table 4. To assess the effect of iron-folic acid supplementation on iron status, data were fitted with a linear model including the above variables and their interaction (TRIM × SULN) as terms, together with a term accounting for the effect of the characteristics of “individual women.” The inclusion of this term enabled the assessment of the effects of the supplement/duration of supplementation and physiological status on the different hematological parameters, controlling for the effect of other characteristics such as age, parity, nutritional status, and socioeconomic level. Because of the inclusion of this term in the model, the least-squares means for each level of the two variables and of their interaction were only slightly affected by the fact that the set of women changed in part from level to level. As a result, the effects of pregnancy and iron-folic acid supplementation were estimated with little or no bias.16,17
Ethical Considerations

Before the study began, women were oriented on the project protocol by the project team. Participation was entirely voluntary. Each woman signed a written consent form. The ethical review committee of the DOH approved the proposal.

RESULTS

At survey 1 (baseline), a total of 744 women (409 non-pregnant and 335 pregnant) were taken as respondents. Table 1 shows the distribution of women by pregnancy status at each survey period. The total number of non-pregnant women seen at the second survey increased, likely reflecting deliveries that had occurred during the interval between surveys. However, a declining trend in participants occurred from survey 3 to survey 4. The high rate of loss of follow-up in both pregnant and non-pregnant women was due to fear of repeated blood collection (48%), no time because of many household chores (42%), or transfer of residency (10%).

Although mean basal iron status blood parameters were within or close to normal ranges, those for pregnant women were lower compared with non-pregnant women (Table 2). The prevalence of anemia at each survey period among non-pregnant women (33%) was lower than the prevalence among pregnant women (54%). The prevalence of iron deficiency, however, was 19% in non-pregnant and 27% in pregnant women (Table 3).

Table 4 presents the pregnancy status of women at the time of survey (TRIM) and the intake, frequency, and duration of iron-folic acid supplements (SULN). The latter variable represents the woman’s history of iron-folic acid supplementation in the period before each survey, and is derived from four variables in the knowledge, attitudes, and practices (KAP) questionnaire, namely: whether she took iron-folic acid tablets, type of tablets taken, frequency of intake, and length of time supplements were taken. The resulting variable indicates the type of iron supplementation taken by the woman (none, daily, or weekly), as well as the duration of supplementation categorized as ≤6 weeks or >6 weeks. A cut-off point of 6 weeks for the duration of supplementation was selected for two reasons. The first was based on the actual distribution of responses to the survey question, in which most women reported that they had been taking iron-folic acid tablets for ≤4 weeks or ≥9 weeks. Using the midpoint of these two time points, 6 weeks, results in clear-cut groups of observations with adequate sample sizes for comparison. The second reason was based on the a priori assumption that a short treatment is unlikely to produce important changes in serum ferritin and Hb levels. More non-pregnant women (1013 or 65%) than pregnant women (259 or 44%) across all trimesters took supplements, and more women took the weekly dose (non-pregnant: 907; pregnant: 194) than the daily dose (non-pregnant: 106; pregnant: 65). An increased intake of supplements occurred as the trimester of pregnancy progressed and duration of intake increased. Weekly rather than daily supplementation, therefore, was the preferred regimen by both pregnant and non-pregnant women, and the number of women taking weekly iron-folic acid supplements increased with time. Pregnant women taking weekly iron-folic acid supplements increased from 5.7% in the first survey to 95.2% in the fourth survey; among non-pregnant women, this percentage increased from 6.1% to 98.6% (Table 5).

Table 6 shows the estimated differences in serum ferritin levels for different comparisons made among different sub-groups of women according to physiological status (TRIM) and previous iron-folic acid supplementation (SULN). Serum ferritin levels were lower by 7.0 ± 2.2 μg/L (mean ± SE) in pregnant women compared with non-pregnant women. They were higher by 20.4 ± 2.2 μg/L in women who took iron-folic acid tablets compared with those who did not. Among women who took tablets, those supplemented for more than 6 weeks had serum ferritin levels higher by 11.8 ± 3.5 μg/L compared with those who took iron-folic acid supplements for under 6 weeks. Compared with those who took daily iron-folic acid supplements, women administered weekly supplements had serum ferritin levels higher by 17.6 ± 3.5 μg/L. The difference between weekly and daily administration was similar in non-pregnant (15.9 ± 3.1 μg/L; P < 0.01) and pregnant women (18.2 ± 4.5 μg/L; P < 0.01). Since neither linear trend nor lack of fit were significant, it can be deduced that gestational age does not exert prominent effects on serum ferritin levels in the populations studied.

Although iron-folic acid supplementation appears to exert significant effects on serum ferritin levels, no analogous effects were observed on Hb levels. On the whole, pregnant women had Hb levels lower by 8.7 ± 1.0 g/L (P < 0.01) compared with non-pregnant women. There was a negative linear relationship between Hb and gestational age, with a mean decrease of 4.0 ± 1.1 g/L per trimester (P < 0.01). In particular, the mean Hb levels of women in their first trimester of pregnancy were

Table 1. Number of Women Studied By Pregnancy Status and Survey Period

<table>
<thead>
<tr>
<th>Pregnancy Status</th>
<th>Survey 1</th>
<th>Survey 2</th>
<th>Survey 3</th>
<th>Survey 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not pregnant</td>
<td>409</td>
<td>419</td>
<td>383</td>
<td>357</td>
</tr>
<tr>
<td>Pregnant</td>
<td>335</td>
<td>109</td>
<td>83</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>744</td>
<td>528</td>
<td>466</td>
<td>420</td>
</tr>
</tbody>
</table>
lower by 3.8 ± 1.9 g/L (P < 0.05) compared with those who were not pregnant. Women in their second trimester of pregnancy had lower Hb levels (7.0 ± 2.2 g/L, P > 0.01) compared with those in the first trimester. No difference was seen between the mean Hb levels of women in their third and second trimesters of pregnancy (1.0 ± 1.8 g/L).

With regard to the other hematologic parameters, Hct values were lower by 3.6 ± 0.3% (P < 0.01) in pregnant compared with non-pregnant women, with an average decrease of 0.16 ± 0.04 million/mm³ of RBC (P < 0.01) and 1.7 ± 0.3% of Hct per trimester (P < 0.01). However, it is worth noting that Hct values were higher by 1.2 ± 0.3% (P < 0.01) in women who took iron-folic acid tablets compared with those who did not. This was true for both pregnant (1.0 ± 0.4; P < 0.01) and non-pregnant (1.7 ± 0.3; P < 0.01) women.

Statistical analysis of the correlation between WBC numbers and serum ferritin and Hb was done to understand if infection played an important role in determining high serum ferritin values and anemia (that is, to see if serum ferritin and WBC were positively correlated and if Hb and WBC were negatively correlated).

Correlations between serum ferritin and WBC, as well as the number of granulocytes, lymphocytes, and monocytes were negative, except in the case of pregnant women, in whom the correlation of ferritin with monocytes was positive but weak (r = 0.099; P = 0.02, both with Pearson’s and Spearman’s coefficients). Therefore, infection does not seem to play an important role in determining high serum ferritin values in this population.

If anemia was partly caused by infection, there would be a negative correlation between Hb or Hct and various WBC numbers. A modest negative correlation was found between Hb or Hct and WBC total number, as well as with the number of granulocytes, but not with the number of lymphocytes and monocytes. In conclusion, infection appears to play a minor role as a cause of anemia in this population.

Table 7 shows the prevalence of self-reported adverse side effects, which ranged from 3.4% among those who were not taking any supplementation to 14.5% among those who had taken weekly iron-folic acid supplementation for more than 6 weeks. Notable findings with respect to the occurrence of adverse side effects were as follows: 1) there was no significant difference in the occurrence of adverse side effects between daily and weekly supplementation; b) adverse side effects were higher when supplements were taken than in the absence of supplementation (P < 0.01); and 3) adverse side effects were higher by 4.15 ± 1.92% for prolonged treatments (>6 weeks) than for short treatments (P < 0.01).

### Table 2. Selected Blood Parameters of Pregnant and Non-Pregnant Women at Survey 1

<table>
<thead>
<tr>
<th>Physiological Status</th>
<th>Blood Parameter</th>
<th>No. Samples</th>
<th>Mean Value</th>
<th>Standard Deviation</th>
<th>Minimum Value</th>
<th>Maximum Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Pregnant</td>
<td>Red blood cells*</td>
<td>397</td>
<td>4.49</td>
<td>0.45</td>
<td>2.80</td>
<td>5.99</td>
</tr>
<tr>
<td></td>
<td>Hemoglobin (g/L)</td>
<td>402</td>
<td>12.37</td>
<td>1.23</td>
<td>7.50</td>
<td>15.50</td>
</tr>
<tr>
<td></td>
<td>Hematocrit (%)</td>
<td>403</td>
<td>37.24</td>
<td>3.36</td>
<td>22.60</td>
<td>46.20</td>
</tr>
<tr>
<td></td>
<td>Ferritin (µg/L)</td>
<td>401</td>
<td>34.34</td>
<td>17.07</td>
<td>11.00</td>
<td>92.00</td>
</tr>
<tr>
<td></td>
<td>Transferrin receptor (mg/L)</td>
<td>401</td>
<td>5.11</td>
<td>1.67</td>
<td>2.20</td>
<td>11.20</td>
</tr>
<tr>
<td>Pregnant</td>
<td>Red blood cells*</td>
<td>330</td>
<td>3.87</td>
<td>0.45</td>
<td>2.66</td>
<td>5.46</td>
</tr>
<tr>
<td></td>
<td>Hemoglobin (g/L)</td>
<td>330</td>
<td>10.89</td>
<td>1.27</td>
<td>7.00</td>
<td>15.10</td>
</tr>
<tr>
<td></td>
<td>Hematocrit (%)</td>
<td>329</td>
<td>32.28</td>
<td>3.34</td>
<td>23.30</td>
<td>42.10</td>
</tr>
<tr>
<td></td>
<td>Ferritin (µg/L)</td>
<td>328</td>
<td>31.20</td>
<td>15.76</td>
<td>8.00</td>
<td>88.00</td>
</tr>
<tr>
<td></td>
<td>Transferrin receptor (mg/L)</td>
<td>328</td>
<td>4.85</td>
<td>1.64</td>
<td>2.10</td>
<td>11.00</td>
</tr>
</tbody>
</table>

*10⁶/mm³ blood
†Non-pregnant median and 1st and 3rd quartiles (in parentheses): 29 (22, 44); pregnant: 26 (19, 40) as median (1st and 3rd quartile).

*Anemia was considered in non-pregnant women to be hemoglobin under 120 g/L; in pregnant women it was when hemoglobin was under 110 g/L.
Iron supplementation for target populations is the most common strategy for the control of iron deficiency and iron-deficiency anemia in developing countries. The Philippines has implemented an iron supplementation program for nearly three decades, with only limited effectiveness due in part to inadequate compliance with daily iron supplementation and lack of supply.

In effectiveness studies implemented through the usual primary health care approach, programmatic issues are likely to be encountered related to women’s participation and behavior, leading to a high rate of loss to follow-up among both pregnant and non-pregnant women. For example, women associated blood examination with sickness, and thus considered it of least priority when they were not sick in bed. Femina and all other iron supplements were viewed as medicines. Therefore, pregnant women recruited in survey 1 may not have participated in the following surveys due to reasons such as fear of repeated blood collection, no time, and transfer of residency. The higher number of non-pregnant women in survey 2 was due to births that occurred during the interval from survey 1. Since attending health centers for preventive purposes is not a top priority for families in the Philippines, the preventive once-weekly dose of iron and multi-micronutrients is more practical, efficient, and less demanding of the organizational, financial, and administrative branches of the health system.19-21

The lower mean values of all blood parameters among pregnant compared with non-pregnant women reflect normal physiological expansion in erythrocyte volume that is exceeded by plasma volume expansion, causing the concentration of Hb to fall as much as 2 g/dL.22 Pregnancy is a period of increased demand for iron; the median total needs of iron during pregnancy are 840 mg.7

The high prevalence of low serum ferritin values in both pregnant and non-pregnant women, as well as the high rates of anemia among WRA at baseline, imply that these are public health problems that warrant serious concern by all sectors: government, non-government organizations (NGOs), international agencies, and industry. The data support findings from the National Nutrition Survey of 1998, which reported the prevalence of anemia in the province at the alarmingly high rate of 64% in pregnant women.1 Iron-deficiency anemia during pregnancy can lead to inadequate pregnancy weight gain and poor pregnancy outcome.23,24 Among WRA, low productivity25,26 and frequent occurrence of illness27,28 are reported.

Although dietary data were not assessed in this study, possible factors that might have contributed to the high prevalence of iron-deficiency anemia at survey 1 are the low dietary intake of nutrients involved in erythropoiesis, such as iron, vitamin A, riboflavin, vitamin B12, and folic acid.7 Filipinos have low intakes (as a percentage of the RDA) of iron (64.7%), vitamin C (73.2%; which enhances the bioavailability of plant iron), vitamin A (88%), and riboflavin (57%).1

The number of women who took the weekly dose increased rapidly with time; this number was greater than the number of women who took the daily dose, and more women took the supplements for longer than 6 weeks. This positive change in practice was likely due to the effect of the social marketing and social mobilization activities conducted by both the public and private sectors.13

The effects of the Philippine community-based weekly iron-folic acid supplementation pilot project for WRA and pregnant women resulted in marked improvements in serum ferritin but no significant improvement in Hb levels. These findings are not in agreement with the

### Table 4. Distribution of Subjects According to Pregnancy Status by Iron-Folic Acid Intake and Duration of Supplementation

<table>
<thead>
<tr>
<th>Pregnancy Status (TRIM)</th>
<th>None</th>
<th>Daily ≤6 Weeks</th>
<th>Daily &gt; 6 Weeks</th>
<th>Weekly ≤6 Weeks</th>
<th>Weekly &gt; 6 Weeks</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not pregnant</td>
<td>555</td>
<td>35</td>
<td>71</td>
<td>145</td>
<td>762</td>
<td>1568</td>
</tr>
<tr>
<td>1st trimester</td>
<td>73</td>
<td>6</td>
<td>4</td>
<td>12</td>
<td>24</td>
<td>119</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>145</td>
<td>10</td>
<td>12</td>
<td>17</td>
<td>65</td>
<td>249</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>113</td>
<td>12</td>
<td>21</td>
<td>16</td>
<td>60</td>
<td>222</td>
</tr>
<tr>
<td>Total</td>
<td>886</td>
<td>63</td>
<td>108</td>
<td>190</td>
<td>911</td>
<td>2158</td>
</tr>
</tbody>
</table>

### Table 5. Percentage of Women Taking Weekly Iron-Folic Acid Supplementation by Pregnancy Status and Survey Period

<table>
<thead>
<tr>
<th>Pregnancy Status</th>
<th>Survey 1</th>
<th>Survey 2</th>
<th>Survey 3</th>
<th>Survey 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant</td>
<td>5.7</td>
<td>63.3</td>
<td>84.3</td>
<td>95.2</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>6.1</td>
<td>64.0</td>
<td>88.5</td>
<td>98.6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>5.9</td>
<td>63.8</td>
<td>87.8</td>
<td>98.1</td>
</tr>
</tbody>
</table>

DISCUSSION

Iron supplementation for target populations is the most common strategy for the control of iron deficiency and iron-deficiency anemia in developing countries. The Philippines has implemented an iron supplementation program for nearly three decades, with only limited effectiveness due in part to inadequate compliance with daily iron supplementation and lack of supply.

In effectiveness studies implemented through the usual primary health care approach, programmatic issues are likely to be encountered related to women’s participation and behavior, leading to a high rate of loss to follow-up among both pregnant and non-pregnant women. For example, women associated blood examination with sickness, and thus considered it of least priority when they were not sick in bed. Femina and all other iron supplements were viewed as medicines. Therefore, pregnant women recruited in survey 1 may not have participated in the following surveys due to reasons such as fear of repeated blood collection, no time, and transfer of residency. The higher number of non-pregnant women in survey 2 was due to births that occurred during the interval from survey 1. Since attending health centers for preventive purposes is not a top priority for families in the Philippines, the preventive once-weekly dose of iron and multi-micronutrients is more practical, efficient, and less demanding of the organizational, financial, and administrative branches of the health system.

The lower mean values of all blood parameters among pregnant compared with non-pregnant women reflect normal physiological expansion in erythrocyte volume that is exceeded by plasma volume expansion, causing the concentration of Hb to fall as much as 2 g/dL.22 Pregnancy is a period of increased demand for iron; the median total needs of iron during pregnancy are 840 mg.7

The high prevalence of low serum ferritin values in both pregnant and non-pregnant women, as well as the high rates of anemia among WRA at baseline, imply that these are public health problems that warrant serious concern by all sectors: government, non-government organizations (NGOs), international agencies, and industry. The data support findings from the National Nutrition Survey of 1998, which reported the prevalence of anemia in the province at the alarmingly high rate of 64% in pregnant women.1 Iron-deficiency anemia during pregnancy can lead to inadequate pregnancy weight gain and poor pregnancy outcome.23,24 Among WRA, low productivity25,26 and frequent occurrence of illness27,28 are reported.

Although dietary data were not assessed in this study, possible factors that might have contributed to the high prevalence of iron-deficiency anemia at survey 1 are the low dietary intake of nutrients involved in erythropoiesis, such as iron, vitamin A, riboflavin, vitamin B12, and folic acid.7 Filipinos have low intakes (as a percentage of the RDA) of iron (64.7%), vitamin C (73.2%; which enhances the bioavailability of plant iron), vitamin A (88%), and riboflavin (57%).1

The number of women who took the weekly dose increased rapidly with time; this number was greater than the number of women who took the daily dose, and more women took the supplements for longer than 6 weeks. This positive change in practice was likely due to the effect of the social marketing and social mobilization activities conducted by both the public and private sectors.

The effects of the Philippine community-based weekly iron-folic acid supplementation pilot project for WRA and pregnant women resulted in marked improvements in serum ferritin but no significant improvement in Hb levels. These findings are not in agreement with the
findings of some earlier research, where weekly iron supplementation in pregnant and non-pregnant women resulted in improved levels of both Hb and serum ferritin.5,29,30 An increase in Hb is the immediate response to iron supplementation in deficient individuals, because changes in serum ferritin concentrations do not occur until optimal Hb concentrations are reached.31 Previous studies attributed the phenomenon to concurrent infection and/or vitamin A deficiency. 32,33 During infection, serum ferritin is elevated because of the accumulation of iron in the liver and spleen. This is accompanied by depression of retinol-binding protein, the synthesis of which is dependent on vitamin A status. Since in this study, infection did show any significant influence on serum ferritin (r = 0.0994), it can be deduced that vitamin A deficiency might be the hindering factor. The National Nutrition Survey (1998) revealed that vitamin A deficiency prevalence in the province under study was 7% among pregnant women and 16.5% among lactating women.1

Vitamin A has been implicated in the synthesis of transferrin that makes iron available for hematopoiesis.34 The addition of vitamin A to the supplement formula should be considered in future anemia intervention programs to facilitate efficient mobilization and utilization of iron, likely resulting in greater benefits in improving iron status among population groups. The ratio of iron to vitamin A is an important factor to be considered in pill formulations to avoid high costs and unnecessary risks of excessive vitamin A.35

The longer duration of supplementation (>6 weeks) was associated with greater increments of serum ferritin, both in pregnant and non-pregnant women. It can be postulated that iron supplementation for more than 6 weeks may lead to the deposition of iron in the liver. This is consistent with the findings that supplementation for

| Table 6. Effects of Iron-Folic Acid Intake on Serum Ferritin Levels by Duration and Frequency of Supplementation and Physiological Status |
|---------------------------------|-----------------|-----------------|
|                                  | Estimate        | Probability     | Standard Error |
| Pregnant vs not pregnant         | −7.007          | 0.0015†         | 2.201          |
| Trimester (linear trend)*        | −3.809          | 0.0943          | 2.275          |
| Trimester (lack of fit)†         | 1.952           | 0.6001          | 3.723          |
| Iron vs no iron                  | 20.407          | 0.0001†         | 2.161          |
| ≥6 weeks vs <6 weeks             | 11.848          | 0.0007†         | 3.468          |
| Weekly vs daily                  | 17.623          | 0.0001†         | 3.533          |
| Weekly: ≥6 weeks vs <6 weeks     | 14.056          | 0.0001†         | 3.469          |
| Daily: ≥6 weeks vs <6 weeks      | 9.640           | 0.1072          | 5.981          |
| Not pregnant: Iron vs no iron    | 21.704          | 0.0001†         | 1.989          |
| Pregnant: Iron vs no iron        | 19.975          | 0.0001†         | 2.801          |
| Not pregnant: ≥6 weeks vs <6 weeks| 10.180        | 0.0010†         | 3.076          |
| Pregnant: ≥6 weeks vs <6 weeks   | 12.404          | 0.0055†         | 4.456          |
| Not pregnant: weekly vs. daily   | 15.938          | 0.0001†         | 3.135          |
| Pregnant: weekly vs. daily       | 18.185          | 0.0001†         | 4.539          |
| Not pregnant weekly: ≥6 weeks vs <6 weeks | 15.322 | 0.0001†         | 2.386          |
| Pregnant weekly: ≥6 weeks vs <6 weeks | 13.633 | 0.0027†         | 4.529          |
| Not pregnant daily: ≥6 weeks vs <6 weeks | 5.037 | 0.3744          | 5.669          |
| Pregnant daily: ≥6 weeks vs <6 weeks | 11.175 | 0.1446          | 7.654          |

*Mean variation per trimester of pregnancy.
†Since both linear trend and lack of fit are not significant, gestational age does not exert prominent effects on serum ferritin levels.
‡Highly significant difference.

| Table 7. Occurrence of Adverse Side Effects by Frequency and Duration of Iron-Folic Acid Intake |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                  | Adverse Side Effects | 95% Confidence Interval |
| Type and Duration of Iron/Folic Acid Supplementation |                  | Lower Limit | Upper Limit  |
| No Treatment                     | 3.4%              | 2.2%         | 4.6%          |
| Daily ≤6 Weeks                   | 11.1%             | 4.6%         | 21.6%         |
| Daily >6 Weeks                   | 13.9%             | 7.2%         | 20.6%         |
| Weekly ≤6 Weeks                  | 10.0%             | 5.6%         | 12.4%         |
| Weekly >6 Weeks                  | 14.5%             | 12.2%        | 16.8%         |

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12 weeks with a weekly low dose of iron further increased serum ferritin values (5 μg/L) compared with 8 weeks of supplementation. Another study, however, showed that increasing the duration of supplementation for more than 17 weeks resulted in no further significant increase in iron stores. Differences in results could be attributed to factors such as infection, pill composition, screening criteria, baseline iron status, and other nutritional deficiencies that might confound the biological mechanism of iron metabolism. The actual duration of preventive supplementation needed to allow for improvement in iron parameters of at-risk population groups, as well as the period of re-supplementation when values of blood parameters start to decline, urgently call for further research as a basis for program planning. One study revealed that 6 months after termination of supplementation for 12 weeks, the iron parameters of female adolescents started to decline, indicating the need for repeat supplementation.

In our study, women who took weekly supplementation had higher serum ferritin and Hct levels than those who took daily supplements. Controversies continue regarding the existence of iron blockage occurring during daily supplementation. From our study, it is difficult to infer that an increase in the weekly dose is attributable to more efficient absorption, because there was no strict monitoring of the number or amount of the iron doses ingested by the two groups. A study on weekly versus daily iron supplementation among pregnant women in Indonesia revealed no significant differences in iron status between the two groups. Additional well-designed and controlled studies should be conducted to clarify the extent of effects of weekly and daily supplementation.

The increasing compliance to weekly iron-folic acid supplementation with increasing time of supplementation suggests that women became accustomed to taking the pills. Therefore, weekly iron-folic acid supplementation can be considered a feasible alternative to preventing anemia among WRA in the Philippines. The information, education, and communication (IEC) materials distributed to all women, coupled with the joint promotional campaigns conducted by private industry (UNILAB) and government (DOH) personnel aided women’s increasing compliance in taking the supplements.

Women who had taken iron-folic acid supplements for a longer period of time experienced more negative side effects than those who took them for a shorter time. The occurrences of side effects were similar in women who took the supplements daily and those who took them weekly. Another study, however, reported more adverse effects in girls who took a lower daily dose (60 mg elemental Fe) and weekly high-dose (120 mg elemental Fe) than those who took weekly low-dose (60 mg elemental Fe) supplements. The occurrence of side effects is therefore apparently dose dependent.

**CONCLUSIONS AND RECOMMENDATIONS**

This project showed that iron status, as expressed by serum ferritin, can be significantly improved, both in pregnant and non-pregnant women, by taking weekly iron-folic acid supplements for at least 6 weeks. The insignificant effect on Hb levels suggests that supplements that include other micronutrients involved in the absorption, utilization, and mobilization of iron should be considered. Weekly multi-micronutrient supplements containing vitamin A, vitamin C, vitamin B12, and B12 could be considered by pharmaceutical companies in the development of the pill formula. A dose ratio of iron to vitamin A needs further investigation to avoid unnecessary risks of overdose and increased cost.

The project duration was not sufficient to show what might be the minimal period of weekly supplementation before pregnancy that would allow continued effective weekly iron-folic acid supplements during pregnancy. This aspect needs to be considered in additional research. The supplementation program used in this study could also be used in secondary schools, factories, and other places where WRA are found. Social marketing messages should introduce weekly supplements as part of a healthy lifestyle for WRA. Intensive motivation and encouragement of health workers are required to encourage WRA to buy weekly iron-folic acid supplements. However, the weekly supplement should first be made available for purchase as an over-the-counter supplement at an affordable price in village drug stores and village variety stores ("sari-sari" stores).

Weekly iron supplementation is feasible in the Philippines and could be adopted as a preventive strategy in the prevention of iron deficiency and iron-deficiency anemia. A policy statement from the DOH is necessary for implementation on a national scale. The strategy should target all WRA who are not pregnant because they need sufficient iron reserves before they become pregnant.

**REFERENCES**


Koum Kanal, Jennifer Busch-Hallen, Tommaso Cavalli-Sforza, Byron Crape, Suttilak Smitasiri, and the Cambodian Weekly Iron-Folic Acid Program Team

Social marketing and community mobilization approaches were applied in a pilot program to introduce weekly iron-folic acid supplementation to prevent anemia in Cambodian women of reproductive age. The program was implemented in three very different environments: secondary school girls, women working in garment factories in the vicinity of Phnom Penh, and women in rural villages. Each population provided its own challenges and obstacles. However, all three groups of women showed substantial improvements in knowledge about the causes, consequences, and prevention of anemia, and the large majority reported interest in continuing to take the supplements.

Key words: anemia, weekly iron-folic acid supplementation, multisectoral collaboration, social marketing, community mobilization, Cambodia

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INTRODUCTION

Anemia is a widespread public health problem in Cambodia. The Cambodian Demographic and Health Survey of 2000 estimated that 58% percent of Cambodian women of reproductive age (WRA) were anemic. The Cambodian Ministry of Health provides daily iron-folic acid supplements for pregnant women to prevent low birth weight and reduce maternal mortality. However, only 38% of the women in Cambodia receive antenatal care, and compliance in taking iron-folic acid supplements is poor.1

Anemia is now recognized as a serious and preventable public health problem worldwide, with consequences for the health and well-being of a community and its development, especially affecting women and children.2-4 Anemia may have multiple causes, some of which may occur concurrently. In addition to iron deficiency, other nutrients associated with anemia include deficiencies in vitamins A, C, B12, folate, and zinc. However, the leading cause of anemia worldwide is iron deficiency.5 One approach to the prevention of nutritional anemia is weekly iron-folic acid supplementation.5-9

The rationale for using weekly iron doses is presented by Viteri and Berger elsewhere in this issue.10 Several studies support the underlying assumptions upon which the weekly approach is based, and have demonstrated efficacy under supervised conditions.11-21 Effectiveness under unsupervised community conditions, however, needs to be validated.

In 2001–2002, with the financial and technical support of the World Health Organization (WHO) Western Pacific Regional Office (WPRO) and the Japanese government, the Cambodian Ministry of Health, in collaboration with other ministries and agencies, undertook a pilot weekly iron-folic acid supplementation program for WRA. This program was implemented without supervised control among women in selected secondary schools, garment factories, and rural villages.

The weekly iron-folic acid supplementation program utilized social marketing and community mobilization approaches to: 1) reach non-pregnant WRA who are not easily accessible through existing health system delivery channels; 2) educate women about the benefits of iron and folic acid, emphasizing the positive effects on health and beauty; 3) achieve a high coverage and compliance...
to supplementation over a long time frame; and 4) enhance sustainability of ongoing supplementation.

This paper reports the effectiveness of the social marketing and participatory communications methodologies applied in the Cambodian weekly iron-folic acid supplementation project and their impact on knowledge, attitudes, and practices (KAP) that may prevent the development of anemia. The paper also examines differences and similarities between participating schools, factories, and communities in order to provide direction for long-term program implementation.

**PROGRAM DESIGN, IMPLEMENTATION, MONITORING, AND EVALUATION**

The National Nutrition Program of the Ministry of Health (the program team), with support of a WHO advisor, the Occupational Health Department (Ministry of Social Affairs), and staff of the inter-ministerial Seth Kuma program in Kompong Speu Province (supported by UNICEF), worked in close collaboration to implement the weekly iron-folic acid supplementation program and to conduct ongoing monitoring and informal evaluation. Two independent external consultants were contracted for the duration of the pilot program. One consultant designed and coordinated the collection of the baseline, midterm, and final evaluation surveys, analyzed the data, and reported on hemoglobin (Hb) levels and changes in KAP of women participating in the pilot program. The second consultant, an expert in social marketing strategies, served as the program’s social marketing advisor.

**Social Marketing Strategies to Promote Weekly Iron-Folic Acid Supplementation**

Developing an attractive name and image for the supplement was an important first step to its promotion. During initial formative field research in the three target areas at schools, factories, and rural villages, WRA complained of fatigue and tiredness during their monthly menstrual period, which caused some to reduce activities; for example, schoolgirls were often absent from school. The observation was also made that Cambodian WRA relate beauty with good health and a positive self-image, and they also associated a good complexion with good health.

During the pre-testing exercises to identify a suitable name for the product, the Cambodian women surveyed selected “Kolap Krahorm” (“red rose”) as the most attractive name because it portrayed a product that would enhance women’s health and beauty. The program team, with technical help from the National Centre for Health Promotion, Ministry of Health, worked collaboratively to design an attractive tertiary package for the supplement and a program poster, sticker, and logo. A photogenic factory worker “glowing with good health” was selected to be the model for the supplement package, posters, and stickers. This young woman was photographed with an attractive and popular female Cambodian singer, who held a pack of the supplement. A program logo was designed that showed a beautiful hand holding a red rose. This logo was displayed on all information, education, and communication (IEC) materials, including the supplement package. The picture of the two selected young women and the program logo was also used to produce large factory billboards, which were erected in prominent locations at each factory and unveiled during the factory program launches.

The program team composed three program songs and key messages, which were recorded on a cassette tape. This tape was played over the public broadcast system at regular intervals throughout the week in each factory and on players in the schools. A program T-shirt and bags containing the program logo and a key message were also printed and distributed to many of the women participating in the program.

**Choice of Supplement and Packaging**

The weekly iron-folic acid supplementation supplement came from United Laboratories (UNILAB) in Manila, Philippines. It contained 60 mg of elemental iron and 3.5 mg folic acid encapsulated in a small elliptical, film-coated pink tablet, which was easy to swallow. Cambodian women surveyed during the field research chose pink as the most attractive color for the supplement. The film coating masked the taste and reduced side effects. The supplement was packed in blisters of four tablets (a 1-month supply) to ensure stability and protection. Although blister packaging is more expensive than flexible foil packaging, it was preferred by WRA in Cambodia. The Ministry of Health packing station in Phnom Penh prepared the tertiary packages, both small (containing one blister pack of four tablets) and large (containing 50 small packs), which were produced by a private company in Phnom Penh.

**SUBJECTS**

**Secondary Schoolgirls**

The weekly iron-folic acid supplementation program specifically designed for schoolgirls of reproductive age was launched in five secondary schools in January 2002. Schools were decorated with banners carrying messages about the weekly iron-folic acid supplementation. Dignitaries gave supportive speeches, which were followed by games and the presentation of gifts and recognitions. As a result of local consultations, a decision was made to charge a nominal fee of 10 cents US for one package of supplements (four iron-folic acid tablets providing 1 month’s supply).

Schoolgirls who showed leadership were selected to be peer educators in the weekly iron-folic acid supplementation program for the schools. Schoolteachers were
also selected to attend peer educator training in order to provide support for the student leaders. A weekly iron-folic acid supplementation committee consisting of teachers and students managed the funds raised from the sale of the iron-folic acid supplements.

Questionnaires were administered and Hb was measured at baseline and at a follow-up visit approximately 6 months later. Of the 423 schoolgirls participating in both baseline and follow-up evaluation visits, 232 (55%) provided stool samples at baseline and were given 500 mg mebendazole for deworming if they tested positive for worms.

Initially, 581 schoolgirls from five schools were recruited to participate in the program evaluation. Six of these students did not complete the baseline questionnaire. Out of the remaining 575, 152 did not complete the follow-up questionnaire 6 months later. Data from the remaining 423 students were included in the analysis.

Garment Factory Workers

There are 130 garment factories in the vicinity of Phnom Penh. Because of few employment opportunities for young women in the rural areas of Cambodia, thousands of women migrate to Phnom Penh to find work in these factories. Most women earn around $50 to $60 US a month, and approximately half of their wages are sent back to their families in the countryside.

The social marketing strategy for the garment factories included peer education training for 50 peer team leaders. Factory workers were divided into teams, each led by one of the trained team leaders. The team leaders were selected based on the respect held by their peers. Team leader training included peer counseling and organizing educational activities to promote the iron-folic acid supplements and improved nutrition. Every month, the team leaders distributed to their teams packets of four tablets for 1 month's supply of iron-folic acid supplements. The team leaders provided the supplements to the garment factory workers without cost, because local regulations require factory owners to care for the health of their staff, and it is not permissible to sell drugs and supplements to WRA inside a factory.

To generate excitement for the weekly iron-folic acid supplementation, news releases were prepared and a heavily publicized opening celebration was held at one of the participating factories. Special lotteries were held for factory workers who successfully took the supplement for 3 consecutive months.

To evaluate the weekly iron-folic acid supplementation in the garment factories, 1181 of the workers completed a baseline questionnaire. Because of garment factory closures, conflicts with working schedules or lack of participation in the weekly iron-folic acid supplementation, 703 of these women did not complete the follow-up evaluation questionnaires 6 months and 1 year after the start of the weekly iron-folic acid supplementation program. The final data analysis included 478 garment factory workers.

Rural Village Women

Respected rural villagers were selected for the weekly iron-folic acid supplementation peer educator training. Two peer educators were chosen to be responsible for village development committee health activities, and in this capacity their weekly iron-folic acid supplementation work was combined with other health activities. The supplements were sold to rural village women at the nominal cost of 10

Table 1. Baseline Characteristics of the Secondary School Students, Garment Factory Workers, and Rural Village Women Given Weekly Iron-Folic Acid Supplements in a Study in Cambodia

<table>
<thead>
<tr>
<th>Baseline Characteristic*</th>
<th>Secondary School Students (N = 423)</th>
<th>Garment Factory Workers (N = 478)</th>
<th>Rural Village Women (N = 639)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (yrs)</td>
<td>16</td>
<td>21</td>
<td>32</td>
</tr>
<tr>
<td>Median height (cm)</td>
<td>149</td>
<td>153</td>
<td>150</td>
</tr>
<tr>
<td>Median body mass (kg)</td>
<td>40.2</td>
<td>48.3</td>
<td>44.2</td>
</tr>
<tr>
<td>Median body mass index (kg/m²)</td>
<td>18.1</td>
<td>20.7</td>
<td>19.4</td>
</tr>
<tr>
<td>Median earnings (US $ per month)</td>
<td>not applicable</td>
<td>60</td>
<td>not available</td>
</tr>
<tr>
<td>Attending school</td>
<td>100%</td>
<td>96.2%</td>
<td>73.4%</td>
</tr>
<tr>
<td>Median highest grade attained among school attendees</td>
<td>not applicable</td>
<td>6th</td>
<td>4th</td>
</tr>
<tr>
<td>Median initial hemoglobin level (g/L)</td>
<td>120</td>
<td>127</td>
<td>116</td>
</tr>
<tr>
<td>Married</td>
<td>0%</td>
<td>17.4%</td>
<td>not available</td>
</tr>
<tr>
<td>Diarrhea during past 2 weeks unless otherwise stated</td>
<td>19.1%</td>
<td>14.9% (last 24 h)</td>
<td>32.9%</td>
</tr>
<tr>
<td>Fever during past 2 weeks</td>
<td>36.4%</td>
<td>46.7%</td>
<td>59.5%</td>
</tr>
</tbody>
</table>

*Weights, heights, and hemoglobin concentrations were measured. The participants reported all other characteristics.
cents US for 1 month’s supply (four tablets). In some villages, these supplements were sold at regular monthly village meetings. In other villages, peer educators went door to door to educate and promote the supplement. The most impoverished families received the supplements without cost. Funds received from the sales of the supplements went to a village revolving fund.

WRA living in 13 randomly selected villages (all located in Kong Pisei and Samraong Tong districts, Kampong Spue Province) participated in the weekly iron-folic acid supplementation program. From the 1021 rural village women recruited for evaluation, 383 were not available to participate in the follow-up visit 6 months later or were removed from analyses because they were pregnant. Data from the remaining 638 rural village women were available for program evaluation.

RESULTS

Table 1 shows the baseline characteristics of the three study groups. Secondary school students, as expected, were youngest and had the lowest body mass index (BMI). Only 75% of rural women attended school, in contrast to 96% and 100% of factory workers and schoolgirls, respectively. Rural women had the highest incidence of diarrhea and fever in the 2 weeks prior to the survey.

Tables 2 to 4 show the questions on behaviors related to reported use of weekly iron-folic acid supplements. In all three groups, the majority of women reported that they felt the need for iron supplementation and that they intended to continue purchasing and taking supplements. Almost all of the women who were taking the supplements were taking them on a weekly basis at the time of the 6-month follow-up. An estimate of compliance in taking the supplements, as stated by the women in the three settings, was about 55% for the schoolgirls, 57% for the factory workers, and 71% for the rural women.

<table>
<thead>
<tr>
<th>Question*</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you need to take iron tablets?</td>
<td>66.7% (282/423) answered yes</td>
<td>95.3% (402/422) answered yes</td>
</tr>
<tr>
<td>Will you continue to take iron tablets?</td>
<td>not applicable</td>
<td>96.3% (222/228) answered yes</td>
</tr>
<tr>
<td>How many times did you take the tablets?</td>
<td>not applicable</td>
<td>100.0% (232/232) answered once a week</td>
</tr>
</tbody>
</table>

*The first question was addressed to all participants, including those taking iron-folic acid supplements and those not taking supplements. The next two questions were only addressed to those persons who reported taking the supplements at the time of follow-up. Other differences between denominators are due to missing data.

Table 3. Questions Related to Behavior Change in the Use of Iron-Folic Acid Supplements in Rural Village Women in Cambodia

<table>
<thead>
<tr>
<th>Question*</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you need to take iron tablets?</td>
<td>63.1% (403/639) answered yes</td>
<td>92.3% (589/638) answered yes</td>
</tr>
<tr>
<td>Will you continue to take iron tablets?</td>
<td>not applicable</td>
<td>98.7% (312/316) answered yes</td>
</tr>
<tr>
<td>How many times did you take the tablets?</td>
<td>not applicable</td>
<td>97.8% (445/455) answered once a week; 1.8% (8/455) answered less than once a week; 0.4% (2/455) answered twice a week</td>
</tr>
</tbody>
</table>

*The first question was addressed to all participants, including those taking iron-folic acid supplements and those not taking supplements. The next two questions were only addressed to those persons who reported taking the supplements at the time of follow-up. Other differences between denominators are due to missing data.
Figures 1 to 3 show the number of subjects in each of the three populations who correctly answered questions related to anemia. Of the 11 questions, few correct answers were given at baseline, but the number of questions correctly answered markedly increased at follow-up 6 months after initiation of the social marketing intervention.

Figure 4 shows the replies to a question requiring participants to identify iron-rich foods at baseline and at the 6-month follow-up. Knowledge in all three groups improved substantially after the educational campaign. Women from the rural communities, however, had the least knowledge of iron-rich foods. Figures 5 and 6 show the increased knowledge of consequences of anemia and its prevention among all three populations.

**DISCUSSION**

The weekly iron-folic acid supplementation pilot program increased awareness and support about anemia and the benefits of preventative iron-folic acid supplementation among policy makers, government, non-government organizations (NGOs), and WRA in urban and rural settings in Cambodia. The majority of Cambodian women in the program areas enthusiastically adopted the practice of taking preventive weekly iron-folic acid supplements. Through the use of social marketing strategies, an attractive image was created for the supplements and was widely recognized in the program areas. Women and adolescent schoolgirls in rural areas who participated in the program demonstrated that they were willing and able to purchase the supplement.

Mobilizing women in all program settings through existing community and workplace structures increased knowledge of the causes and consequences of anemia, as well as ways to prevent it. Multiple collaborating partners from the national level down to the community level demonstrated that they could successfully work together to develop and implement strategies to prevent and control anemia.

The factory setting proved a challenging environment for introducing weekly iron-folic acid supplementation. Large numbers of young WRA in each factory were either highly mobile or inaccessible during working hours. Nearly 60% of the original survey group was lost to follow-up. Access to factories was also a limitation for follow-up, monitoring, and evaluation. Despite these constraints, women working in factories enthusiastically adopted the use of weekly iron-folic acid supplementation. Even though the supplement was provided free in the factory setting, a large percentage of women interviewed during the follow-up expressed interest in purchasing the supplement in the future.

The weekly iron-folic acid supplementation program’s success in schools showed that this is a highly supportive environment in which to improve knowledge and behavior practices to control and prevent anemia. The educational training and social marketing strategies implemented were effective in increasing knowledge, awareness, and practices to prevent anemia.

However, unlike other weekly iron-folic acid supplementation interventions in schools in which supplements were provided free and under supervised conditions, the

**Table 4. Questions Related to Behavior Change in the Use of Iron-Folic Acid Supplements in Garment Factory Workers in Cambodia**

<table>
<thead>
<tr>
<th>Question*</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you need to take iron tablets?</td>
<td>57.2% (318/556) answered yes</td>
<td>96.8% (539/557) answered yes</td>
</tr>
<tr>
<td>Will you continue to take iron tablets?</td>
<td>not applicable</td>
<td>96.3% (441/458) answered yes</td>
</tr>
<tr>
<td>How many times did you take the tablets?</td>
<td>not applicable</td>
<td>100.0% (316/316) answered once a week</td>
</tr>
</tbody>
</table>

*The first question was addressed to all participants, including those taking iron-folic acid supplements and those not taking supplements. The next two questions were only addressed to those persons who reported taking the supplements at the time of follow-up. Other differences between denominators are due to missing data.

**Figure 1.** Schoolgirls (N = 423) in Cambodia who correctly answered a number of questions related to anemia. P < 0.0001 based on a t-test for the difference in counts of correct answers between baseline ( ) and follow-up 6 months later ( ).
supplements were sold to Cambodian female students. These schoolgirls, therefore, voluntarily chose to purchase and take the supplement since they had to pay for it.

The three populations of women, secondary schoolgirls, factory workers, and rural villagers, were very different. The secondary students were much younger and the women in the villages much older. The women in the garment factories were less educated than the schoolgirls. Rural village women suffered more health problems, at least from infectious agents that caused fevers and diarrhea. Rural village women also had the highest proportion with low baseline Hb. Villages and factories posed special logistical problems compared with the schools, with the villages having the least formal structure. The garment factories’ priorities were primarily economic. Regardless, all three populations were very responsive to learning and understanding about anemia.

Eleven questions testing knowledge related to anemia demonstrated substantial improvement at follow-up after 6 months of the weekly iron-folic acid supplementation. All three groups showed improvement in the identification of iron-rich foods and in their knowledge of the consequences and prevention of anemia.

Loss to follow-up was high for several reasons, such as factory closures and working schedules. Those lost may have been different from those remaining in the program.

The large majority of women who reported taking weekly iron-folic acid supplements at the 6-month follow-up indicated that they would continue to take the supplement. Though compliance to weekly supplementation over the entire program period is unknown, the women’s interest in continuing supplementation and their feeling that they needed iron was a positive result.

CONCLUSIONS

The weekly iron-folic acid supplementation pilot program, utilizing social marketing strategies in the context...
of a complex of multisector collaborators, demonstrated effectiveness in the dissemination of knowledge about anemia and nutrition. Although the three environments were very different and posed different challenges to success, the indicators for increased knowledge and behavior changes as a result of weekly iron-folic acid supplementation were positive. The program also inspired a reported interest in continuing supplementation in all three populations of women.

The weekly iron-folic acid supplementation pilot program, utilizing social marketing strategies, proved extremely worthwhile in providing future direction and generating further support relating to issues that impact on prevention and control of anemia. The weekly iron-folic acid supplementation program showed that a multisectoral collaborative approach to preventing iron-deficiency anemia in WRA in Cambodia is feasible and should be expanded through channels and partnerships that are more likely to succeed, such as schools. However, there were some constraints that need to be considered for future programming. One constraint was the difficulty in getting access to factories due to busy work schedules, which suggests that future support to factories might need to be provided outside the factory environment. Another constraint was that it took longer to implement the project at the rural community level. These women needed more time to absorb information and new knowledge, and village committees needed more support to provide health education and to conduct follow-up activities with women enrolled in the project.

**FUTURE PLANS**

With positive results from the pilot program, the Cambodian Ministry of Health agreed in principle with the need to provide weekly iron-folic acid supplementation to WRA, and is developing the means to introduce the program on a larger scale. The National Nutrition
The Program of the Ministry of Health has received some funding from UNICEF and WHO to further examine the delivery mechanism through the school system. In 2003-2004, the National Nutrition Program implemented the weekly iron-folic acid supplementation program in eight secondary schools in one operational district, with 1500 schoolgirls enrolled in the program. So far, the program has shown very encouraging results, including high coverage and compliance and improved knowledge about the causes, effects, and prevention of anemia. The program has excellent coordination among all partners involved in the program.

Even though only 30% of WRA attend secondary schools, the National Nutrition Program, with its limited human and financial resources, plans to first expand the weekly iron-folic acid supplementation program through the school system before further expansion to other settings, such as rural villages and factories. In 2005, with support from the Health Sector Support Project, the National Nutrition Program will expand the weekly iron-folic acid supplementation program in three provinces where other nutrition interventions are also implemented. The program will cover approximately 35,000 schoolgirls.

ACKNOWLEDGMENTS

We thank Mr. Eric Keneffick, who designed and conducted the original analyses of the data.

REFERENCES

Positive Impact of a Weekly Iron-Folic Acid Supplement Delivered with Social Marketing to Cambodian Women: Compliance, Participation, and Hemoglobin Levels Increase with Higher Socioeconomic Status

Byron L. Crape, Eric Kenefick, Tommaso Cavalli-Sforza, Jennifer Busch-Hallen, Silvano Milani, and Koum Kanal

A social marketing program promoting weekly iron-folic acid supplementation improved hemoglobin levels in women of reproductive age in Cambodia. Supplementation was increasingly effective among women of higher socioeconomic status (SES). Among higher SES schoolgirls, 58% took the supplements, compared with 49% for lower SES (P = 0.07). Garment factory workers with an 11th- or 12th-grade education had a mean improvement in hemoglobin of 0.72 g/dL over those with a 5th-grade education or less (P = 0.04). The percentage of rural village women taking supplements increased with increasing SES (linear trend P = 0.046). These results suggest that women with lower SES be given special attention for future programs.

Key words: social marketing, iron-folic acid, socioeconomic status, Cambodia

INTRODUCTION

The weekly iron-folic acid supplementation program in Cambodia utilized social marketing and community mobilization approaches to educate women about iron-deficiency anemia and to promote taking the supplements. The social marketing-mobilization program is described in detail in an accompanying paper. The objective of this paper is to evaluate the impact of weekly iron-folic acid supplementation on hemoglobin (Hb) levels for Cambodian women of reproductive age and to evaluate the impact of SES on program participation and compliance.

METHODS

Hemoglobin Measurement

Hb was measured at baseline and at follow-up 6 months later using the HemoCue analyzer (HemoCue AB, Angelholm, Sweden), which requires a finger prick and a few drops of blood drawn into a microcuvette. Hb levels are read immediately by a photometer in the analyzer, which provides a measure of circulating Hb concentrations but does not directly measure iron stores.

In an anemia survey in Kandal Steung/Kandal Province, Cambodia among 159 children ages 6 to 69 months, the HemoCue analyzer was compared with the gold standard, the ABX Micro-60 (Horiba ABX Co., Montpellier, France). Using a cutoff for anemia of ≤110 g/L, Pasteur Laboratories in Cambodia reported an anemia prevalence of 30% using the ABX test, while the HemoCue test identified an anemia prevalence rate of 42% in the same population (Institut Pasteur du Cambodge, Ministry of Health, Kingdom of Cambodia, ...
World Health Organization, National Institute of Public Health of Cambodia, World Vision, Cambodia. A anaemia survey in Kandal Steung/Kandal, preliminary unpublished results 2002). Based on these numbers, the HemoCue test has a sensitivity of 89% and a specificity of 82% to detect anemia.

Because the HemoCue test set-point for the measurement of Hb level was somewhat higher than that of the ABX test, the unit for the analyses used in this paper is the change in Hb, which requires only that the Hb be reliable between repeat measures.

Measurement of Socioeconomic Status

SES status among both the secondary school students and rural village women was measured as the sum of items owned by their households based on a predefined list. This list included household ownership of a bicycle, cart, motorcycle, water pump, boat, machine, radio, or television. Household automobile ownership was also included on the list for the secondary students.

SES for garment factory workers was measured by educational grade level attained. The number of listed items of household ownership was not available for garment factory workers, since most live in temporary accommodations such as hostels.

Both the listing of household items and information on attained educational grade level was acquired from participant reporting. The variability in the socioeconomic measures for secondary school students was considerably less than that found among the rural village women. Thus, secondary students were grouped into two SES categories, while rural village women were grouped into three SES categories.

Subjects

The subjects of this study were described in detail in an accompanying paper.2

Statistical Analysis

The Wilcoxon rank sum test was applied to data concerning changes in Hb levels in secondary school students and garment workers in lieu of the Student’s t-test because changes in Hb level are not normally distributed. Due to multiple comparisons, the Bonferroni correction was applied to the statistics for changes in Hb levels.

Comparisons were made between women of different SES (based on number of listed household items) and participant-reported compliance rates for taking the weekly iron-folic acid supplements 6 months after baseline. A chi-squared test was used for statistical testing of the differences for the secondary school students, and a chi-squared test for linear trend was applied to the differences in rural village participants. The association between the educational grade attained and the change in Hb level over 1 year of the weekly iron-folic acid supplementation among garment factory workers was assessed by a multivariable linear regression model. To remove the potential confounding effects of other factors (which can cover up the true association between education and change in Hb), the variables initial Hb level, age, salary, body mass index (all in quartiles), having a fever during the 2 weeks prior to baseline, and having diarrhea 24 hours prior to baseline (both dichotomous) are also included in the model.

The statistical package SAS 8.2 (SAS, Inc., Cary, NC) was used for statistical analyses. SPSS software (version 10.0, SPSS, Inc., Chicago, IL) was used for conversion of the original databases to a SAS database.

RESULTS

Baseline characteristics of the subjects were described in detail in the accompanying paper.2 Figure 1 shows that rural women at baseline had the highest proportion of moderate to severe anemia and mild anemia. The factory workers had the lowest proportion of mild and moderate to severe anemia. Prevalence of anemia among secondary school students fell between that of the rural village women and the factory workers.

The median age for rural village women was 16 years greater than the median age for secondary school students. The median age of garment factory workers was 5 years greater than that of the students. Rural village women reported the highest prevalence of diarrhea and fever, whereas the secondary school students reported the lowest rates.

Figure 1. Percentage of Cambodian women not anemic (Hb ≥ 12 g/dL), mildly anemic (Hb 9–12 g/dL), or moderately to severely anemic (Hb < 9 g/dL).
The impact of the weekly iron-folic acid supplementation and deworming treatments on changes in Hb level after 6 months for secondary school students are shown in Figure 2. Four groups were compared. Group 1 neither received the mebendazole treatment nor took the weekly iron-folic acid supplements (N = 57); group 2 received mebendazole but did not take iron-folic acid supplements (N = 51); group 3 took the weekly iron-folic acid supplements but received no mebendazole treatment (N = 134); and group 4 received the mebendazole and took the weekly iron-folic acid supplements (N = 181). Hb declined in group 1 by 1.2 g/L, but increased in groups 2, 3, and 4 by 1.7, 6.4, and 2.8 g/L, respectively. Comparison of group 1 with groups 2, 3, and 4 yielded P values for differences (Wilcoxon rank sum test) of 0.220, 0.006, and 0.089, respectively. The only statistically significant difference (Bonferroni correction, alpha = 0.05/6 = 0.008) in Hb change occurred between group 1 and group 3 (P = 0.006).

Figure 3 shows the change in Hb among the secondary school students who reported taking the iron-folic acid supplements at follow-up (N = 232) and those who reported not taking the supplements (N = 191). The improvement in mean Hb was significantly greater for those students who took the weekly iron-folic acid supplements (3.6 g/L) than for those who did not (0.8 g/L) (Wilcoxon rank sum P value slightly less than 0.05).

Table 1 shows the association in secondary school students between SES differences and the use of weekly iron-folic acid supplementation 6 months after the program started. A borderline significant improvement in use of weekly iron-folic acid supplements was found for the highest SES group compared with the lowest SES group. The initial median Hb levels, based on measurements using the HemoCue analyzer, were 119 g/L and 120 g/L for the low and high SES groups, respectively.

All garment factory women answering the evaluation questionnaires reported taking the supplement at the time of follow-up. Table 2 summarizes results of the multivariable linear regression that models the change in Hb level from baseline to follow-up as the outcome, adjusting for potential confounding due to initial Hb level, age, salary, body mass index (BMI), and the existence of fever and diarrhea. After adjustment for potential confounders, the most highly educated group (11th- and 12th-grade education), showed a mean elevation in Hb of 0.74 g/dL over that of the lowest educated group (no education to 4th-grade education). This difference was statistically significant.

Table 3 assesses the association between the SES (count of listed household items) of rural women and the use of the weekly iron-folic acid supplements at follow-up. Rural village women participants in the weekly iron-folic acid supplementation evaluation were increasingly more likely to report taking iron-folic acid supplements with increasing SES. The initial median Hb level from baseline to follow-up as the outcome, adjusting for potential confounding due to initial Hb level, age, salary, body mass index (BMI), and the existence of fever and diarrhea. After adjustment for potential confounders, the most highly educated group (11th- and 12th-grade education), showed a mean elevation in Hb of 0.74 g/dL over that of the lowest educated group (no education to 4th-grade education). This difference was statistically significant.

<table>
<thead>
<tr>
<th>SES</th>
<th>Taking WIFS</th>
<th>Not Taking WIFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>High SES (N = 259)</td>
<td>58.3%</td>
<td>41.7%</td>
</tr>
<tr>
<td>Low SES (N = 164)</td>
<td>49.4%</td>
<td>50.6%</td>
</tr>
</tbody>
</table>

*SES was computed as the sum of household ownership of the following items as reported by the participants: bicycle, cart, motorcycle, water pump, boat, machine, radio, television and car. High SES was considered to be the possession of 4 to 7 of these items; low SES was 0 to 3 items.
DISCUSSION

The results from the secondary schools indicate that in the Cambodian context, a social marketing and community mobilization strategy promoting weekly iron-folic acid supplementation is effective in improving Hb levels; however, the magnitude of the impact depended on SES. Based on number of listed household items or on education, with increasingly higher SES, participants were more likely to take the weekly iron-folic acid supplements and were more likely to take them consistently over time. For all three weekly iron-folic acid supplementation participant groups in Cambodia, the secondary school girls, the garment factory workers, and the rural village women, this pattern was consistent across settings, populations, and weekly iron-folic acid supplementation program differences. Poorer participation and compliance among lower SES women reduced the hematological impact of the weekly iron-folic acid supplementation for these women.

The secondary school students and the rural village women paid a nominal fee for the iron-folic acid supplements. For the poorest rural village women, this fee was waived. Regardless, lower SES women were less likely to actually take the supplements. Though SES distribution was different between students and rural village women, the pattern among those who chose to take the supplements was similar. This is of special concern because lower SES women tended to have lower average Hb levels and are at greater risk for anemia.

All participants in the garment factories were provided weekly iron-folic acid supplements free of charge, and everyone participated in the educational and motivational programs throughout the year. Among those factory workers who completed the final follow-up questionnaires, essentially all indicated that they were taking the weekly iron-folic acid supplements. However, those women with the highest educational status, another indicator of SES, showed the largest improvements in Hb levels. If women with the highest educational attainment took the weekly iron-folic acid supplements more consistently during the evaluation period of 1 year than women with less education, this would explain the differences in change in Hb levels.

CONCLUSIONS AND RECOMMENDATIONS

These findings indicate that the weekly iron-folic acid supplementation positively impacted Hb levels. For all three participating groups, the supplementation program was more effective among those who were better off socioeconomically. This may be explained by greater participation and better compliance in taking the supplements weekly. This suggests that to improve program effectiveness, the program should be especially designed to target lower SES women.

REFERENCES

Weekly Iron and Folic Acid Supplementation As a Tool to Reduce Anemia among Primary School Children in Cambodia

Philippe Longfils, Ung Kim Heang, Hay Soeng, and Muth Sinuon

The prevalence of anemia decreased from 62% to 12% and from 57% to 26% in children 5 to 11 years of age in two rural primary schools in Kampot Province, Cambodia, after oral weekly supplementation with iron-folic acid tablets for 20 weeks and with vitamin A and mebendazole twice per year. In 12- to 15-year-old children, success was less marked. The prevalence of hookworm infestation did not change, but the number of eggs in the stool decreased drastically. The intervention had no significant influence on stunting and wasting. An integrated community approach including mass deworming, health education, and multi-micronutrient supplementation was very effective in reducing anemia in Cambodian schoolchildren and should be adopted on a larger scale.

Key words: anemia, hemoglobin concentration, stunting, wasting, age determination, parasites

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INTRODUCTION

The quality of the diet in Cambodia is poor. It starts with inappropriate breastfeeding and then is hampered by food taboos. Weaning food frequently consists of white rice soup without meat, vegetables, or fruit. The majority of people in rural areas, including many young children, eat only twice per day, mainly plain rice with small amounts of fish. Vegetables and fruits are often absent in the diet. Using a cutoff point of 110 g hemoglobin (Hb)/L, the UNICEF baseline survey of Community Action for Social Development in Cambodia in 1998 showed that 81% of 1348 children 6 to 59 months of age were anemic, with a mean Hb concentration of 96 g/L. In a follow-up survey in May 2000, 74% of 1588 children under 5 years of age were anemic. The prevalence is even higher for children under 2 years of age. Deficiencies of vitamins A, B, and iodine, and infections with intestinal parasites are frequent. In the first National Micronutrient Survey of Cambodia in 2000, children in 7 out of 10 survey provinces showed a prevalence of night blindness of over 1%. The National Goiter Survey in 1996–1997 revealed a goiter rate of over 12% in children ages 8 to 14. The prevalence of malnutrition is high and is the main factor undermining healthy growth and intellectual development of children in Cambodia.

In 1996, the Integrated Food Security Program was started to coordinate the efforts of national and international agencies as well as non-governmental organizations (NGOs) on the improvement of the nutritional situation in Cambodia. As part of this program, the German Technical Cooperation (GTZ) started community health activities in Kampot Province. The activity included a growth-monitoring program for children under 5 years of age, which was soon expanded with many older children in poor health condition. To take care of these older children, the Integrated Food Security Program started a school health program in 1999 in nine schools in rural areas, which was later extended to 25 schools in Kampot Province. The program included medical examination of the eyes, ears, mouth, hands, feet, and skin, as well as six monthly administrations of vitamin A (200,000 IU) and mebendazole (500 mg). Health education was also part of the program, as poor hygiene was the main cause for scabies and other skin diseases.

The only data on prevalence of anemia in Cambodia available in 1999 concerned children under 5 and adults over 15 years of age. Therefore, a school health survey was performed to collect data for the age group 5 to 14.
years. The prevalence of anemia was 64% during baseline Hb determinations in this age group, so iron-folic acid tablets were given in school once a week over a period of 20 weeks to all children in first grade between the end of 1999 and June 2000. Hb concentration, anthropometric measures, and stool samples were re-examined after this intervention.

METHODS

The baseline school survey was performed in July 1999 before the end of the school term, and was repeated after the intervention in July 2000. Age, sex, weight, height, Hb concentration, and stool parasites were analyzed before and after the intervention.

Description of Study Population

Two cluster schools were selected for the study: the Wat Ang Chork primary school in Trapiang Reang (Chum Kiri District) with 1083 pupils, and the Dang Tung primary school in Dang Tung district with 609 pupils. Early dropout from school is a common problem in Cambodia. Therefore, in order to keep attrition rates low, only grade-one pupils were included in the survey. All grade-one pupils present on the day of the baseline survey were included. None of these children showed clinical signs of chronic diseases at medical examination. Moreover, micronutrient supplements that could possibly interfere with this intervention were not available in the Kampot area. For these two reasons, no particular exclusion criteria were applied.

Age Assessment

To relate Hb concentrations to age and for the assessment of stunting using height for age, correct ages are essential. This is a problem in rural Cambodian schoolchildren. In 1999, “school registration age” was not accurate and family records were not available. However, parents knew their children’s “traditional zodiac date of birth.” The accurate age of the children, therefore, was assessed by home visiting surveys. A special questionnaire was used, which included traditional lunar Khmer calendars for months and Chinese calendar animals for years. These data were cross-matched with questions regarding main events in the year to confirm the results.

Anthropometry

Weight was measured to the nearest 100 g using a floor scale distributed by UNICEF (Seca Corp., Hanover, MD), and height was determined to the nearest 0.1 cm by use of a locally made tool. The indicators weight-for-height and height-for-age, respectively, were used to define “wasting” (acute malnutrition) and “stunting” (chronic malnutrition). The indicator weight-for-age was used to define “underweight” (general undernutrition). All pupils below a cutoff point of minus two standard deviations compared with an international reference population were considered malnourished. Data analysis software (Epi Info, CDC, Atlanta, GA) provided the percentage of malnourished children, based on Z-scores, referring to the standard deviation of the frequency distribution of this reference population.

Stool Analysis

Before July 1999, no mass deworming was done in the school population under investigation. During the July 1999 baseline survey, 162 stools were collected in Dang Tung School only and analyzed immediately according to Kato-Katz to assess the intensity of the infestation, and according to the sodium acetate-acetic acid-formalin (SAF) method developed by Ritchie to assess the prevalence of all intestinal parasites including protozoa. The Baermann method was used to assess the prevalence of Strongyloides stercoralis. In July 2000, 146 stools were collected and the same examinations were repeated after two deworming sessions. In addition, pupils answered a questionnaire regarding living conditions, water supply, and behavior during defecation. Stools from other schools were not analyzed in this pilot project.

Hemoglobin Assessment

The Hb concentration was estimated using the hemoglobinometer undiluted method (Lovibond, Tintometer, Salisbury, UK), which does not require a reliable electric power supply. Capillary blood was obtained by pricking a finger with a sterile lancet. The blood ran directly into the observation cell of the hemoglobinometer, where the color was compared with a series of colored glasses. Double, even triple readings were taken for all cases, with borderline results. Results obtained by this method correlated surprisingly well with corresponding certified cyanmethemoglobin determinations in an earlier study, though no value for the correlation coefficient was given. Specificity was between 66% and 99%, sensitivity between 70% and 94%, and the predictive value was between 82% and 98% when systematically compared in populations from different parts of the world. The Hb cutoff to define anemia was according to WHO guidelines: under 115 g/L for children ages 5 to 11 years and under 120 g/L for children 12 to 14 years of age. Based on the correlation between the undiluted
hemoglobinometer method and the cyanmethemoglobin method, these cutoff values correspond to a range of 105 to 132 g/L and 110 to 137 g/L, respectively (confidence interval: 95%). Though this comparison shows sufficient reliability on which to base Hb estimates, certified methods for Hb determinations should be used in future studies if electricity is reliably available.

**Intervention**

Starting in June 1999, vitamin A (200,000 IU) and mebendazole (500 mg) were distributed every 6 months in nine schools. Vitamin B complex (1 mg each of B₁, B₂, and B₆ in two tablets/day) was provided only to those children who showed angular gingivitis as a clinical sign of vitamin B₂ deficiency. From December 1999, all children in nine schools, including the 451 pupils from this survey, received a UNICEF iron-folic acid tablet once a week (60 mg of Fe as ferrous sulfate and 0.25 mg folic acid). Teachers distributed the tablet and supervised its consumption during the teaching period of 20 weeks. No iron or folic acid was distributed during school holidays, so supplementation stopped in June 2000. The follow-up survey was done in early July 2000.

**Compliance**

At the end of the intervention period in 2000, tablets of vitamin A and mebendazole were shown to each subject. The pupils were asked how many of each they had taken during the past 12 months to estimate compliance with the vitamin A/mebendazole program; the same process was used for the iron-folic acid tablets. Teachers supervised intake of iron-folic acid tablets for those children who were at school but did not record the number of children absent.

**Pharmaceutical Supply**

All supplements came from the Central Medical Store of the Ministry of Health. The National Mother and Child Health Department provided iron-folic acid tablets and vitamin A (200,000 IU/capsule). The parasitology department of the "Centre National de Malaria" provided mebendazole (500 mg/tablet). Vitamin B complex tablets were imported from the Netherlands.

**Data Analysis**

The software programs EPI Info 6™ and EpiNut Anthropometry for Nutrition (CDC, Atlanta, GA) were used to analyze weight and height in terms of respective indicators for stunting (height-for-age), wasting (weight-for-height), and general undernutrition (weight-for-age). Data are given as means ± SD. Means of two corresponding groups were compared by use of Student’s unpaired t-test to assess the statistical significance of differences.

**RESULTS**

Included in the study of grade-one pupils were 234 children in Trapiang Reang (121 male and 113 female) and 217 in Dang Tung (113 male and 104 female). The same set of parameters assessed at baseline was reassessed in the same group of children 12 months later after weekly oral iron-folic acid administration during the 20-week trial period ending with the end of term. In Trapiang Reang, 215 out of 234 pupils completed the study, as did 197 out of 217 in Dang Tung. The attrition rate was as low as 9%. In 1999, according to the pupil’s age assessed prior to the study, 15% of the pupils were 12 to 15 years old, while 1 year later 31% of the pupils were in this age range. This is a very high percentage of comparably old children in grade one, and is the consequence of frequent class repetition and late entry into primary school. In Dang Tung, more than half of the children repeat grade one instead of passing on to grade two.

**Age Assessment**

Two-hundred-twenty-eight children had their age assessed in Trapiang Reang, and 184 in Dang Tung. A large discrepancy was found between "school registration age" and the age identified by our survey questionnaire (real age). In Trapiang Reang, the mean school-registered age was 2 years below the real age. In Dang Tung, the difference between the two means was 1 year. Only 7 out of 440 children started school at the recommended age of 6 years, while a few older pupils aged 12 to 15 were still repeating grade one.

**Anthropometry**

At baseline, height, weight, and age were assessed, and related indicators of malnutrition were determined in 207 children in Dang Tung and in 233 children in Trapiang Reang. Detailed results of the survey can be seen in Tables 1 and 2. Little change occurred in the prevalence of malnutrition between 1999 and 2000.

**Stool Analysis**

In 1999, 162 fresh stool specimens were analyzed out of a total of 217 subjects in Dang Tung. In this study, 62% out of 162 specimens were parasite positive: 42% of the stools contained hookworm, 12% S. stercoralis, 7%
Trichuris trichiura, 6.5% Entamoeba histolitica, 4% Enterobius, 2.5% Hymenolepis nana, 2% Ascaris lumbricoides, and 1% Giardia. Stools with mixed infection were common. In 2000, parasite infestation was still a prevalent problem: 49% of stool specimens were parasite positive compared with 62% in 1999. Although 40% of stools remained hookworm infected, the infestation intensity decreased considerably. Infestation of over 1000 eggs/g decreased from 2% to zero, infestation of 100 to 1000 eggs/g decreased from 20% to 9%, and infestation of 100 eggs/g increased from 20% to 30% in all specimens under inspection.

Hemoglobin Assessment

Two-hundred-thirty-four blood samples were collected in Trapiang Reang, 217 in Dang Tung. About two-thirds of pupils in both schools were anemic in 1999 (Table 3). Anemia was more prevalent in both sites in 12- to 14-year-old children compared with younger age groups. No significant difference was seen between sexes. All cases of “severe” anemia in Trapiang Reang (Hb < 9.7 g/L) seen in 1999 had disappeared after the intervention. The distribution of Hb concentration showed a marked shift towards higher values between 1999 and 2000 in Trapiang Reang (Figure 1).

### Compliance

Based on recall by children, the mean number of iron-folic acid tablets taken in Trapiang Reang was 18 out of 20; this number was 14 out of 20 in Dang Tung. These figures signal good or satisfactory compliance, respectively. However, the estimate is based on a comparably small random sample, which permits no valid statistical evaluation.

### DISCUSSION

This study took advantage of an opportunity to obtain important information before and after intervention with supplements and drugs that reduce the risk of anemia caused by inadequate iron intake, parasitic infections, and vitamin A deficiency. These data provide useful information as a basis for future work among schoolchildren in Cambodia. Moreover, the prevalence of incorrect age data was estimated, which is important

### Table 1. Anthropometric Data in Grade-One Children in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999

<table>
<thead>
<tr>
<th>Place and Year</th>
<th>N</th>
<th>Mean Age*</th>
<th>Mean Weight</th>
<th>Mean Height</th>
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<tr>
<td>Trapiang Reang School</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>234</td>
<td>9.4 yrs</td>
<td>19.4 kg</td>
<td>117.6 cm</td>
</tr>
<tr>
<td>(6-15)†</td>
<td></td>
<td>(12.4-32.6)</td>
<td>(100-140)</td>
<td></td>
</tr>
<tr>
<td>6-11 years</td>
<td>211</td>
<td>9.0 yrs</td>
<td>19.4 kg</td>
<td>117.6 cm</td>
</tr>
<tr>
<td>(6-11)†</td>
<td></td>
<td>(12.4-32.6)</td>
<td>(100-140)</td>
<td></td>
</tr>
<tr>
<td>12-15 years</td>
<td>23</td>
<td>12.7 yrs</td>
<td>23.9 kg</td>
<td>127.9 cm</td>
</tr>
<tr>
<td>(12-15)†</td>
<td></td>
<td>(16.1-32.6)</td>
<td>(116-140)</td>
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</tr>
<tr>
<td>Dang Tung School</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>217</td>
<td>10 yrs</td>
<td>21.7 kg</td>
<td>122.7 cm</td>
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<td>(6-15)†</td>
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<td>(14.2-35.4)</td>
<td>(99-144.3)</td>
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<tr>
<td>6-11 years</td>
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<td>9.4 yrs</td>
<td>21.0 kg</td>
<td>121.0 cm</td>
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<td>(6-11)†</td>
<td></td>
<td>(14.2-35.4)</td>
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<td>12-15 years</td>
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<td>12.5 yrs</td>
<td>24.4 kg</td>
<td>129.1 cm</td>
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<td>(12-15)†</td>
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<td>(17.6-32.7)</td>
<td>(113-142)</td>
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</tr>
</tbody>
</table>

*Mean age is the calculated “real age,” as opposed to mainly biased “school registered age.”
†Numbers in parentheses are ranges.

Trichuris trichiura, 6.5% Entamoeba histolitica, 4% Enterobius, 2.5% Hymenolepis nana, 2% Ascaris lumbricoides, and 1% Giardia. Stools with mixed infection were common. In 2000, parasite infestation was still a prevalent problem: 49% of stool specimens were parasite positive compared with 62% in 1999. Although 40% of stools remained hookworm infected, the infestation intensity decreased considerably. Infestation of over 1000 eggs/g decreased from 2% to zero, infestation of 100 to 1000 eggs/g decreased from 20% to 9%, and infestation of 100 eggs/g increased from 20% to 30% in all specimens under inspection.

### Hemoglobin Assessment

Two-hundred-thirty-four blood samples were collected in Trapiang Reang, 217 in Dang Tung. About two-thirds of pupils in both schools were anemic in 1999 (Table 3). Anemia was more prevalent in both sites in 12- to 14-year-old children compared with younger age groups. No significant difference was seen between sexes. All cases of “severe” anemia in Trapiang Reang (Hb < 9.7 g/L) seen in 1999 had disappeared after the intervention. The distribution of Hb concentration showed a marked shift towards higher values between 1999 and 2000 in Trapiang Reang (Figure 1).

### Compliance

Based on recall by children, the mean number of iron-folic acid tablets taken in Trapiang Reang was 18 out of 20; this number was 14 out of 20 in Dang Tung. These figures signal good or satisfactory compliance, respectively. However, the estimate is based on a comparably small random sample, which permits no valid statistical evaluation.

### DISCUSSION

This study took advantage of an opportunity to obtain important information before and after intervention with supplements and drugs that reduce the risk of anemia caused by inadequate iron intake, parasitic infections, and vitamin A deficiency. These data provide useful information as a basis for future work among schoolchildren in Cambodia. Moreover, the prevalence of incorrect age data was estimated, which is important

### Table 2. Prevalence of Acute (Wasting) and Chronic (Stunting) Malnutrition and Undernutrition in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999 and July 2000 Before and After Weekly Iron-Folic Acid Supplementation*

<table>
<thead>
<tr>
<th>Place and Year</th>
<th>N</th>
<th>Acute Malnutrition (Weight-for-Height)</th>
<th>Chronic Malnutrition (Height-for-Age)</th>
<th>General Undernutrition (Weight-for-Age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% pupils &lt; -2 SD</td>
<td>% pupils &lt; -2 SD</td>
<td>% pupils &lt; -2 SD</td>
</tr>
<tr>
<td>Trapiang Reang School</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>233</td>
<td>9%</td>
<td>60%</td>
<td>59%</td>
</tr>
<tr>
<td>2000</td>
<td>215</td>
<td>10%</td>
<td>55%</td>
<td>53%</td>
</tr>
<tr>
<td>Dang Tung School</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>207</td>
<td>4%</td>
<td>45%</td>
<td>42%</td>
</tr>
<tr>
<td>2000</td>
<td>197</td>
<td>4%</td>
<td>43%</td>
<td>38%</td>
</tr>
</tbody>
</table>

*No significant improvement of anthropometric data was observed after the intervention.
for the assessment of stunting, wasting, and overall nutritional status.

Correct assessment of the age is a prerequisite for valid comparison of growth measurements to a corresponding reference population. As most official birth registers were lost during the war in Cambodia, parents registered their children at school when they perceived they had reached an appropriate height. Since the majority of children are small for their age, their parents tend to send them to school late. Obtaining correct age data involved interviewing parents and caretakers during home visits to determine the correct birth date. Our data showed that the school registration age in rural Cambodia could not be used for comparative studies of anthropometric measurements based on age. Proper data on age for school registration need to be derived.

### Prevalence of Stunting and Wasting

Roughly half of the children 5 to 11 years of age, and close to 90% of those 12 years and over were stunted. Supplementation with iron, folic acid, vitamin A, and vitamin B complex for those with clinical vitamin B deficiency symptoms did not significantly improve the situation. This finding suggests that protein, calories, and perhaps other micronutrients that were not supplemented were still in short supply. Moreover, improvement of growth in height after nutrition intervention was mostly seen in younger children and infants, not in school-age children. Accurate data on food intake were not available, so we could not analyze differences in this parameter between the two locations. Clinical symptoms such as anemic pallor were frequent, and angular gingivitis was seen in 10% to 15% of pupils in both schools during the health surveys.

### Experience and Compliance with Iron-Folic Acid Intervention

This is the first Hb survey done in rural schools in Cambodia. It showed a high prevalence of anemia, which is likely to impair children’s health and school performance. This probably contributed to the high number of children (approximately 50%) repeating grade one.

The low Hb values suggested the need to start an intervention program immediately. Thus, the interven-

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**Table 3. Prevalence of Anemia among Grade-One Pupils in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999 and July 2000 Before and After Weekly Iron-Folic Acid Supplementation**

<table>
<thead>
<tr>
<th></th>
<th>Trapiang Reang</th>
<th>Dang Tung</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before Intervention (1999)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-11 yrs</td>
<td>(N = 211)</td>
<td>(N = 171)</td>
</tr>
<tr>
<td>Anemia†</td>
<td>130 (62%)</td>
<td>98 (57%)</td>
</tr>
<tr>
<td>12-14 yrs</td>
<td>(N = 23)</td>
<td>(N = 46)</td>
</tr>
<tr>
<td>Anemia†</td>
<td>19 (83%)</td>
<td>42 (91%)</td>
</tr>
<tr>
<td>All</td>
<td>149 (64%)</td>
<td>140 (65%)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-11 yrs</td>
<td>(N = 160)</td>
<td>(N = 70)</td>
</tr>
<tr>
<td>Anemia</td>
<td>19 (12%)</td>
<td>32 (26%)</td>
</tr>
<tr>
<td>12-14 yrs</td>
<td>(N = 52)</td>
<td>(N = 122)</td>
</tr>
<tr>
<td>Anemia</td>
<td>23 (44%)</td>
<td>38 (55%)</td>
</tr>
<tr>
<td>All</td>
<td>42 (20%)</td>
<td>70 (37%)</td>
</tr>
</tbody>
</table>

*The sample size in group 12-14 years of age increased in 2000 as children 5-11 years of age in 1999 became 1 year older.
†Anemia was defined as hemoglobin <115 g/L for age group 5-11 years; <120 g/L for age group 12-14 years. Anemia was significantly more prevalent in the older age group at both locations (Student’s t-test; P < 0.0001). No significant differences were seen between sexes (data not shown).
tion was not part of a preplanned trial, but rather a response to an urgent need. This situation, as well as ethical considerations, explains the lack of a placebo group, which would have been desirable to assess the specific impact of the intervention. However, in spite of this, a marked impact of the intervention on Hb concentration and a marked reduction in the prevalence of anemia became obvious.

The reduction in prevalence of anemia strongly supports the usefulness of iron-folic acid supplementation in schoolchildren 6 to 12 years of age. At the beginning of the intervention, some children complained about stomachache after ingestion of the iron-folic acid pills. The frequency of gastrointestinal side effects is known to relate to the iron dose, but symptoms were most common in pupils who came to school without breakfast. Interviews with pupils showed that 30% went to school on an empty stomach. Although it was recommended that students eat some food prior to weekly iron distribution, this was not possible in all cases, leading to about 5% of schoolchildren avoiding school on the day tablets were distributed. During the 20-week school period in 1999–2000, tablets were handed out 20 times. On average, schoolchildren accepted the tablets 18 times and 14 times in Trapiang Reang and Dang Tung, respectively, corresponding to a compliance of approximately 90% and 70%, respectively. Weak teacher supervision in some classrooms in Dang Tung was identified as the main cause of the lower compliance and effectiveness at this location.

A problem with the interpretation of these data is that we cannot separate the impact of iron supplementation on anemia reduction from that of the vitamin A and mebendazole interventions. As the compliance with vitamin A and mebendazole distribution was high in both schools (because of the supervised distribution by health center staff), it is likely that the lower compliance with iron intake in Dang Tung was the main cause of the lower success regarding anemia reduction in that school. Nevertheless, the regimen of one tablet of iron per week handed out at school was satisfactory.

Regarding the degree of malnutrition, no significant changes were observed before or after intervention. Both surveys were done in July at the beginning of the rainy season. Without famine or war, wasting is mainly caused by diarrhea due to unsafe water and food. As the pupils were living in the same environmental conditions during both surveys, no change was expected. The small decrease observed in the prevalence of stunting may be interpreted as an indication of slightly improved food security or as the consequence of the intervention. Further work needs to be done to improve food security to insure proper nutrition for children before and after birth.

**Stool Analysis**

During the baseline survey in 1999, 42% of the children were infected with hookworms and 12% with *S. stercoralis*. Both parasites enter the body from contaminated soil via the skin of feet. The reason for such high prevalence is that 84% of the homes had no latrines. As 90% of the children did not wear shoes during defecation, frequent re-infection with hookworms was likely. Indeed, the follow-up survey in 2000 found little reduction in the prevalence of hookworm infestation, although the number of hookworm eggs counted in the stool had decreased markedly. This is a success regarding the impact of hookworm infestation on anemia, as the extent of intestinal bleeding correlates with the number of hookworms in the intestine. *S. stercoralis* infestation decreased by 50%. Therefore, intervention with mebendazole is a useful tool to reduce intestinal blood losses, but needs to be given on a regular basis to cope with frequent reinfection.

**CONCLUSIONS**

An integrated community approach including mass deworming, health education, and multi-micronutrient supplementation was very effective in reducing anemia in schoolchildren in Cambodia and should be adopted on a larger scale.

A number of lessons can be learned from the observations reported:

1. Growth assessment needs to be related to correct age. This is a critical issue in Cambodia, as birth registers are often missing or inaccurate, resulting in parents sending their children to school late.

2. The Cambodian diet is deficient in many ways. The results suggest that the supplementation of iron, folic acid, vitamin A, and B vitamins are not sufficient to reduce the prevalence of stunting. Additional nutrients are needed, including a sufficient supply of protein, calories, and other micronutrients.

3. Anemia in this study occurred in two-thirds of grade-one schoolchildren 5 to 11 years of age and in up to 80% to 90% of children >12 years of age. Though the database is limited, supplementation of iron and folic acid in these age groups seems urgently needed on a larger scale.

4. Weekly iron-folic acid supplementation is a useful tool to mitigate the extent and prevalence of anemia in grade-one Cambodian children. Supplementation with other micronutrients, such as vitamin A and possibly others, as well as hookworm control, are likely to be helpful in this effort. To improve compliance, however, it may be advisable to use a lower single dose of iron than the 60 mg used in this study. It may also help to provide the iron supplement...
together with or shortly after school meals, since many children come to school without breakfast.

5. Regular mebendazole administration proved useful in reducing the number of hookworm eggs in the intestine. To improve the hygienic situation and to reduce hookworm infestation, latrine programs and education on how to maintain them are needed. In addition, children should wear shoes to reduce infestation with hookworms.

Based on results from the pilot weekly iron supplementation program reported herein, the program has been expanded to 25 Cambodian schools supported by GTZ’s Rural Development Program. Fifteen thousand primary school children receive weekly supplementation, many of them since late 1999. The results of this survey suggest that such an intervention is very cost-effective, since iron-folic acid tablets cost around 5 cents US per child per year.

ACKNOWLEDGEMENTS

The program was supported by GTZ (German Technical Cooperation). The survey was performed with the help of the Nutrition Department, National MCH; the Parasitology Department, “Centre National de Malaria”; UNICEF; and the Provincial Health Direction of Kampot Province. We take this opportunity to thank Dr. Barbara Underwood for her expert advice in recommending the weekly iron-folic acid supplementation in this study and for her editing of this paper. We thank Dr. Klaus Schuemann from the Institute for Physiology of Nutrition, Technical University of Munich, for his help in drafting the manuscript.

REFERENCES

Industry Experience in Promoting Weekly Iron-Folic Acid Supplementation in the Philippines
Josel Garcia, Eva Datol-Barrett, and Maynilad Dizon

After participating in a pilot project under a government-industry partnership to promote the adoption of weekly iron-folic acid supplementation among women of reproductive age in the Philippines in 1998, United Laboratories (UNILAB), the Philippines’ largest private pharmaceutical company, decided in April 2002 to launch a weekly iron-folic acid supplement for pregnant and non-pregnant women under the brand name Femina™. The business objective set for the Femina brand was to build the category of preventive iron-folic acid supplements in line with the Philippine Department of Health’s advocacy on weekly supplementation as an alternate to daily dosing to reduce the prevalence of anemia in the country. The brand was supported with an integrated mix of traditional advertising media with complementary direct-to-consumer educational programs that aimed to create awareness of iron-deficiency anemia, its causes and effects, and the role of weekly intake of iron-folic acid in preventing the condition. Aggressive marketing support for 1 year was successful in creating awareness among the target women. Significant lessons derived from consumers identified opportunity areas that can be further addressed in developing advocacy programs on weekly iron supplementation implemented on a nationwide scale in the future.

Key words: industry experience, marketing, iron-folic acid supplement, industry-government partnership

1998 PANGASINAN, PHILIPPINES PILOT PROJECT

In 1998, the Philippine Department of Health (DOH) and the World Health Organization (WHO) Regional Office for the Western Pacific Region (WPRO) launched a pilot project in Pangasinan, a province in the Philippines, to assess the impact of weekly iron-folic acid supplementation in improving the iron status of women of reproductive age (WRA). Details of the pilot project are reported elsewhere in this volume. Since the type of weekly supplement proposed by WHO was not available on the market, United Laboratories (UNILAB), Manila, Philippines, was asked to manufacture one. This paper describes UNILAB’s experience in this industry-government partnership. We first discuss the product, key marketing activities, and key results on consumer behavior during the 1998 test market, followed by marketing activities and key lessons learned from the national launch.

THE PRODUCT

Two preparations of iron-folic acid were used in the project: Femina 60 (60 mg elemental iron and 3.5 mg folic acid) for non-pregnant women and Femina OB (120 mg elemental iron and 3.5 mg folic acid) for pregnant women. The following factors were considered in the choice of the final product appearance: ease of swallowing, size, and color. Elliptical-shaped tablets of small size were chosen for ease of swallowing; light pink color was chosen for the 60 mg preparation and red for the 120 mg format (Table 1 gives more detailed information about the supplements).

Flexible foil packaging was used to ensure better stability and protection for the tablets. UNILAB packaged the tablets by four pieces attached to a catch cover, as it was intended for 1 month’s supplementation. Such packaging was made to encourage women to buy the entire 1-month package. The package also contained information about the product, the importance of iron and folate in the body, food sources of iron and folate, product indication, and dosage.

DISTRIBUTION

Femina OB was donated by UNILAB for the project and was given free to all pregnant and lactating women...
through the rural health units of the participating areas. Femina 60 was made available for sale at the local drugstores and through the village (“barangay”) health workers. Owners of the local drugstores were oriented on the project and on the importance of their role in making the supplements available. Local barangay health workers and rural health unit staff were made part of the marketing system in the project sites as direct sellers. Aside from the monetary incentives they were given for every sale of the product, local staff were educated on the importance and benefits that could be derived by women who participated in the project, which further enabled them in effective product selling.

**SOCIAL MARKETING PROGRAM**

Social marketing programs were utilized to encourage the female population of the Pangasinan test areas to take the weekly iron-folic acid supplement and, at the same time, to improve their dietary intake of iron and vitamin C-rich foods, as discussed in the two accompanying Philippine papers in this volume. Support and participation was obtained from implementers and key persons in the local area, such as barangay health workers, rural health unit staff, local government officials, and church and school officials, all of whom were mobilized to ensure the effectiveness of the program’s implementation.

UNILAB assisted in the development and production of various information, education, and communication (IEC) materials such as posters, leaflets, streamers, and newsletters for every activity implemented. All materials adopted a common look, such as the basic pink-colored background, a uniform logo bearing the Femina brand name, and a single message consistent with the product’s positioning as a once-weekly iron-folic acid supplement.

Various promotional programs were implemented by UNILAB to encourage both the selling of the product by the barangay health workers, rural health unit personnel, drugstore personnel, teachers, and others, and the purchase of the product by the target female users. Community activities such as games and mini-olympics were sponsored by UNILAB to foster camaraderie among the barangay health workers and rural health unit personnel and to show the organizing committee’s appreciation of their support for the project.

A search for “Ms. Femina” was conducted in the three participating towns, where community members were required to attach empty Femina packages as proof of purchase along with their entry votes for their desired contestant. Entry coupons contained the name of the candidate together with the name of the barangay represented by the contestant, the name, address, and signature of the entry sender, and the name and address of the seller. All coupons presented with Femina packages purchased before and after the contest were raffled and prizes given to both the winning entry sender and the seller.

School-based activities were conducted to generate awareness and involvement of female students, which primarily targeted third- and fourth-year high school students of three schools from each town, since they were most likely to develop iron-deficiency anemia and were most eligible for marriage. To introduce and disseminate information about the project and the product to the targeted schoolgirls, a symposium on iron and iron-deficiency anemia was held in each school.

**Table 1.** Product and Packaging Description of Iron-Folic Acid Supplements Made by United Laboratories (UNILAB), Manila, Philippines, for Non-Pregnant (Femina OB) Women in the Philippines

<table>
<thead>
<tr>
<th></th>
<th>Femina 60 (60 mg iron and 3.5 mg folic acid)</th>
<th>Femina OB (120 mg iron and 3.5 mg folic acid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Format</td>
<td>Film-coated tablet</td>
<td>Film-coated tablet</td>
</tr>
<tr>
<td>Color</td>
<td>Light pink</td>
<td>Dark pink</td>
</tr>
<tr>
<td>Shape</td>
<td>Capsule shape elliptical</td>
<td>Capsule shape elliptical</td>
</tr>
<tr>
<td>Appearance</td>
<td>Bisected on one face</td>
<td>Bisected on one face</td>
</tr>
<tr>
<td>Weight</td>
<td>321 mg</td>
<td>451 mg</td>
</tr>
<tr>
<td>Thickness</td>
<td>168 ± 5 mils</td>
<td>185 ± 5 mils</td>
</tr>
<tr>
<td>Packaging Format</td>
<td>Four tablets individually wrapped in flexible foil packaging with catch cover (packer)</td>
<td>Four tablets individually wrapped in flexible foil packaging with catch cover (packer)</td>
</tr>
<tr>
<td>Packaging Design and Color</td>
<td>Packaging design conforming with the Philippine Bureau of Food and Drug’s generic packaging guidelines, predominantly light pink-colored background, use of an image of a young girl to represent target users</td>
<td>Packaging design conforming with the Philippine Bureau of Food and Drug’s generic packaging guidelines, predominantly red-colored background, use of an image of a pregnant woman to represent target users</td>
</tr>
</tbody>
</table>
and health economics teachers were in charge of project implementation and also served as product sellers. The process of convincing and motivating students to buy and take Femina was strengthened during the health/science classes, where continuous information about the importance of iron supplementation, as well as dietary improvement among WRAs, was disseminated through IEC materials such as flipcharts, posters, leaflets, newsletters, and streamers. A “Club Femina” for the female students of the schools was established. Quarterly Club Femina newsletters were released to approximately 2000 student members, and contained articles of high interest to the target students, such as grooming tips, fashion trends, literary articles, and especially the importance of improving diet and of taking weekly iron-folic acid supplements to prevent anemia.

RESULTS OF THE PILOT MARKET

Consumer measures gathered during the pilot market showed good potential for launching the product on a national scale, as reflected by favorable results in a consumer usage, attitude, and imagery study among the study area’s female population. Femina attained a brand awareness rate of 40% despite the absence of mass media support; a conversion rate (percentage of females who tried the product among those aware of brand) of 44%; and a brand retention or loyalty rate (percentage of those who used the product often among those who tried) of 59%. Key success factors of the Pangasinan test market included social mobilization (involvement of the entire community with strong support from the authorities from local schools and government) and the public-private sector partnership (DOH and UNILAB) in the advocacy campaign for the prevention of iron-deficiency anemia.

NATIONWIDE LAUNCH

It was a strategic decision to expand the distribution and promotion of Femina 60 nationwide after UNILAB’s participation in the Pangasinan test market. Although by virtue of its formulation, Femina belongs to the iron/hematins product category, it has no direct competition because of its unique once-a-week dosage and preventive approach; most of the products in this segment are therapeutic and dosed daily.

The Philippine iron market is close to P300M (300 million Philippine pesos) in value and is composed of single iron, iron with folic acid, and iron with vitamins/minerals products. Dominant brands are Iberet™ and UHP Fersulfate™ (the latter is also a UNILAB product). As of 2002, the iron category was growing on par with the pharmaceutical industry (10%). Consumer tracking data showed that this segment is still not fully saturated, as the current penetration level is barely 20% (i.e., 80% non-users).

MARKETING SUPPORT

Femina’s marketing communications plan was a mixture of traditional and non-mainstream media. The following were implemented simultaneously during the launch:

- Advertising (TV, radio, print, various informational advertorials);
- Merchandising at point of sale;
- Merchandising in other points of contact with target females (female toilets/comfort rooms);
- Equity-building creative media buys;
- Hospital detailing and sampling;
- Strategic alliances;
- Trade promotions;
- Massive education and sampling program in offices and schools; and
- A heavy public relations campaign.

LAUNCH RESULTS

Education via advertising was instrumental in creating awareness of iron-deficiency anemia and the use of iron supplements as a preventive measure. The communications strategy was to first educate the market on iron-deficiency anemia before fully introducing Femina. An infomercial campaign showing iron-deficiency anemia as a potential serial killer victimizing all menstruating women was an influential, strong ad that reached a fairly high level of awareness. “Biktima ka ba?” (“Are you a victim?”) was the catch phrase in that campaign. The second phase of the campaign established the problem-solution idea. Preliminary tracking results (with a sample size of 360) showed a 30% “top of mind ad awareness” only 2 weeks after airing the thematic TV commercial (Figure 1). Femina was the most recalled ad

![Top of Mind Ad Awareness](Image)

Figure 1. Tracking study among the female target market for the launch of Femina, a weekly iron-folic acid supplement, in May-June 2002, in the Philippines. Source: NFO-Trends as contracted by UNILAB: “Project Myriad Brands and Ad Development Tracking Study on Adult Vitamins/Multivitamins and Iron Supplement (May-June 2002 Reading),” conducted in metro Manila, Philippines. ■ = Week 1; ■ = Week 2.
of brands for iron-deficiency anemia, its spontaneous awareness being even higher than for the traditional leader, UHP Fersulfate.

Very focused and ownable benefits communicated in advertisements led to achieving fairly high scores in the tracking study, specifically measuring the association of Femina with the desirable strategic attributes. Table 2 shows that initial results indicated Femina’s ownership of the once-a-week attribute. Unavoidably, most of the strategic attributes Femina hoped to own were shared with the market leader, UHP Fersulfate.

Heavy media weights (high share of investment, the budget for media initiatives, and high share of voice, a measure of “TV noise” compared with other advertising brands) indicated that Femina’s TV advertising was the primary force in achieving high advertising and brand awareness for the brands reflected in the brand tracking results mentioned above. The high share of voice was necessary, as Femina had to undertake a two-pronged approach during its launch: an education drive on iron-deficiency anemia and brand building.

Professional marketing showed early indications of being successful in achieving Femina’s objective to educate the market on iron-deficiency anemia prevention, which cannot be fully explained in TV advertising. Key strategies implemented were: hospital detailing covering the top 1000 general practitioners and pediatricians nationwide; an office education program on women’s health covering 75,000 employees in the greater Manila area alone; and a school program targeting 700,000 students by year’s end. Some qualitative feedback from doctors and consumers after 4 months of promotional efforts among health professionals included:

- Doctors’ feedback:
  - General practitioners showed interest and support for Femina.
  - The once-a-week dosage caught most of their attention.

- Consumers’ feedback:
  - Most of the office employees were already aware of Femina due to advertising.
  - Brand recall for iron-deficiency anemia, Femina, and “Biktima ka ba?” was enormous.
  - Seminars established the need for iron-folic acid supplementation.
  - Male employees wanted to share information with their wives, daughters, and mothers.
  - Strategic alliances were forged with relevant and respectable government institutions to lend more credibility to the brand (Table 4).

Table 2. Ownership of Strategic Attributes from Major Iron-Folic Acid Supplements in the Philippines

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Femina</th>
<th>UHP Fersulfate</th>
<th>Iberet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevents iron-deficiency anemia</td>
<td>67%</td>
<td>67%</td>
<td>43%</td>
</tr>
<tr>
<td>Ensures sufficient iron bank</td>
<td>62%</td>
<td>72%</td>
<td>45%</td>
</tr>
<tr>
<td>Once-a-week dosage</td>
<td>62%</td>
<td>40%</td>
<td>38%</td>
</tr>
<tr>
<td>Combination formula (iron + other nutrients)</td>
<td>61%</td>
<td>61%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Table 3. Share of Voice (SOV) in First Six Months of the Nationwide Launch of Femina in 2002 in the Philippines*

<table>
<thead>
<tr>
<th>Brand</th>
<th>SOV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femina™</td>
<td>23%</td>
</tr>
<tr>
<td>M yra™ 300 E</td>
<td>23%</td>
</tr>
<tr>
<td>UHP™</td>
<td>11%</td>
</tr>
<tr>
<td>Cecon™</td>
<td>4%</td>
</tr>
<tr>
<td>Calci-Aid™</td>
<td>9%</td>
</tr>
<tr>
<td>Caltrate™</td>
<td>6%</td>
</tr>
</tbody>
</table>

AGB Media Monitoring System in the Philippines provides companies with technological solutions for monitoring television broadcasts.

- Doctors viewed Femina as a product committed to uplifting the health and well-being of women.
- Consumers’ feedback:
  - Most of the office employees were already aware of Femina due to advertising.
  - Brand recall for iron-deficiency anemia, Femina, and “Biktima ka ba?” was enormous.
  - Seminars established the need for iron-folic acid supplementation.
  - Male employees wanted to share information with their wives, daughters, and mothers.
  - Strategic alliances were forged with relevant and respectable government institutions to lend more credibility to the brand (Table 4).

**KEY LESSONS FROM THE NATIONWIDE LAUNCH**

Combined strategies of advertising and professional marketing contributed to the high awareness of Femina and iron-deficiency anemia. There is no doubt that Femina’s campaigns stirred the market’s awareness on iron-deficiency anemia and consequently stimulated the need to prevent it. It generated the highest share of mind with respect to ads for iron-deficiency anemia (above 30%), as well as high unaided/spontaneous brand awareness (78%). The challenges after having created product awareness were: 1) to further increase trial and maintain retention by convincing the targets to sustain the weekly Femina habit, and 2) for consumers to see Femina as an indispensable, integral part of their healthy lifestyles.

A strong, compelling message on iron-deficiency anemia is needed to encourage regular use of an iron-folic acid product. Consumers need to fully understand iron-deficiency anemia and the role of once-weekly iron-folic acid supplements for prevention, and to know the causes, symptoms, and consequences of iron-deficiency anemia to be able to relate to the issue. Further education is needed to make women realize that symptoms often mistaken as normal adverse effects of modern busy
lifestyles or improper eating, such as dizziness, fatigue, and paleness, may be symptoms of a more serious health condition such as iron-deficiency anemia.

In the Philippines, iron-deficiency anemia is considered an ailment; therefore, Femina and all other iron supplements are viewed as medicines that cure anemia, and as such, do not need to be taken unless one is sick. The challenge is to effect a total mindset change by strongly reinforcing Femina’s preventive actions rather than having it be seen as a therapeutic product. The importance of iron to one’s body is not clear to the majority of Filipino females, more so because it has no strong perceivable benefits.

Implementing on a national scale the social marketing efforts in Pangasinan entails a substantial investment of resources. Table 5 provides a comparative chart of the activities undertaken in the Pangasinan test market and the national launch.

It is important to segment the very wide target market and determine the best communications approach for each group. The younger segment (female adolescents) were the most indifferent to the concept of iron supplementation and iron-deficiency anemia. However, test market results in Pangasinan showed that the key to their compliance was their teachers, who emerged as not only credible nutrition counselors but were also effective in influencing the girls to take the supplements. Therefore, a school program component is critical in addressing this specific age market. Women in their 20s to mid-30s (pre-conception stage) are the most receptive.

Table 5. A Comparative Chart of the Pangasinan Test Market and National Launch Efforts for Femina in the Philippines

<table>
<thead>
<tr>
<th>Pangasinan Test Market*</th>
<th>National</th>
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<tbody>
<tr>
<td>• Advocacy campaign with town mayor and rural health unit heads</td>
<td>• Orientation and training of barangay health workers</td>
</tr>
<tr>
<td>• Use of village (“barangay”) health workers as sales channels</td>
<td>• Advocacy campaign with school officials</td>
</tr>
<tr>
<td>• Training of health education teachers</td>
<td>• Teaching aid production and dissemination</td>
</tr>
<tr>
<td>• Use of teachers as sales channels</td>
<td>• Integration of iron-deficiency anemia in the nutrition curriculum</td>
</tr>
<tr>
<td>• Availability of Femina in school cooperatives/canteens</td>
<td>• Orientation of drugstore owners and distributors</td>
</tr>
<tr>
<td>• Product symposium in town plazas for community orientation</td>
<td>• Merchandising at point of sale</td>
</tr>
<tr>
<td>• Conduct of school-based promotional activities (essay-writing, marathon, search for “Ms. Femina”)</td>
<td>• Trade and consumer promotions</td>
</tr>
<tr>
<td>• Mobilization of parent-teachers’ association as support group</td>
<td>• Consumer education and sampling program in offices (GMA)</td>
</tr>
<tr>
<td>• Establishment of “Club Femina” in schools</td>
<td>• Mass media advertising</td>
</tr>
<tr>
<td>• Orientation and training of barangay health workers</td>
<td>• Below-the-line activities (e.g., product sampling)</td>
</tr>
<tr>
<td>• Advocacy campaign with school officials</td>
<td>• Hospital detailing</td>
</tr>
<tr>
<td>• Teaching aid production and dissemination</td>
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<tr>
<td>• Integration of iron-deficiency anemia into the nutrition curriculum</td>
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<tr>
<td>• Orientation of drugstore owners and distributors</td>
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<td>• Below-the-line activities (e.g., product sampling)</td>
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<td>• Hospital detailing</td>
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</table>

*Consumer education and sampling programs in offices (GMA), mass media advertising below-the-line activities (e.g., product sampling), and hospital detailing were not done in this test market.
and sensitive segment to Femina’s initiatives, and should therefore be prioritized with respect to advertising communications.

The once-a-week dosage is a habit that needs to be further built among women. Evidently, there is still confusion and lack of complete knowledge on the benefits of once-a-week iron-folic acid supplementation. Feedback from trade representatives indicate that even salesclerks have difficulty properly articulating the rationale for the weekly dosage. There is a need to conduct refresher product seminars for trade and lay advertisers for consumers in print media. An active and regular habit-building campaign is needed to remind women to take Femina habitually. The once-a-week schedule may be harder to remember compared with daily dosing. A doctor’s prescription is needed to compel trial usage. Focus group discussants and even salesclerks interviewed claimed that consumers hesitate to take Femina without a doctor’s advice. Again, this springs from the general contention that Femina is a drug. Hospital detailing efforts are imperative in this case and must therefore be ongoing until the whole medical community becomes strongly convinced to prescribe weekly supplements for WRA.

CONCLUSION AND RECOMMENDATIONS

The 1998 Pangasinan pilot project and the nationwide launch of Femina in 2002 demonstrated that weekly iron-folic acid supplementation among WRA for the prevention of anemia could be encouraged through a marketing campaign. Educating the target market and the market influencers on the importance of iron and the symptoms/effects of iron deficiency played an essential role in inducing trial and usage of the weekly iron-folic acid supplements. The two programs also showed that weekly iron supplementation could be an alternative to daily intake of iron supplements for the prevention of anemia. However, our experience showed that there is much work yet to be done to promote weekly iron-folic acid supplementation.

Given the lessons learned from the pilot study and from the nationwide launch, the following recommendations can be made:

1. Programs for promoting weekly iron-folic acid supplementation must cover aspects such as product formulation and presentation, distribution, and marketing activities, which should comply with the existing policies promulgated by the government. Partnership with relevant government institutions (e.g., departments of health, education, local governments) may help in the implementation of the programs.
2. The target market and the market influencers must be educated on the importance of iron-folic acid and the symptoms/effects of iron deficiency, as this is essential in inducing trial and usage of the weekly iron-folic acid supplement.
3. Social marketing programs and hospital detailing in promoting weekly iron-folic acid supplementation must be implemented.
4. Availability of the promoted iron-folic acid supplement in outlets easily accessible to consumers with due regard to regulations set by the government on dispensing of drugs/supplements must be ensured.

REFERENCES

**SUMMARY**

**Weekly Iron-Folic Acid Supplementation of Women of Reproductive Age: Impact Overview, Lessons Learned, Expansion Plans, and Contributions Toward Achievement of the Millennium Development Goals**

Tommaso Cavalli-Sforza, Jacques Berger, Suttilak Smitasiri, and Fernando Viteri

**INTRODUCTION**

In this special supplement to Nutrition Reviews, the efficacy of weekly iron-folic acid supplementation in a supervised environment for the prevention and control of iron deficiency and iron-deficiency anemia is reported in young children, and among adolescent and adult women of reproductive age (WRA), whether or not they were pregnant. Most efficacy studies provided the tablets free of charge. Community-based effectiveness studies in which participants have to purchase iron supplements and consume them on a weekly schedule without supervision are rare. Iron supplementation notoriously is viewed as therapeutic and taken on doctor’s orders from medical providers, rather than as a preventive supplement available from non-medical community sources. Therefore, a mindset change is required to convince consumers, particularly WRA and the medical profession, to view weekly iron supplement consumption as part of a normal routine to avoid the risk of ill effects from iron deficiency and anemia. The effectiveness studies reported in this supplement to Nutrition Reviews demonstrate in three Asian countries that a mindset change among WRA is feasible when social marketing and community mobilization accompany affordable supplements available from local providers.

**IMPACT OVERVIEW**

The knowledge, attitudes, and practices (KAP) surveys in all three countries showed that combining social marketing and community mobilization greatly improved women’s understanding of anemia, the type of diets that can prevent it, and the need to take weekly iron-folic acid supplements. Furthermore, the combined approach succeeded in promoting the purchase and use of weekly iron-folic acid supplements by WRA over the year-long project period. Self-reported compliance also increased rapidly and in most cases remained high. The exception was in Vietnam, where the average number of tablets taken decreased slightly over time (and therefore compliance decreased), while the percentage of women in the district buying tablets increased. The increased purchases and compliance resulted in improved hemoglobin (Hb) levels in Vietnam and Cambodia, improved iron status in Vietnam and the Philippines (where iron deficiency was measured), and a reduction in iron-deficiency anemia in Vietnam and anemia in Cambodian schoolgirls.

Some impact findings were specific to country context and to adaptations in the master protocol project design. The Vietnam project showed that regular intake of weekly supplements by menstruating women can ensure that they begin pregnancy with adequate iron stores and Hb concentrations, and demonstrated the effectiveness and safety of weekly iron-folic acid supplementation to prevent and control iron deficiency and iron-deficiency anemia before and during pregnancy. On the other hand, under non-supervised conditions, daily iron-folic acid supplementation was less efficient than weekly iron-folic acid supplementation, since Hb concentrations were lower and anemia prevalence higher in all trimesters of pregnancy. Among WRA taking weekly iron-folic acid supplements who did not become pregnant, significant decreases in the prevalence of iron deficiency from 46% to 19% and in iron-deficiency...
anemia from 9% to 1% occurred during the 12-month intervention. After 9 months of taking weekly iron-folic acid supplements, no woman who had taken at least 25 tablets had an Hb level under 100 g/L.

In all three studies, iron nutrition during pregnancy was better the longer the period of pre-pregnancy preventive supplementation. When weekly iron-folic acid supplements were taken 6 months before conception and continued during pregnancy, no woman had iron-deficiency anemia or iron deficiency in the first or second trimester. When weekly iron-folic acid supplements were taken 3 months before conception and during pregnancy, no woman had iron-deficiency anemia in the first or second trimester, and iron deficiency prevalence in the second trimester was low. The prevalence of anemia in the first trimester was less than 9% among women who took weekly iron-folic acid supplements for 9 to 12 months. These findings are important, because anemia during the first half of pregnancy is associated with low birth weights and preterm delivery.

In the second trimester of pregnancy, an assessment of daily and weekly iron-folic acid supplementation using a cutoff of Hb < 105 g/L revealed an iron-deficiency anemia prevalence of 54% in the daily group and a significantly lower prevalence in the weekly groups: after taking weekly iron-folic acid supplementation for a total of 4.5, 9, and 12 months, iron-deficiency anemia prevalence was 36%, 17% and 15%, respectively (P < 0.001). When weekly iron-folic acid supplements were started with pregnancy, they were as effective as the daily supplements.

The third trimester of pregnancy is the time when iron needs are highest but the effects on perinatal events is lowest. Neither daily nor weekly supplementation provided enough iron to meet needs in the third trimester. However, the prevalence of iron-deficiency anemia was 13% to 15% in the weekly group and more than twice as high in the daily group (31%) (P = 0.07). Beaton suggested that a target mean Hb level at term of 110 g/L, with a cutoff of 90 to 95 g/L to define moderate anemia, would be relevant to estimate the success of a program rather than the recommended 110 g/L cutoff commonly used. Perinatal risks for mother and newborns begin to increase significantly as Hb levels fall below 90 to 100 g/L at term or exceed 125 to 135 g/L during gestational weeks 24 to 32. In the Vietnam project, less than 1.5% of women had Hb concentrations below 95 g/L in the third trimester.

Noteworthy is the observation that a significant number of subjects who took daily supplements had high serum ferritin values: 17.3% had Hb levels ≥ 100 μg/L in the first trimester and 14% during lactation. Daily iron supplementation, therefore, may be associated with a risk of oxidative stress. Weekly iron supplementation prevented excessive ferritin levels.

Birth weight was monitored among some participants in Vietnam. The prevalence of low birth weight was less than 3% in the weekly supplemented group and about 9% in the daily group (P = 0.08). The difference in mean birth weight was 80 g favoring the weekly group (P = 0.15). Although the differences were not statistically significant, with larger sample sizes they would likely become so.

The Philippines project achieved very significant improvements in serum ferritin: 17.6 ± 3.5 μg/L higher in women who took weekly iron-folic acid supplements compared with those who took daily iron-folic acid tablets. The difference was of similar magnitude in non-pregnant and pregnant women. Serum ferritin values were higher in WRA who took weekly iron-folic acid supplements for 6 or more weeks compared with those who took them for less than 6 weeks (with similar findings before and during pregnancy). Hematocrit values were significantly higher (by 1.2 ± 1.3%) in women who took iron-folic acid tablets (weekly or daily) compared with those who took nothing. There were, however, no significant differences in mean Hb values between women who took iron-folic acid supplements (weekly or daily) and those who did not, either before or during pregnancy. Other micronutrient deficiencies are a possible cause for the discrepancy. Infection did not appear to play an important role, since white blood cell levels did not correlate with serum ferritin or Hb levels. The effect of adding vitamin A and other micronutrients on Hb needs further study in the Philippines and other countries where several micronutrient deficiencies are common.

In Cambodia, a social marketing and community mobilization strategy promoting weekly iron-folic acid supplementation was effective in improving Hb levels among schoolgirls but not among factory workers or rural women. Loss to follow-up was large among WRA factory workers due to the high mobility of the workforce and limited access during working hours. In addition, the absence of a non-supplemented comparison group made it difficult to assess changes in Hb among female factory workers.

Socioeconomic status was a significant determinant of the impact of weekly iron-folic acid supplementation in Cambodia. Weekly iron-folic acid supplements were more effective in controlling iron-deficiency anemia among those who were better off socioeconomically in all three participating groups, i.e., secondary school girls, garment factory workers, and rural village women. Greater participation and better compliance in taking weekly supplements may explain this association. The implication for policy is that to improve the effectiveness
of iron deficiency and iron-deficiency anemia control programs, women of lower socioeconomic status should be targeted for specially designed interventions. This is particularly important because these women tend to be at greater risk for anemia.

The Cambodian project among primary school children, which was sponsored by the German Technical Corporation (GTZ) independently of the WHO protocol for WRA, was remarkably successful. Anemia rates in a 12-month period were reduced by 55% to 80% with a combination of multiple public health interventions (weekly iron-folic acid supplementation, vitamin A capsules, deworming, improved water, and health education). This suggests that in the complex Cambodian environment, where many factors, including a high prevalence of hereditary anemia and parasitism, contribute to much higher rates of anemia than in other countries, multiple interventions are needed, including supplementation with multiple micronutrients.

The success of the GTZ-sponsored program in primary schools provides useful lessons for community programs. Improved water and sanitation and education on personal hygiene are needed to reduce high rates of hookworm infection and help to reduce infections due to fecal-oral contamination and related malnutrition. The program also demonstrated the need to provide weekly iron-folic acid supplementation with or shortly after school meals to reduce side effects and improve compliance; this was important because 30% of children did not have breakfast before going to school and were thus more subject to gastric side effects after taking the supplements in the morning.

An integrated community approach combining mass deworming, health education, and multi-micronutrient supplementation was very effective in reducing anemia in primary school children and should be adopted on a larger scale in Cambodia. Reproductive-hematological-genetic education and screening should complement those efforts.

LESSONS LEARNED IN PROMOTING WEEKLY IRON-FOLIC ACID SUPPLEMENTATION IN COMMUNITIES

WRA are willing and able to purchase supplements when they are widely available and affordable. In all three countries studied, WRA showed that they were willing and able to purchase the supplements and interested in continuing to buy them, including in poor rural areas and schools, as in Cambodia. In the Cambodian factories, where supplements had to be provided free, as local laws forbid their sale, WRA asked that the supplements be sold outside the factories so that they could continue taking them in the future.

The sale of weekly iron-folic acid supplements was economically rewarding for producers and community distributors. In each country, the program’s success led to expanding weekly iron-folic acid supplementation through larger-scale programs. In Vietnam and Cambodia, women’s unions and community organizations were rewarded by establishing revolving funds to continue the program after the project ended. In Vietnam, the funds raised from the sale of the tablets were used to buy more supplements (50%), for more social marketing activities (30%), and as an incentive for the collaborators to sell supplements (20%). The variety of social marketing and community mobilization strategies used in the three countries in schools, factories, and communities (discussed in the papers on program process and in the industry paper in this issue) provide valuable lessons for replicating this approach in other countries.

The Philippines pilot project demonstrated that wide availability of the supplements was important to success. Weekly iron-folic acid supplements were sold through multiple channels, including local drugstores, the local health system (through village or “barangay” health workers and rural health units), and in some schools. Health staff received training on the importance and benefits of preventive supplementation, and had a small financial incentive from every sale; this facilitated and encouraged the sale of the supplements and allowed for the provision of counseling by trained staff when needed. In Vietnam and Cambodia, pricing of the supplement was done in consultation with the local communities to ensure affordability by most WRA. Funds raised remained in the community under local control and were used to sustain and expand the programs.

Community mobilization of local government officials, churches, and community organizations, in combination with social marketing, contributed to spreading the message about preventive supplementation. Community involvement was especially critical in Vietnam and Cambodia, because their market system, particularly in health services, is generally less developed compared with other countries in the region, such as the Philippines. Two well-functioning distribution channels contributed to the success of the Vietnamese project. The Women’s Union is a reliable, well-respected community organization whose collaborators sold the supplements to non-pregnant women, helping to inform and motivate them, while also helping health staff to understand the problems met, through their knowledge of the community. The health station staff distributed the supplement free of charge to pregnant women from a central location. Thus, a social mobilization approach, in combination with social marketing, is critical to increasing awareness and participation in preventive health care programs.

Government/industry/community coalitions are critical to success. The Philippines project highlights the impor-
tance of a strong public/private partnership for success of a preventive public health approach to anemia control. The pharmaceutical company producing the supplements (called “Femina” in that country), United Laboratories (UNILAB), Manila, Philippines, used its resources for the development and production of information, education, and communication (IEC) materials for the social marketing campaign, sponsored fun community activities, such as a “M.s. Femina” contest with a raffle and prizes, and a “Club Femina” for female students in nine schools (including a quarterly Club Femina newsletter for approximately 2000 students). UNILAB also conducted an independent survey to monitor changes in KAP of women and supplement sales. The rapid increase in sales of the product achieved in 12 months and monitoring of various market parameters in the pilot phase led UNILAB to the strategic decision to expand the sale of weekly iron-folic acid supplements nationwide.

Industry’s market strategy to WRA for weekly iron-folic acid supplementation needs to be segmented by age. In drawing lessons from the nationwide launch, UNILAB concluded that the combined strategies of advertising and professional marketing contributed to increasing the market’s awareness on iron-deficiency anemia, and consequently stimulated the need to prevent it. The nationwide launch led to important lessons learned on the marketing strategy required by this product, such as the need for market segmentation to target women of different ages. UNILAB realized that a mindset change must be generated for women to see iron supplements as a preventive rather than a therapeutic product, and that an active and regular habit-building campaign is needed to remind women to keep taking Femina weekly.

UNILAB also saw that the weekly iron-folic acid supplementation occupied a niche in the supplements market with no direct competition because of its unique once-a-week dosage and preventive action within the iron supplements category, which still has a very low level of market saturation (barely 20%).

Economic status is associated with compliance. In Cambodia, rural village women and schoolgirls with higher socioeconomic status were more likely to take supplements than their lower-socioeconomic status counterparts. Garment factory workers with secondary school education (11th or 12th grade) had a significantly greater improvement in Hb than those with elementary education only (5th grade or less). This shows the need to focus future efforts on women of lower-socioeconomic status when the program is expanded.

**EXPANSION PLANS**

The success of the program led to expansion of the project in all three countries. In Vietnam, the project expanded into two additional districts in 2003, and expansion of the new preventive approach to a whole province in the north of the country is under discussion. Consideration is also being given to providing all adolescent girls in high school with weekly iron-folic acid supplements to better prepare them for motherhood. A local weekly iron-folic acid supplement was produced for use in the expansion phase, which was cheaper but less attractive than that supplied by UNILAB. The new supplement was in packages of 30 tablets (a 7-month supply) and sold at a low price, well affordable by Vietnamese rural WRA (US $0.20 per package). Though funds from the pilot phase revolving fund allowed for the purchase of the cheaper local supplement, they were insufficient to continue providing an incentive to Women’s Union collaborators for promotional activities. Between 42% and 65% of WRA in the two districts bought and used the weekly iron-folic acid supplements in the first 9 months of the expansion phase, with progressively increasing rates in the first 6 months. Nonetheless, about a 20% decrease from the pilot phase in percentage of WRA buying the supplements occurred in the expansion phase. This illustrates the need to monitor closely what women thought of the supplements and to sustain promotional activities to counteract any unanticipated negative influences. Investigations during the pilot project showed that a rumor attributing negative effects to the supplements may have played an important role in decreasing sales.

In Cambodia, all three populations of women, schoolgirls, factory workers, and rural WRA, showed substantial improvements in knowledge about the causes and consequences of anemia and its prevention, and the large majority of those involved expressed the desire to continue supplementation. Furthermore, the program led to increased awareness and support among policy makers and to a commitment by the director of health to pay for the weekly iron-folic acid supplements for preventing anemia in WRA and schoolchildren, if other agencies could provide the support needed for sustained social marketing. Multiple partners working together from the national to the community level showed that multisector collaboration for the prevention of anemia through long-term supplementation can be successfully achieved. During a workshop on iron-deficiency anemia held in Phnom Penh in September 2004, it was recommended that weekly iron-folic acid supplementation should be extended to all primary schools in Cambodia. As a result, weekly iron-folic acid supplementation has been introduced in Cambodian schools.

A nationwide launch of a weekly iron-folic acid supplement (Femina) occurred in the Philippines through collaboration among government, industry, and community. UNILAB made the strategic decision to expand the
sale of weekly iron-folic acid supplements nationwide, with commercial campaigns through the mass media (TV, radio, newspapers), using a number of marketing strategies described in the report in this supplement on the industry’s experience. In the expansion phase of the project, the Department of Health gave permission to quote in UNILAB’s ads “UNILAB supports the Government programme on Iron Deficiency Anaemia.”

The Department of Education introduced the supplements in schools, and UNILAB signed a pledge of commitment to support their programs advancing women’s health care. The Junior Chamber International (JCI), Manila, Philippines, partnered with UNILAB and the Philippines’ Department of Health and Department of Education from October 2003 to February 2004 for a metro Manila-wide public information and awareness campaign on iron-deficiency anemia. This campaign included supplement distribution to 180,000 female public school students in 100 high schools in seven major cities of metro Manila, as well as 60,000 young housewives and professionals in selected districts of the city of Manila. The project was very successful and received an award for the “Best Community Development Programme” during the 2004 JCI Asia Pacific Conference in Malaysia, in competition with 71 other bids from the region. JCI chose the project “MJC Fights Iron-Deficiency Anemia” as the best JCI project related to the advancement of the United Nations Millennium Development Goal (MDG) #5 (Improving Maternal Health), and presented it during the second JCI-UN Leadership Summit, on the theme “Youth Leaders Achieving Results in the UN MDG” in July 2004 and at the JCI World Congress in Fukuoka, Japan in November 2004.

In September 2003, the WHO Regional Office for the Western Pacific organized a workshop to review the outcomes and process of the pilot weekly iron-folic acid supplementation effectiveness projects and draw conclusions and recommendations for scaling up the weekly approach for possible extension to other countries in various settings such as school health and safe motherhood programs. It was concluded that the new approach of unsupervised weekly iron-folic acid supplementation, selling the supplements with the support of social marketing and mobilization, is feasible and can reduce the prevalence of anemia and improve iron status in a variety of settings, including rural communities, schools, and factories, and in countries with different socioeconomic structures and cultures. It was suggested that there is sufficient evidence for WHO and countries in the western Pacific region to introduce weekly iron-folic acid supplementation as a preventive approach for WRA’s where anemia is a public health problem.

Participants pointed to the need for a paradigm shift from curative to preventive iron-folic acid supplementation for WRA’s in countries with high anemia prevalence. In these countries, weekly iron-folic acid supplementation should be promoted from menarche to menopause, the high-risk period for anemia, until appropriate diets and effective fortification programs can independently ensure adequate iron and other micronutrient intakes. This would have additional benefits for the prevention of neural tube defects, in places where they constitute a public health problem, for example, China. Long-term weekly iron-folic acid supplementation was considered safe where micronutrient fortification programs, including iron and folic acid, are in place.

**WEEKLY IRON-FOLIC ACID SUPPLEMENTATION AND MILLENNIUM DEVELOPMENT GOALS**

Anemia is one of the most prevalent forms of malnutrition. Preventing anemia by the weekly iron-folic acid supplementation approach can therefore contribute to improve health and development in many ways. This can be shown by analyzing the contribution that successful anemia prevention programs can make towards the achievement of the MDGs:

**MDG #1: Eradicate Extreme Poverty and Hunger**

Iron-deficiency anemia reduces the ability of the blood to carry oxygen from the lungs to the brain, muscles, and other organs. This affects the body’s capacity to do work, as well as the brain’s capacity to think and learn. One of the most pernicious effects of moderate and severe infant anemia is neurological damage, which, like that caused by iodine deficiency, is permanent. The implications for work capacity and educational achievement are very serious, because men, women, and children are affected. It is estimated that for every 10% increase in Hb, there is a 15% increase in physical work capacity. The effect of anemia on productivity can be reversed with improvements in iron nutrition. Preventing anemia, therefore, contributes to improving human capacity and productivity throughout the life cycle and across generations.

**MDG #2: Achieve Universal Primary Education**

Preventing anemia improves nutritional status and reduces the frequency and severity of infection. This not only helps to reduce morbidity and mortality, but also helps to increase school attendance, learning capacity, and school achievement.
MDG #3: Promote Gender Equality and Empower Women

In many countries, where girls are affected by anemia more than boys, especially in adolescence, and have lower attendance and achievement at school, preventing anemia contributes to the elimination of gender disparity in primary and secondary education.

MDG #4: Reduce Child Mortality

Because much of the iron that the infant needs comes from the mother during pregnancy, maternal anemia leads to infant anemia\(^{19,20}\) with serious consequences for infant health and survival, including stillbirth, infant death, and brain damage. Improving iron status and preventing pregnancy anemia thus helps reduce child mortality.

MDG #5: Improve Maternal Health

Women in pregnancy are at increased risk of mortality. Each year, about half a million women die in childbirth or from related causes. It is estimated that 20% of these maternal deaths, some 100,000 per year, are directly attributable to the effects of anemia.\(^{18,21,22}\) By improving iron status and preventing pregnancy anemia, weekly iron-folic acid supplementation helps to reduce maternal mortality.

MDG #6: Combat HIV/AIDS, Malaria, and Other Diseases

The prevention and control of anemia is an important component in the treatment and care of many diseases, and contributes to slowing the progression of AIDS. Resolution of HIV-related anemia has been shown to improve quality of life and physical functioning and to reduce fatigue in individuals with HIV.\(^{23}\)

MDG #7: Ensure Environmental Sustainability

All projects for the prevention of anemia described in this journal (and generally all supplementation projects supported by WHO) combine the promotion of the use of supplements with improved diets rich in iron and other nutrients that contribute to the prevention of anemia and promote iron absorption and utilization. By promoting increased production and consumption of local crops and animals for improved diet diversity and quality, anemia prevention programs contribute to ensuring environmental sustainability.

MDG #8: Develop a Global Partnership for Development

Success in weekly iron-folic acid supplementation programs requires public/private partnerships with pharmaceutical industries, the health and education sectors, non-governmental organizations, and community organizations, and the support of experts and international agencies with experience in applying the new approach. By bringing together many sectors and agencies around a common problem, weekly iron-folic acid supplementation helps to establish partnerships for development. Even beyond unnecessary human suffering, anemia and malnutrition deprive workers and communities of their full physical and mental potential, thereby creating dependence and hindering development. Investments in improved micronutrient nutrition have economic benefits that far outweigh their costs and contribute to sustainable development.\(^{24}\) Anemia prevention will contribute significantly to broader development goals such as child survival, better education, poverty alleviation, and improved reproductive health. All of these will help to bring about the economic and demographic transition that will reduce population growth and contribute to a more equitable, stable, and prosperous world.

CONCLUSION

The effectiveness studies reported herein achieved the goal of improving iron nutrition and reducing iron-deficiency anemia through weekly iron-folic acid supplements voluntarily purchased and used by WRA. Availability and affordability of the product, accompanied by intensive social marketing and community mobilization, contributed to the success of these programs. The next step should be a review of all work done so far on weekly iron-folic acid supplementation, as well as the adoption and promotion by WHO, UNICEF, and the International Nutritional Anemia Consultative Group (INACG) of international guidelines for the use of weekly iron-folic acid supplementation in different settings, such as schools, factories, and the open market, to assist in the development, monitoring, and evaluation of national programs that include preventive supplementation as a new strategy.

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REFERENCES