Anemia is one of the most prevalent public health problems in the world, affecting 42% of pregnant women (56 million) and 47% of children younger than five years of age (293 million). There are three major causes of anemia: inadequate dietary intake of micronutrients, particularly iron, and malaria and helminth infections in some areas of the world. Currently, interventions to address these causes are not operating at-scale in most countries due to lack of interest, funding, and effective management. Implementing these interventions at-scale in developing countries could have the following impact:

<table>
<thead>
<tr>
<th></th>
<th>Impact</th>
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<tbody>
<tr>
<td>Maternal Deaths</td>
<td>Decreased by 20%</td>
</tr>
<tr>
<td>Newborn and Child Deaths</td>
<td>Decreased by 30-50%</td>
</tr>
<tr>
<td>IQ Points and Productivity</td>
<td>Increased by 8 IQ points for populations and by 5-17% for adult productivity</td>
</tr>
</tbody>
</table>

This toolkit recommends an integrated package of services to control the three major causes of anemia and provides background information related to these causes and guidance about
implementing programs to address them. The toolkit also discusses maternal and child health programs that contribute to anemia. Under each TAB there may supporting documents as SUB-TABS that are particularly relevant to the text of the TAB. At the end of each TAB, there are supporting documents related to the TAB. Supporting documents including all the tools and resources also are listed alphabetically in the Tools and Resources TAB.

If you are interested in reviewing WHAT anemia is and its causes, HOW prevalent it is, WHO it affects, and WHY it is a high priority to address, start with the Anemia: Prevalence, Causes & Consequences TAB.

To learn WHAT components are included in an integrated anemia prevention and control package go to Components of the Integrated Package TAB.

To learn about HOW to implement the integrated anemia prevention and control approach take a look at the Program Guidance TAB. You will also want to visit the Tools and Resources TAB.

Lastly, check out the Country and Field Experience TAB to learn more about what countries are doing already. Please do not hesitate to contact us to add new resources or ask any questions you might have. We also welcome your comments regarding the content of this toolkit and any suggestions for improvement.

The Maternal and Child Survival Program (MCSP) is the USAID Bureau for Global Health?s flagship maternal, newborn, and child health (MNCH) program introducing and supporting high-impact health interventions with a focus on 24 high-priority countries. MCSP supports programming in maternal, newborn and child health, immunization, family planning and reproductive health, nutrition, health systems strengthening, water/sanitation/hygiene, malaria, prevention of mother-to-child transmission of HIV, and pediatric HIV care and treatment. Support for this toolkit was made also provided under MCSP?s predecessor, the Maternal and Child Health Integrated Program (MCHIP). For more information about MCSP, visit www.mcsprogram.org.

What are K4Health Toolkits?
K4Health Toolkits are electronic collections of carefully selected information resources on a particular topic for health policy makers, program managers, and service providers. They are based on a continuous publishing principle that allows them to evolve after publication to capture additional resources and to identify and fill remaining information gaps.

**What is the purpose of this toolkit?**

The purpose of this toolkit is to provide information, resources and tools that will assist in advocating for and implementing anemia prevention and control programs using an integrated package of services. The resources in the toolkit will be useful in advocating for increased funding for and attention to anemia prevention and control and in the design, implementation, monitoring, and evaluating of programs.

**Who developed this toolkit?**

The Maternal and Child Integrated Program (MCHIP) Nutrition Team developed the toolkit by selecting published and gray literature on the prevalence, causes, and consequences of anemia and effective programs to address it. The team has identified programmatic experiences malaria and helminth experts, multi-lateral organizations, and universities.

**What types of resources are included?**

The resources include links to scientific articles on the prevalence, causes, and consequences of anemia and program.

**Who are the intended audiences?**

- *Policy makers* can use the information in the Toolkit to identify research and information to develop anemia control strategies and guidelines.

- *Program managers* will find guidance on selecting the best integrated package of interventions to prevent and control interventions. The Toolkit suggests components of an integrated package and gives program guidance for improving program implementation. The toolkit provides information for program managers working in health, education, and agriculture.

- *Communication professionals* will find tools to develop evidence-based behavior change communication messages using qualitative research and some examples of BCC materials developed in some countries.
• Research institutions will find guidance on monitoring and evaluating anemia control programs with some examples of questionnaires that can be adapted for baseline and endline surveys.

How do I get started using this toolkit?

Please visit the Landing Page which gives guidance on how you might want to use the toolkit. To get familiar with the content of this toolkit, use the navigation to view the resources relevant to key program topics. You can also use the search box if you what you are looking for or have a specific item in mind.

Many of the journal articles are under copyright restrictions for the full article. When we cannot provide the full article, we have linked to the abstract which is available for free. In many cases we have provided resources in pdf format. Some of the resources are available in adaptable formats (e.g., Microsoft PowerPoint). We encourage you to adapt these tools so they are useful for you but please credit the original source. If you do use these tools or adapt them, we would love to hear from you. Please email us at toolkits@k4health.org and include the name of the toolkit in the subject line of your message.

How can I suggest a resource to include in this toolkit or comment on the toolkit?

This toolkit is a living resource! Please send us any comments on the toolkit, suggestions for change and materials and tools you have developed. We are interested in reports on the outcomes of anemia prevention and control programs, either an integrated package or single components. Please send any suggested resource here.

New and Noteworthy in Anemia Control

Some of our readers may remember the popular newsletter, "New and Noteworthy in Nutrition," written by Mr. Alan Berg, Nutrition Advisor, at the World Bank in the 1990s. New and Noteworthy in Anemia Control follows the lead of Mr. Berg's newsletter by providing information on new events, publications, and program experience on preventing and controlling anemia. Information will be updated quarterly. If you have suggestions or information which you think would be useful to our readers, please send them to: sstraubinger@path.org and agottwalt@path.org.

See the sub-tabs to the right for what's new and noteworthy in anemia control.
Understanding Anemia: Guidance for Conducting a Landscape Analysis (November 2016)

SPRING Project's "Understanding Anemia: Guidance for Conducting a Landscape Analysis" tool provides guidance to support data collection and analysis to understand the anemia situation and support an evidence-based approach to anemia prevention and reduction. While primarily directed at technical experts planning to carry out a landscape analysis, the guidance will also be of interest to anyone interested in a better understanding of anemia in their country: government staff in anemia-related ministries, nutrition program implementers, and planning staff in anemia-related sectors. This guidance leads readers through the process of conducting a landscape analysis, providing references and examples to further explain each step. The tool is complete and ready for use, but any additional feedback is welcome.

https://www.spring-nutrition.org/publications/series/understanding-anemia
Maternal Anemia and Risk of Adverse Birth and Health Outcomes - Meta Analysis (February 2016)

Anemia is a leading cause of maternal deaths and adverse pregnancy outcomes in developing countries. A systematic review and meta-analysis to estimate the pooled prevalence of anemia, the association between maternal anemia and pregnancy outcomes, and the population-attributable fraction (PAF) of these outcomes that are due to anemia in low- and middle-income countries. PubMed, EMBASE, CINAHL, and the British Nursing Index were searched from inception to May 2015 to identify cohort studies of the association between maternal anemia and pregnancy outcomes. Of 8182 articles reviewed, 29 studies were included in the systematic review, and 26 studies were included in the meta-analysis. Overall, 42.7% of women had anemia during pregnancy in low- and middle-income countries. Pregnant anemic women had 31% higher risk of low birth, 63% higher risk of preterm birth, a 51% higher risk of perinatal mortality and 172% higher risk of neonatal mortality (2 studies only). In low- and middle-income countries, 12% of low birth weight, 19% of preterm births, and 18% of perinatal mortality were attributable to maternal anemia.

IFA Reduces Risk of Stunting - Study from Nepal (January 2016)

The study investigated the effect of antenatal iron-folic acid (IFA) supplementation on child stunting in Nepalese children age <2 years. A retrospective pooled cohort of 5235 most recent live births from 2001, 2006 and 2011 Nepal Demographic and Health Surveys was analyzed. The adjusted relative risk of being stunted was 14% lower in children whose mothers consumed IFA supplements compared to those whose mothers did not consume IFA. The greatest impact on reducing the risk of child stunting was when IFA supplementation was initiated ?6 months and when ?90 supplements consumed during pregnancy, with a 23% reduction in risk of stunting (aRR = 0.77, 95% CI = 0.64-0.92).

Resources:

- Iron-Folic Acid Supplementation during Pregnancy Reduces the Risk of Stunting in Children Less than 2 Years of Age: A Retrospective Cohort Study from Nepal

The study investigated the effect of antenatal iron-folic acid (IFA) supplementation on child
stunting in Nepalese children age <2 years. A retrospective pooled cohort of 5235 most recent live births from 2001, 2006 and 2011 Nepal Demographic and Health Surveys was analyzed. The adjusted relative risk of being stunted was 14% lower in children whose mothers consumed IFA supplements compared to those whose mothers did not consume IFA. The greatest impact on reducing the risk of child stunting was when IFA supplementation was initiated ?6 months and when ?90 supplements consumed during pregnancy, with a 23% reduction in risk of stunting (aRR = 0.77, 95% CI = 0.64-0.92).

Controlling Maternal Anemia and Malaria (June 2015)

The WHO 2012 updated policy on intermittent preventive treatment in pregnancy (IPTp) as well as the RBM Global Call to Action to Increase National Coverage of IPTp of Malaria in Pregnancy for Immediate Impact underscore the importance of increasing IPTp) and iron-folic acid (IFA) coverage to reduce maternal and child mortality. Both documents promote WHO policy-urging program implementers to give pregnant women a dose of folic acid less than 5 mg per day to ensure the effectiveness of IPTp in saving the lives of mothers and their infants. Two new advocacy documents promote acceleration of IPTp uptake and anemia prevention during pregnancy and using a lower dose of folic acid that will ensure a reduction of both malaria and anemia in pregnancy. These include:


2. Program Brief- ?Controlling Maternal Anemia and Malaria: Ensuring Pregnant Women Receive Effective Interventions to Prevent Malaria and Anemia: What Program Managers and Policymakers Should Know.? This brief was developed by USAID?s Maternal and Child Survival Program in collaboration with the President?s Malaria Initiative.

To access these documents, please go to the Components of the Integrated Package Tab and then to either the Malaria Prevention and Control or Iron-Folic Acid Supplementation Sub-Tabs. Under each of these Sub-Tabs, you will find ?Giving Folic Acid with IPTp? with information about the documents. Both these places provide information and links to the Consensus Statement and Brief. They also provide additional resources for IFA supplementation and malaria control, with studies that support the lower dose of folic acid. We suggest visiting both places as the information and resources are different in each place.

Kenya update and interview (Sept 2014)
In August 2013 an interview was conducted with Madame Terrie Wefwafwa, Kenya’s Head of the Division of Nutrition, to discuss Kenya’s approach to anemia prevention and control. You can find the interview with Madame Wefwafwa here as well recently-developed behavior change communication and demand creation resources for pregnant women, health workers and community health workers in Kenya.

**ICN Panel on Giving Iron to Children (Sept 2013)**

MCHIP participated in the 20th International Congress of Nutrition (ICN) from September 15-20, 2013 in Granada, Spain. The ICN occurs every four years and, with more than 4,000 participants registered this year, is considered the largest international nutrition conference. The theme of the five-day Congress was “Joining Cultures through Nutrition” and includes 7 plenary lectures, 32 special lectures, 90 parallel symposia, 4 debates, a living legend session, and 24 sessions of oral communications, as well as 36 sponsored symposia and 16 satellite symposia.

MCHIP staff in attendance contributed to the breadth and depth of experiences and knowledge brought to the international meeting through the hosting of a satellite symposium as well as oral and poster presentations on our work.

On the opening day of the event, MCHIP’s Nutrition Team convened a Symposium Panel on “Giving Iron to Children: Implications for Public Health Programs in Developing Countries.” Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Rae Galloway, MCHIP’s Nutrition Team Lead, the panel featured five experts discussing the “hot topic” of the risks and benefits of giving iron to young children in developing countries.

Links to these presentations are available as resources below. Click here to watch a live webcast of the event.

**Resources:**

- **Does Iron Supplementation Benefit Development in Children Younger than Two Years?**

  On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, "Giving Iron to Children: Implications for Public Health Programs in Developing Countries." Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated Program (MCHIP), five panelists discussed the "hot topic" of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and
• **Giving Iron Supplementation to Malaria Exposed Children: What is the Way Forward?**

On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, “Giving Iron to Children: Implications for Public Health Programs in Developing Countries.” Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated Program (MCHIP), five panelists discussed the “hot topic” of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and Michael Georgieff, University of Minnesota, Minneapolis, MN, USA.

• **The Impact of Zinc and/or Micronutrient Supplementation on Intestinal Flora, Diarrheal Disease Burden, Intestinal Mucosal Integrity and Growth Among Cohorts of Children in Pakistan**

On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, "Giving Iron to Children: Implications for Public Health Programs in Developing Countries." Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated Program (MCHIP), five panelists discussed the "hot topic" of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and Michael Georgieff, University of Minnesota, Minneapolis, MN, USA.

• **The Risks of Giving Young Children Iron on Growth and Infectious Diseases and Possible Mechanisms**
On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, “Giving Iron to Children: Implications for Public Health Programs in Developing Countries.” Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated Program (MCHIP), five panelists discussed the “hot topic” of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and Michael Georgieff, University of Minnesota, Minneapolis, MN, USA.

- The Specific Role of Iron in Early Brain Development

On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, “Giving Iron to Children: Implications for Public Health Programs in Developing Countries.” Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated Program (MCHIP), five panelists discussed the “hot topic” of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and Michael Georgieff, University of Minnesota, Minneapolis, MN, USA.

Anemia Prevalence, Causes, and Consequences

What is anemia?
Anemia is defined as a low level of hemoglobin in the blood, as evidenced by fewer numbers of functioning red blood cells. Hemoglobin in red blood cells is an oxygen-carrying protein that binds oxygen through its iron component. Hemoglobin transports oxygen to most cells in the body for the generation of energy. When hemoglobin levels are low, less oxygen reaches the cells to support the body's activities. The heart and lungs also must work harder to compensate for the blood's low capacity to carry oxygen. Because of oxygen's role in generating energy in the body and hemoglobin's role in transporting oxygen, one of the first symptoms of anemia is feeling tired. Because the heart has to work harder to get blood and oxygen to the tissues, anemia, particularly severe anemia, can result in cardiac arrest. Click here for World Health Organization (WHO) cutoffs of hemoglobin that define all, mild, moderate, and severe anemia.

Who does anemia affect?

Globally, anemia is prevalent in most developing countries and considered of public health significance. Click here for the WHO definitions for the levels of public health significance based on anemia prevalence.

The WHO (2008) has estimated the worldwide prevalence of anemia by regions and population groups. Women and young children are most vulnerable to anemia. The proportion of women and children is highest in the Africa region where 57% of pregnant women (17 million), 48% of non-pregnant women (70 million), and 68% of preschool children (84 million) are anemic. While the proportion of people with anemia is lower in Southeast Asia, the number of people with anemia are higher than in the Africa region. In Southeast Asia, 48% of pregnant women (18 million), 46% of non-pregnant women (182 million), and 66% of preschool children (115 million) suffer from anemia. A pictorial representation of the prevalence of anemia is shown in the map below.

Click here for the WHO global estimates of anemia prevalence. Click here for the WHO estimates of anemia prevalence by vulnerable group and region.

What are the causes of anemia?

There are three main categories of the causes of anemia: 1) poor, insufficient, or abnormal red blood cell production; 2) excessive red blood cell destruction; and 3) excessive red blood cell
loss. In developed countries, iron deficiency is the major cause of anemia and results in insufficient red blood cell production. In some individuals, infections such as peptic ulcers may cause blood loss and anemia. In developing countries, iron deficiency affects all vulnerable groups. Malaria, which can contribute to excessive red blood cell destruction, and helminth infections, a cause of excessive red blood cell loss, are geographically specific. Other infectious diseases also may be at play. There are contributing causes of anemia which include inadequate knowledge about the problem of anemia, environmental factors, lack of access to services, and poverty. Click here for a more complete list of direct and contributing causes of anemia.

Because there are different causes of anemia, an integrated package of interventions is recommended. In some cases, diagnosis of anemia may be warranted and appropriate to determine the cause of anemia.

**What are the consequences of anemia?**

An early symptom of anemia is fatigue and decreased ability to work (Haas & Brownlie, 2001). Yet, being anemia also is associated with an increased risk of mortality and cognitive loss in those who survive (Stoltzfus et al, 2005; Lozoff et al, 1988, 2000). Maternal anemia is associated with 20% of maternal deaths (Black et al, 2008), with greater evidence that anemia may cause increased blood loss at delivery and put women at risk of postpartum hemorrhage (Kavle et al, 2008). Anemic mothers are at greater risk of delivering premature and low-birth-weight babies who have an increased risk of dying (Kozuki, 2012; Zeng et al, 2008, 2009).

Giving iron during pregnancy reduces anemia and improves child outcomes. Indonesian children of mothers taking iron during pregnancy had a decreased risk of dying in their first five years of life, with a 40% decreased risk of dying in the first day of life (Dibley et al, 2012). Studies that administered iron and folic acid (IFA) supplements during pregnancy resulted in substantial impacts—halving neonatal mortality in China (Zeng et al, 2008) and markedly decreasing the risk of death in the first seven years of life (Christian et al, 2009).

Children younger than two years of age with severe anemia, caused by malaria and iron deficiency, are at increased risk of mortality (Brabin et al, 2001), and less milder forms, even if corrected, cause permanent cognitive damage by decreasing attention span and shortening memory. Children with anemia have, on average, IQs that are two points lower per every 10 g/L decrease in hemoglobin than other children (Black et al, 2008; Stoltzfus et al, 2004). Iron deficiency in U.S. school-age children is associated with poorer performance on math tests (Halterman et al, 2001).

Anemia has devastating costs to individual and national productivity. A 10% increase in hemoglobin in a moderately anemic person results in a 10-20% increase in work output (Levin, 1986). Eliminating anemia would increase adult productivity by 5-17% and gross domestic product by 2% in countries where anemia prevalence is high (Strauss et al, 1998; Horton et al, 2000). To achieve strides in preventing the consequences of anemia, an integrated package of interventions needs to be delivered at-scale to address all the causes of anemia.

**Resources:**
The Global Prevalence of Anaemia in 2011

This document describes estimates of the prevalence of anaemia for the year 2011 in preschool-age children (6?59 months) and women of reproductive age (15?49 years), by pregnancy status, and by regions of the United Nations and World Health Organization (WHO), as well as by country.

This document may serve as a resource for estimating the baseline prevalence of anaemia in women of reproductive age, in working towards achieving the second global nutrition target 2025, a 50% reduction of anaemia in women of reproductive age, as outlined in the Comprehensive implementation plan on maternal, infant and young child nutrition and endorsed by the Sixty-fifth World Health Assembly, in resolution WHA65.6.

Anaemia, Prenatal Iron Use, and Risk of Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis

Objectives: To summarise evidence on the associations of maternal anaemia and prenatal iron use with maternal haemotological and adverse pregnancy outcomes; and to evaluate potential exposure relations of dose of iron, duration of use, and haemoglobin concentration in prenatal period with pregnancy outcomes.

Design: Systematic review and meta-analysis.

Data Sources: Searches of PubMed and Embase for studies published up to May 2012 and references of review articles.

Study Selection Criteria: Randomised trials of prenatal iron use and prospective cohort studies of prenatal anaemia; cross-sectional and case-control studies were excluded.

Results: 48 randomised trials (17,793 women) and 44 cohort studies (1,851,682 women) were included. Iron use increased maternal mean haemoglobin concentration by 4.59 (95% CI 3.72 to 5.46) g/L compared with controls and significantly reduced the risk of anaemia (relative risk 0.50, 0.42 to 0.59), iron deficiency (0.59, 0.46 to 0.79), iron deficiency anaemia (0.40, 0.26 to 0.60), and low birth weight (0.81, 0.71 to 0.93). The effect of iron on preterm birth was not significant (relative risk 0.84, 0.68 to 1.03). Analysis of cohort studies showed a significantly higher risk of low birth weight (adjusted odds ratio 1.29, 1.09 to 1.53) and preterm birth (1.21, 1.13 to 1.30) with anaemia in the first or second trimester. Exposure-response analysis indicated that for every 10 mg increase in iron dose/day, up to 66 mg/day, the relative risk of maternal anaemia was 0.88 (0.84 to 0.92) (P for linear trend<0.001). Duration of use was not significantly associated with the outcomes after adjustment for dose.
Furthermore, for each 1 g/L increase in mean haemoglobin, birth weight increased by 14.0 (6.8 to 21.8) g (P for linear trend=0.002); however, mean haemoglobin was not associated with the risk of low birth weight and preterm birth. No evidence of a significant effect on duration of gestation, small for gestational age births, and birth length was noted.

**Conclusions:** Daily prenatal use of iron substantially improved birth weight in a linear dose-response fashion, probably leading to a reduction in risk of low birth weight. An improvement in prenatal mean haemoglobin concentration linearly increased birth weight.

- **Maternal Iron Status: Relation to Fetal Growth, Length of Gestation, and Iron Endowment of the Neonate**

Anemia prevalence is highest in preschool children, women of reproductive age, and women who are pregnant. While the etiology of anemia is multifactorial, iron deficiency is the most commonly recognized nutritional cause. Observational studies imply that supplementation with iron or iron-folic acid should be started early in pregnancy, if not before, in order to prevent low-birth-weight and preterm delivery. Despite this, findings from clinical trials, even those conducted during early pregnancy, are equivocal. Recent follow-up studies of children born to women supplemented with iron-folic acid suggest that mortality is decreased and that the infant's iron endowment reflects the mother's iron status during pregnancy.

- **Why Nutritional Iron Deficiency Persists as a Worldwide Problem**

The earliest studies of food iron absorption employing biosynthetically incorporated radioisotopes were published in the 1950s. Wheat flour has been fortified with iron in Canada, the United Kingdom, and the United States since the 1940s. However, half a century later, nutritional iron deficiency (ID) is estimated to affect 1.5-2 billion people worldwide. The reasons for the apparently limited impact of health and nutrition policies aimed at reducing the prevalence of ID in developing countries are complex. They include uncertainty about the actual prevalence of ID, particularly in regions where malaria and other infections are endemic, failure of policy makers to recognize the relationships between ID and both impaired productivity and increased morbidity, concerns about safety and the risks to iron-sufficient individuals if mass fortification is introduced, and technical obstacles that make it difficult to add bioavailable iron to the diets of those at greatest risk. It is, however, likely that the next decade will see a marked reduction in the prevalence of ID worldwide. More specific assessment tools are being standardized and applied to population surveys. The importance of preventing ID during critical periods of the life cycle is receiving increased attention. Innovative approaches to the delivery of bioavailable iron have been shown to be efficacious. The importance of integrating strategies to improve iron nutrition with other health measures,
and economic and social policies addressing poverty as well as trade and agriculture, are receiving increasing consideration.

**Moderate to Severe, but not Mild, Maternal Anemia is Associated with Increased Risk of Small-for-Gestational-Age Outcomes**

Anemia is highly prevalent globally, estimated at 40-50% in women of reproductive age. Prior studies have produced inconclusive evidence as to the association between maternal anemia and intrauterine growth restriction (IUGR). We conducted a systematic review of the literature containing associations between maternal anemia and small for gestational age (SGA) outcomes (as a proxy for IUGR). A meta-analysis was performed to pool associations, categorized by the hemoglobin cutoffs presented by the authors. We identified 12 studies reporting associations between maternal anemia and SGA. For the meta-analysis, there were 7 associations with a hemoglobin cutoff 110 g/L, 7 with a cutoff 100 g/L, and 5 with a cutoff 80 g/L. Although the categories showed no significant relationship with SGA, the <90- or <80-g/L category was associated with a 53% increase in risk of the newborn being SGA OR = 1.53 (95% CI: 1.24-1.87); \( P < 0.001 \). Moderate to severe, but not mild, maternal anemia appears to have an association with SGA outcomes, but the findings must be viewed with caution due to the great heterogeneity of the studies. Further examination should be conducted using datasets with better standardized definitions and measurements of exposure and outcome.

**Iron Status of Women is Associated with the Iron Concentration of Potable Groundwater in Rural Bangladesh**

Women of reproductive age are at a high risk of iron deficiency, often as a result of diets low in bioavailable iron. In some settings, the iron content of domestic groundwater sources is high, yet its contribution to iron intake and status has not been examined. In a rural Bangladeshi population of women deficient in dietary iron, we evaluated the association between groundwater iron intake and iron status. In 2008, participants (n = 209 with complete data) were visited to collect data on 7-d food frequency, 7-d morbidity history, 24-h drinking water intake, and rice preparation, and to measure the groundwater iron concentration. Blood was collected to assess iron and infection status. Plasma ferritin (mg/L) and body iron (mg/kg) concentrations were [median (IQR)] 67 (46, 99) and 10.4 6 2.6, respectively, and the prevalence of iron deficiency (ferritin , 12 mg/L) was 0%. Daily iron intake from water [42 mg (18, 71)] was positively correlated with plasma ferritin \( r = 0.36 \) and total body iron \( r = 0.35 \) (\( P , 0.001 \) for both). In adjusted linear regression analyses, plasma ferritin increased by 6.1%
(95% CI: 3.8, 8.4%) and body iron by 0.3 mg/kg (0.2, 0.4) for every 10-mg increase in iron intake from water (P < 0.001). In this rural area of northern Bangladesh, women of reproductive age had no iron deficiency likely attributable to iron consumed from drinking groundwater, which contributed substantially to dietary intake. These findings suggest that iron intake from water should be included in dietary assessments in such settings.

• Are We Making Progress on Reducing Anemia in Women? Cross-country Comparison of Anemia Prevalence, Reach, and Use of Antenatal Care and Anemia Reduction Interventions

Purpose: The purpose of this report is to assess the progress being made on reducing the burden of anemia in women. It also aims to stimulate global and national action to improve the reach and delivery of proven anemia reduction interventions targeting pregnant women.

Methods: Data from DHS surveys conducted from 2004 to 2008 were used for cross-country and over-time comparisons of anemia prevalence in pregnant and non-pregnant women. These data were also used to make cross-country comparisons of the major service delivery platform for maternal anemia interventions, including antenatal care visits, and the coverage and/or reach of evidence-based anemia reduction interventions—iron tablet consumption, use of intermittent presumptive treatment for malaria, use of insecticide-treated mosquito nets, and the use of de-worming medicines.

Findings:

- The burden of anemia in pregnant women remains serious and unacceptably high.
- Reducing the anemia burden in pregnant women has progressed little, especially in African countries.
- The burden of anemia in non-pregnant women, while somewhat lower than that for pregnant women, puts women at risk of anemia when they become pregnant.
- A high proportion of pregnant women participate in at least one antenatal care (ANC) visit, but the correlation between ANC use and iron tablet consumption is weak.
- In places where access to and participation in ANC care clinics is adequate, other factors need to be examined such as inadequate supply of iron tablets, which can be affected by cost and weak logistic systems; poor quality of counseling by health workers about the need for iron supplementation and its potential benefits and side-effects; lack of knowledge and concern about maternal anemia by both pregnant women and health care providers; and low motivation and some resistance among pregnant women to consume the iron supplement because of undesirable characteristics of the iron tablets or side effects experienced by women.
- Access to and participation in ANC services is not high in all countries.
- Strong evidence of inequitable access to and participation in ANC exist for poorer, less educated, and/or rural women in countries such as Bangladesh, Chad, Egypt, Ethiopia,
- Improved coverage of intermittent preventive treatment for pregnant women (IPTp) in areas with high malaria endemicity is needed.
- There is a need to increase use of insecticide-treated bednets (ITN) among all household members in malaria-endemic areas.
- There is a need to increase presumptive treatment of hookworms in areas where hookworms are known to be endemic.

### Anaemia in Low-Income and Middle-Income Countries

**Background:** Anaemia affects a quarter of the global population, including 293 million (47%) children younger than 5 years and 468 million (30%) non-pregnant women. In addition to anaemia’s adverse health consequences, the economic effect of anaemia on human capital results in the loss of billions of dollars annually.

**Methods:** In this paper, we review the epidemiology, clinical assessment, pathophysiology, and consequences of anaemia in low-income and middle-income countries. Our analysis shows that anaemia is disproportionately concentrated in low socioeconomic groups, and that maternal anaemia is strongly associated with child anaemia.

**Results:** Anaemia has multifactorial causes involving complex interaction between nutrition, infectious diseases, and other factors, and this complexity presents a challenge to effectively address the population determinants of anaemia.

**Conclusions:** Reduction of knowledge gaps in research and policy and improvement of the implementation of effective population-level strategies will help to alleviate the anaemia burden in low-resource settings.

### Maternal Iron-Folic Acid Supplementation Programs: Evidence of Impact and Implementation

**Background:** According to a World Health Organization (WHO) review of nationally representative surveys from 1993 to 2005, 42% of pregnant women have anemia worldwide. Almost 90% of anemic women reside in Africa or Asia. Most countries have policies and programs for prenatal iron-folic acid supplementation, but coverage remains low and little emphasis is placed on this intervention within efforts to strengthen antenatal care services. The evidence of the public health impact of iron-folic acid supplementation and documentation of the potential for scaling up have not been reviewed recently.
Objective: The purpose of this review is to examine the evidence regarding the impact on maternal mortality of iron-folic acid supplementation and the evidence for the effectiveness of this intervention in supplementation trials and large-scale programs.

Methods: The impact on mortality is reviewed from observational studies that were analyzed for the Global Burden of Disease Analysis in 2004. Reviews of iron-folic acid supplementation trials were analyzed by other researchers and are summarized. Data on anemia reduction from two large-scale national programs are presented, and factors responsible for high coverage with iron-folic acid supplementation are discussed.

Results: Iron-deficiency anemia underlies 115,000 maternal deaths per year. In Asia, anemia is the second highest cause of maternal mortality. Even mild and moderate anemia increase the risk of death in pregnant women. Iron-folic acid supplementation of pregnant women increases hemoglobin by 1.17 g/dL in developed countries and 1.13 g/dL in developing countries. The prevalence of maternal anemia can be reduced by one-third to one-half over a decade if action is taken to launch focused, large-scale programs that are based on lessons learned from countries with successful programs, such as Thailand and Nicaragua.

Conclusions: Iron-folic acid supplementation is an under-resourced, affordable intervention with substantial potential for contributing to Millennium Development Goal 5 (maternal mortality reduction) in countries where iron intakes among pregnant women are low and anemia prevalence is high. This can be achieved in the near term, as policies are already in place in most countries and iron-folic acid supplements are already in lists of essential drugs. What is needed is to systematically adopt lessons about how to strengthen demand and supply systems from successful programs.

The Inherited Disorders of Hemoglobin: An Increasingly Neglected Health Burden

An estimated 300,000 babies are born each year with a severe inherited disease of haemoglobin and that over 80 per cent of these births occur in low- or middle-income countries. As these countries go through the epidemiological transition, characterized by a reduction in childhood and infant mortality due to improved public health measures, infants who had previously died of these conditions before they were recognised are now surviving to present for diagnosis and treatment. For a variety of reasons, even in the rich countries there are limited data about the true frequency, natural history, and survival of patients with these disorders, information that is absolutely critical towards providing governments and international health agencies with accurate information about the true global health burden of these conditions. The situation can only be improved by major action on the part of the rich countries together with the formation of partnerships between rich and poor countries and input from the major international health agencies and funding organisations.
Maternal Anemia and Preterm Birth: A Prospective Cohort Study

**Background:** The role of maternal anaemia in preterm birth remains poorly defined, and the association between anaemia and preterm birth clinical subtypes remain unclear. We examined if maternal anaemia exposure both within and across trimesters during gestation is associated with preterm birth.

**Methods:** This was a secondary analysis of data from a population-based prospective cohort study in 13 counties of East China (1993-96). All singleton live births delivered at 20-44 weeks to women with at least one haemoglobin measure during pregnancy were included (n = 160,700). Risk of preterm birth (<37 weeks) was examined by clinical subtypes, namely, preterm premature rupture of membranes (PROM), spontaneous preterm labour and medically indicated preterm birth. Haemoglobin changes across trimesters were assessed as proxy of haemo-dilution and haemo-concentration. Multivariable Cox proportional hazards regression models were fitted.

**Results:** Preterm birth rates of preterm birth were 4.1% for anaemic and 5% for non-anaemic women (P < 0.05). Compared with haemoglobin of 11 g/dl (reference), values <5 g/dl in the first trimester were associated with increased risk for preterm PROM [hazard ratio (HR) 3.3, 95% confidence interval (CI) 1.4-7.7], whereas low haemoglobin in the third trimester was associated with reduced risk of spontaneous preterm labour. Haemodilution was associated with reduced risk for preterm birth.

**Conclusions:** Anaemia in early pregnancy was found to be associated with increased risk for preterm PROM, whereas exposure in late pregnancy was associated with reduced risk for spontaneous preterm labour.

• **Worldwide Prevalence of Anaemia 1993-2005: WHO Global Databases on Anaemia**

Anaemia is a public health problem that affects populations in both rich and poor countries. Although the primary cause is iron deficiency, it is seldom present in isolation. More frequently it coexists with a number of other causes, such as malaria, parasitic infection, nutritional deficiencies, and haemoglobinopathies.

**Objective:** To provide current global and regional estimates of anaemia prevalence and number of persons affected in the total population and by population subgroup.

**Setting and design:** We used anaemia prevalence data from the WHO Vitamin and Mineral Nutrition Information System for 1993–2005 to generate anaemia prevalence estimates for countries with data representative at the national level or at the first administrative level that is below the national level. For countries without eligible data, we employed regression-based estimates, which used the UN Human Development Index (HDI) and other health indicators. We combined country estimates, weighted by their population, to estimate anaemia prevalence at the global level, by UN Regions and by category of human development.

**Results:** Survey data covered 48.8% of the global population, 76.1% of preschool-aged children, 69.0% of pregnant women and 73.5% of non-pregnant women. The estimated global anaemia prevalence is 24.8% (95% CI 22.9%, 26.7%), affecting 1.62 billion people (95% CI 1.50, 1.74 billion). Estimated anaemia prevalence is 47.4% (95% CI 45.7, 49.1%) in preschool-aged children, 41.8% (95% CI 39.9, 43.8%) in pregnant women and 30.2% (95% CI 28.7, 31.6%) in non-pregnant women. In numbers, 293 million (95% CI 282, 303 million) preschool-aged children, 56 million (95% CI 54, 59 million) pregnant women and 468 million (95% CI 446, 491 million) non-pregnant women are affected.

**Conclusion:** Anaemia affects one-quarter of the world’s population and is concentrated in preschool-aged children and women, making it a global public health problem. Data on relative contributions of causal factors are lacking, however, which makes it difficult to effectively address the problem.

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**Maternal and Child Undernutrition: Global and Regional Exposures and Health Consequences**

Maternal and child undernutrition is highly prevalent in low-income and middle-income countries, resulting in substantial increases in mortality and overall disease burden. In this paper, we present new analyses to estimate the effects of the risks related to measures of undernutrition, as well as to suboptimum breastfeeding practices on mortality and disease. We estimated that stunting, severe wasting, and intrauterine growth restriction together were responsible for 2.2 million deaths and 21% of disability-adjusted life-years (DALYs) for children younger than 5 years. Deficiencies of vitamin A and zinc were estimated to be responsible for 0.6 million and 0.4 million deaths, respectively, and a combined 9% of global childhood DALYs. Iron and iodine deficiencies resulted in few child deaths, and combined were responsible for about 0.2% of global childhood DALYs. Iron deficiency as a risk factor for maternal mortality added 115,000 deaths and 0.4% of global total DALYs. Suboptimum breastfeeding was estimated to be responsible for 1.4 million child deaths and 44 million DALYs (10% of DALYs in children younger than 5 years). In an analysis that accounted for co-exposure of these nutrition-related factors, they were together responsible for about 35% of child deaths and 11% of the total global disease burden. The high mortality and disease
burden resulting from these nutrition-related factors make a compelling case for the urgent implementation of interventions to reduce their occurrence or ameliorate their consequences.

• **Gap Analysis: Information Needed for Consensus on Policies and Programs to Improve Iron Nutrition**

Despite over 50 years of research, nutritional iron deficiency remains the most prevalent micronutrient deficiency disorder worldwide. As stated in a recent UNICEF/UNU/WHO publication (2001): "Iron deficiency affects a significant part, and often a majority, of the population in nearly every country in the world. Programs for the prevention of iron deficiency, particularly iron supplementation for pregnant women, are under way in 90 of 112 countries as reported to WHO in 1992 (WHO, 1992). Most of these programs, however, are neither systematically implemented nor well monitored or evaluated. Nevertheless, significant advances in addressing iron deficiency anemia have been made in the last 10-15 years, by applying established scientific observations to the design, implementation, and evaluation of interventions. At the same time, the increased emphasis on outcome analysis has uncovered new problems that require more rigorous scientific evaluation, the most urgent being the possible risks of delivering iron in regions where malaria is endemic. There is also a pressing need to find safe and effective mechanisms for providing iron to infants and young children. This paper seeks to identify the key gaps in information that must be filled to move towards consensus on policies and programs to improve iron nutrition.

• **An Overview of Evidence for a Causal Relation Between Iron Deficiency during Development and Deficits in Cognitive or Behavioral Function**

**Background:** This review, intended for a broad scientific readership, summarizes evidence relevant to whether a causal relation exists between dietary iron deficiency with (ID+A) or without (ID-A) anemia during development and deficits in subsequent cognitive or behavioral performance. An overview of expert opinion and major evidence in humans and animals is provided.

**Methods:** Cognitive and behavioral effects observed in humans with ID-A and in animals with ID+A are provided in tables. The degree to which 5 conditions of causality are satisfied and whether deleterious effects of ID-A might be expected to occur are discussed.

**Results:** On the basis of the existing literature, our major conclusions are as follows. Although most of the 5 conditions of causality (association, plausible biological mechanisms, dose response, ability to manipulate the effect, and specificity of cause and effect) are partially satisfied in humans, animals, or both, a causal connection has not been clearly
established. In animals, deficits in motor activity are consistently associated with severe ID+A, but adverse effects on performance in tests that target cognitive function have not been clearly shown. Resistance to iron treatment was observed in most trials of children <2 y of age with ID+A, but not in older children. Similar observations were made in rodents when ID-A occurred before rather than after weaning.

Conclusions: In children <2 y of age and in adolescents with ID-A, evidence suggests cognitive or behavioral deficits; however, the surprisingly small number of studies conducted in either humans or animals prevents a thorough assessment.

The Burden of Anemia in Rural Bangladesh: The Need for Urgent Action

Many surveys in the past have shown that anemia is a severe problem in Bangladesh among most age, population and geographic groups. Findings from a survey conducted by the Nutritional Surveillance Project (NSP) of Helen Keller International (HKI) in collaboration with the Institute of Public Health Nutrition (IPHN) in 2004 show that 68% of children under five years of age are anemic, with the highest prevalence among those 6-11 months old (92%). Approximately 40% of adolescent girls and 31% of adolescent boys suffer from anemia as well as 46% of non-pregnant and 39% of pregnant women. The prevalence of anemia increased in comparison to a similar survey conducted in 2001. This bulletin calls for urgent need for action to reduce anemia, especially in view of the high risks for maternal health and mortality, the devastating impact on cognitive and motor development of an entire generation of children and the vast economic losses at present as in the future.

Women's Perceptions of Iron Deficiency and Anemia Prevention and Control in Eight Developing Countries

The World Health Organization estimates that 58% of pregnant women in developing countries are anemic. In spite of the fact that most ministries of health in developing countries have policies to provide pregnant women with iron in a supplement form, maternal anemia prevalence has not declined significantly where large-scale programs have been evaluated. During the period 1991-98, the MotherCare Project and its partners conducted qualitative research to determine the major barriers and facilitators of iron supplementation programs for pregnant women in eight developing countries. Research results were used to develop pilot program strategies and interventions to reduce maternal anemia. Across-region results were examined and some differences were found but the similarity in the way women view anemia and react to taking iron tablets was more striking than differences encountered by region, country or ethnic group. While women frequently recognize symptoms of anemia, they do not know the clinical term for anemia. Half of women in all countries consider these symptoms to
be a priority health concern that requires action and half do not. Those women who visit prenatal health services are often familiar with iron supplements, but commonly do not know why they are prescribed. Contrary to the belief that women stop taking iron tablets mainly due to negative side effects, only about one-third of women reported that they experienced negative side effects in these studies. During iron supplementation trials in five of the countries, only about one-tenth of the women stopped taking the tablets due to side effects. The major barrier to effective supplementation programs is inadequate supply. Additional barriers include inadequate counseling and distribution of iron tablets, difficult access and poor utilization of prenatal health care services, beliefs against consuming medications during pregnancy, and in most countries, fears that taking too much iron may cause too much blood or a big baby, making delivery more difficult. Facilitators include women's recognition of improved physical well being with the alleviation of symptoms of anemia, particularly fatigue, a better appetite, increased appreciation of benefits for the fetus, and subsequent increased demand for prevention and treatment of iron deficiency and anemia.

- **Defining Iron-Deficiency Anemia in Public Health Terms: A Time for Reflection**

This paper provides a historical context for this meeting, which aimed to examine critically the way we have defined iron-deficiency anemia as a public health problem. The terms and concepts used to define the problem are reviewed first, followed by estimates of the global prevalence of the problem from 1985 to 2000. It is argued that recent estimates are not credible and that we must redefine the problem in terms that are important, measurable and addressable. This meeting was designed to take first steps toward that goal, namely, to identify the causal factors (e.g., iron deficiency vs. iron-deficiency anemia vs. severe anemia from any cause) that link iron-deficiency anemia to important health outcomes and to estimate the magnitude of their effects in public health terms.

- **Iron Deficiency and Reduced Work Capacity: A Critical Review of the Research to Determine a Causal Relationship**

The causal relationship between iron deficiency and physical work capacity is evaluated through a systematic review of the research literature, including animal and human studies. Iron deficiency was examined along a continuum from severe iron-deficiency anemia (SIDA) to moderate iron-deficiency anemia (MIDA) to iron deficiency without anemia (IDNA). Work capacity was assessed by aerobic capacity, endurance, energetic efficiency, voluntary activity and work productivity. The 29 research reports examined demonstrated a strong causal effect of SIDA and MIDA on aerobic capacity in animals and humans. The presumed mechanism for this effect is the reduced oxygen transport associated with anemia; tissue iron
deficiency may also play a role through reduced cellular oxidative capacity. Endurance capacity was also compromised in SIDA and MIDA, but the strong mediating effects of poor cellular oxidative capacity observed in animals have not been demonstrated in humans. Energetic efficiency was affected at all levels of iron deficiency in humans, in the laboratory and the field. The reduced work productivity observed in field studies is likely due to anemia and reduced oxygen transport. The social and economic consequences of iron-deficiency anemia (IDA) and IDNA have yet to be elucidated. The biological mechanisms for the effect of IDA on work capacity are sufficiently strong to justify interventions to improve iron status as a means of enhancing human capital. This may also extend to the segment of the population experiencing IDNA in whom the effects on work capacity may be more subtle, but the number of individuals thus affected may be considerably more than those experiencing IDA.

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A Review of Studies on the Effect of Iron Deficiency on Cognitive Development in Children

Studies on the effect of iron deficiency on children's cognition and behavior are selectively reviewed, looking for evidence of a causal relationship. More correlational studies have found associations between iron-deficiency anemia and poor cognitive and motor development and behavioral problems. Longitudinal studies consistently indicate that children anemic in infancy continue to have poorer cognition, school achievement, and more behavior problems into middle childhood. However, the possible confounding effects of poor socioeconomic backgrounds prevent causal inferences from being made. In anemic children <2 y old, short-term trials of iron treatment have generally failed to benefit development. Most longer trials lacked randomized placebo groups and failed to produce benefits. Only one small randomized controlled trial (RCT) has shown clear benefits. It therefore remains uncertain whether the poor development of iron-deficient infants is due to poor social backgrounds or irreversible damage or is remediable with iron treatment. Similarly, the few preventive trials have had design problems or produced no or questionable benefits only. For children <2 y old, the evidence from RCT is reasonably convincing but not conclusive. RCT of iron treatment are warranted especially in younger children.

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Malaria is an Important Cause of Anaemia in Primigravidae: Evidence from a District Hospital in Coastal Kenya

A study was undertaken in order to determine the prevalence and aetiology of anaemia in pregnancy in coastal Kenya, so as to establish locally important causes and enable the development of appropriate intervention strategies. 275 women attending the antenatal clinic at Kilifi district hospital, Kenya, were recruited in November 1993. The prevalence of anaemia (haemoglobin 11 g/dL) was 75.6%, and the prevalence of severe anaemia (7g/dL) was 9.8%
among all parities; 15.3% of 73 primigravidae were severely anaemic, compared with 7.9% of 202 multigravidae (P = 0.07). In primigravidae, malaria infection (Plasmodium falciparum) was strongly associated with moderate and severe anaemia (chi 2 test for trend, P = 0.003). Severe anaemia was more than twice as common in women with peripheral parasitaemia as in those who were aparasitaemic, and parasitaemia was associated with a 2.2g/dL decrease in mean haemoglobin level (0.001). In multigravidae, iron deficiency and hookworm infection were the dominant risk factors for anaemia. Folate deficiency and human immunodeficiency virus infection were not strongly associated with anaemia. It is suggested that an intervention that can effectively reduce malaria infection in primigravidae could have a major impact on the health of these women and their infants.

Iron Deficiency Anaemia

Iron deficiency is a highly prevalent form of undernutrition, affecting around one-fourth of the world’s women and children, and is one of the most common causes of anaemia. We conducted comprehensive reviews of published literature linking iron deficiency to disability and death for four potential outcomes: child mortality, perinatal mortality, maternal mortality and mild mental retardation. For all of these outcomes, the best available data were prospective observational studies in which anaemia or haemoglobin concentration was the risk factor. Data on child mortality were not adequate for this task, although a true risk cannot be precluded by the data. Summary relative risks for perinatal mortality (10 studies), maternal mortality (six studies) and mental retardation (five studies) were estimated using random effects models (both mortality outcomes) or a fixed-effects model (retardation) and weighting individual estimates by the inverse of their within-study variance. For mortality outcomes, the bivariate relations between haemoglobin and death were used. In two studies of perinatal mortality, unadjusted and multivariate adjusted odds ratios were compared to assess the potential degree of bias in the unadjusted associations. For mental retardation, published multivariate adjusted relations between haemoglobin and IQ were used. Global anaemia prevalence data were supplied by the World Health Organization (WHO), and converted to mean haemoglobin concentrations, assuming normal distribution and observed standard deviations from a large number of studies. To estimate the haemoglobin distribution if iron deficiency were corrected, we assumed the prevalence of anaemia in women and children would be reduced by 50%. On average, for the world, this would increase haemoglobin concentration by about 0.45 g/dl (range: 0.0 g/dl to 1.28 g/dl).

Worldwide Prevalence
Resources:

- The Global Prevalence of Anaemia in 2011

This document describes estimates of the prevalence of anaemia for the year 2011 in preschool-age children (6-59 months) and women of reproductive age (15-49 years), by pregnancy status, and by regions of the United Nations and World Health Organization (WHO), as well as by country.

This document may serve as a resource for estimating the baseline prevalence of anaemia in women of reproductive age, in working towards achieving the second global nutrition target 2025, a 50% reduction of anaemia in women of reproductive age, as outlined in the Comprehensive implementation plan on maternal, infant and young child nutrition and endorsed by the Sixty-fifth World Health Assembly, in resolution WHA65.6.

DHS Anemia Prevalence and Anemia Control Programs, January 2013

WHO Hemoglobin Cut-Offs
Public Health Significance of Anemia

Prevalence of Anemia by Vulnerable Group and Region
Direct and Contributing Causes of Anemia

Anemia Profiles - Countries

SPRING developed National Anemia Profiles which provide country-specific information on:

- The causes and burden of anemia
- The policy environment
- Program indicators that allow monitoring of progress against anemia targets

The profiles can be used by country leaders, stakeholders, and the broader public health community to raise the visibility of anemia and encourage coordination of anemia efforts across multiple sectors. The profiles highlight a multi-sectoral approach to prevent and control anemia for mothers, infants, and children.

17 country profiles are available:

- **Benin**? English, French
- **Burkina Faso**? English, French
- **Cameroon**? English, French
- **Congo**? English, French
- **Guinea**? English, French
Nepal National Anemia Profile

Anemia has substantial negative effects on the health and economic wellbeing of nations and communities. Children with anemia experience irrevocable cognitive and developmental delays and exhibit decreased worker productivity as adults. Globally, maternal anemia increases the risk of pre-term delivery and low birth weight, and iron-deficiency anemia underlies 115,000 maternal deaths and 591,000 perinatal deaths each year.

Niger National Anemia Profile

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• **Senegal National Anemia Profile**

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• **Rwanda National Anemia Profile**

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• **Kyrgyz Republic National Anemia Profile**

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• **Tanzania National Anemia Profile**

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• **Uganda National Anemia Profile**

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- **Zimbabwe National Anemia Profile**

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- **Benin National Anemia Profile**

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- **Burkina Faso National Anemia Profile**

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- **Cameroon National Anemia Profile**

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Congo National Anemia Profile

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Guinea National Anemia Profile

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Haiti National Anemia Profile

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Madagascar National Anemia Profile

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Malawi National Anemia Profile

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Mali National Anemia Profile

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Components of the Integrated Package

Because there are multiple causes of anemia in most developing countries, a single intervention such as iron supplementation will be ineffective in reducing anemia. Delivering an integrated package of interventions to address the main causes of anemia will be most effective. The components of the package can be delivered through both public and private sectors.

Knowing the causes of anemia is important in designing an integrated package to reduce anemia. This package will be specific to the geographic setting because some of the causes vary by region and country. Click here for the major causes of anemia by region.

Knowing who is most vulnerable to anemia will help in targeting the integrated package. Based on the prevalence and consequences of anemia, pregnant women and children younger than two years of age are the most vulnerable individuals worldwide. Click here for information on the prevalence of anemia. Anemia does exist in other groups, including reproductive-age women,
adolescents, school-age children, and men, particularly those affected by helminths and malaria and doing heavy physical labor. These other groups also should be targeted with interventions, when resources are available.

However, two interventions need to be part of the integrated package due to their cost-effectiveness in reducing anemia and other morbidities in entire populations or large groups of individuals, including fortification and family planning. When a centrally-processed staple food is available, this food should be fortified with iron because it will benefit most of the population. Family planning services need to be offered to all couples because family planning, including birth spacing of at least two years, will reduce anemia. These interventions will not be enough to satisfy the iron needs of women during pregnancy or their vulnerability to malaria, particularly those in their first and second pregnancies, so targeted interventions during pregnancy will continue to be needed.

Components of the integrated package include:

- **Birth spacing** of less than 24 months is associated with poor maternal, newborn, and child health outcomes. Stunting and underweight in children increase as birth intervals decrease (Rutstein, 2005 and 2008). Optimal birth spacing allows for the mother’s body to fully recover from birth and build stores of nutrients lost during delivery including iron. In many countries, women stop breastfeeding when they become pregnant. Ensuring the mother does not become pregnant before her current child reaches his/her second birthday will ensure that the child is adequately cared for during this vulnerable period and continues to receive breast milk. Breast milk continues to be an important source of nutrition until two years of age and decreases the risk of diarrhea and other infections which increase iron requirements and loss. Continued breastfeeding delays subsequent pregnancy, when the three criteria of the Lactational Amenorrhea Method (LAM) are met. Click here to go to the K4Health Toolkit on Maternal Infant Young Child Nutrition and Family Planning Integration Toolkit.

- **Delayed cord clamping** allows blood flow to continue between the mother and newborn for 1-3 minutes after birth or until the cord stops pulsing. This practice can be done while initiating simultaneous essential newborn care. This delay in clamping can build iron stores in the infant to last up to six months after birth, which is particularly relevant for infants living in low-resource settings whose mothers have less
access to iron-rich foods. Delayed cord clamping particularly increases iron stores in low birth weight infants and infants of anemic mothers. Click here for more information on delayed cord clamping.

- **Food-based approaches** to reduce anemia include increasing the availability and access to iron-rich foods and other nutrients that play a role in preventing anemia. Increasing agriculture production of crops with higher iron content, raising animals to consume, or fortifying foods with iron are all effective food-based approaches. Food-based approaches also include food processing to increase the absorption of iron and changing dietary habits by avoiding the intake of iron inhibitors and ensuring that vulnerable groups are consuming iron-rich foods when they are available. Click here for more information on food-based approaches.

- **Helminth prevention and control** should be part of the integrated anemia prevention and control package where helminths are prevalent. Hookworm and schistosome are the two most common types of helminth infections that can cause excessive red blood cell loss and result in iron-deficiency anemia. Endemic hookworm infection is a significant cause of anemia in children. Click here for more information on helminth prevention and control.

- **Iron-Folic Acid Supplementation** during pregnancy is a policy in most developing countries and in most countries some pregnant women receive iron-folic acid supplements but coverage is still limited. Harmonizing the dose of folic acid with malaria control and treatment programs using sulphadoxine-pyrimethamine (SP) is imperative to ensure the effective treatment of malaria. The World Health Organization recommends giving a dose of folic acid less than 5 mg. A combined iron-folic acid supplement contains much less folic acid---only 400 mcg of folic acid. Giving iron routinely to children is less common, although giving iron as drops or syrup is a policy in some countries. Giving iron with other micronutrients in the form of micronutrient powders, which can be incorporated into the child’s porridge, is being tested as an alternative to iron drops. Click here for more information on iron-folic acid supplementation.

- **Malaria prevention and control** is another important intervention to help address anemia. Pregnant women living in stable and unstable malaria transmission areas, who get malaria are at higher risk of severe anemia, and are at the greatest risk in their first and second pregnancies. Malaria infection - usually accompanied by iron deficiency - causes life-threatening, severe anemia in children younger than two years of age. Click here for more information on malaria prevention and control.

In thinking about an integrated anemia prevention and control package, one should think of the contact point at which each component is delivered. This contact point may be health contacts or may be the contacts women have with other sectors or channels. A useful document titled Essential Interventions, Commodities and Guidelines for Reproductive, Maternal, Newborn and Child Health
has been adapted for the anemia integrated package that can be delivered to women and children younger than five years at different contact points and channels. However, other interventions can be delivered by different sectors such as education and agriculture and by the private sector. In the section below, we have described and provided resources for some of these health and other sector interventions. This section has focused on providing in-depth information in SUB-TABS on addressing iron deficiency and helminth and malaria infections. There also are resources below on birth spacing and delayed cord clamping, a neglected but important action to build iron stores in newborns.

Resources:

- **Interventional Strategies for Prevention of Nutritional Anemia**

Iron supplementations are the iron formulations in the form of tablets, syrups, capsules or injections recommended by physicians to prevent and/or treat iron deficiency anemia. It is the effective technique to combat iron deficiency anemia among vulnerable population in developing countries. Iron and folic acid (IFA) supplementation has been advocated as a measure to resolve the nutritional deficiency in the target population at a national level. Food fortification is the food enrichment method with the micronutrients. It might help improve the micronutrient status of the target population provided the fortified foods should be easily accessible and affordable and must be available at the local distribution network. Dietary pattern and selection of foods from the food groups should be so as to balance the presence of iron absorption inhibitors and enhancers. Albendazole, an antihelminthic drug, is suggested for deworming of children. Infants up to 6 months of age should be fed on breast milk. It provides immunity to the child and reduces the prevalence of diarrhoeal episodes. Hand washing, defecation in latrines and safe and proper disposal of human excreta are other good practices that help prevent and/or minimize diarrhoeal episodes in children.

- **Effects of Birth Spacing on Maternal, Perinatal, Infant, and Child Health: A Systematic Review of Causal Mechanisms**

This systematic review of 58 observational studies identified hypothetical causal mechanisms explaining the effects of short and long intervals between pregnancies on maternal, perinatal, infant, and child health, and critically examined the scientific evidence for each causal mechanism hypothesized. The following hypothetical causal mechanisms for explaining the association between short intervals and adverse outcomes were identified: maternal nutritional depletion, folate depletion, cervical insufficiency, vertical transmission of infections, suboptimal lactation related to breastfeeding, pregnancy overlap, sibling competition,
transmission of infectious diseases among siblings, incomplete healing of uterine scar from previous cesarean delivery, and abnormal remodeling of endometrial blood vessels. Women's physiological regression is the only hypothetical causal mechanism that has been proposed to explain the association between long intervals and adverse outcomes. We found growing evidence supporting most of these hypotheses.

Why Nutritional Iron Deficiency Persists as a Worldwide Problem

The earliest studies of food iron absorption employing biosynthetically incorporated radioisotopes were published in the 1950s. Wheat flour has been fortified with iron in Canada, the United Kingdom, and the United States since the 1940s. However, half a century later, nutritional iron deficiency (ID) is estimated to affect 1.5–2 billion people worldwide. The reasons for the apparently limited impact of health and nutrition policies aimed at reducing the prevalence of ID in developing countries are complex. They include uncertainty about the actual prevalence of ID, particularly in regions where malaria and other infections are endemic, failure of policy makers to recognize the relationships between ID and both impaired productivity and increased morbidity, concerns about safety and the risks to iron-sufficient individuals if mass fortification is introduced, and technical obstacles that make it difficult to add bioavailable iron to the diets of those at greatest risk. It is, however, likely that the next decade will see a marked reduction in the prevalence of ID worldwide. More specific assessment tools are being standardized and applied to population surveys. The importance of preventing ID during critical periods of the life cycle is receiving increased attention. Innovative approaches to the delivery of bioavailable iron have been shown to be efficacious. The importance of integrating strategies to improve iron nutrition with other health measures, and economic and social policies addressing poverty as well as trade and agriculture, are receiving increasing consideration.

Iron Interventions for Women and Children in Low-Income Countries

The WHO estimates that 41% of women and 27% of children suffer from anemia due to iron deficiency. The consequences of iron deficiency anemia include suboptimal mental and motor development in young children, increased risk of maternal mortality, and decreased economic productivity of adults. Recent research also provides evidence that maternal iron deficiency in pregnancy increases neonatal morbidity and mortality. This short review briefly highlights how iron interventions might be positioned within 4 global health initiatives: making pregnancy safer, saving newborn lives, infant and young child feeding, and fortification. The importance of iron nutrition is recognized in the context of child nutrition, fortification, and biofortification, and it is likely that meaningful advances will be made through these initiatives.
in the coming decade. However, iron nutrition is not yet well integrated into the programmatic agendas for reducing morbidity and mortality of pregnant women and neonates. Iron supplementation in pregnancy has been advocated for decades as a means of controlling anemia, but this outcome has not been sufficient to motivate strong programs and policies, and the evidence base is still sparse for high-priority clinical outcomes. To act on the current evidence for maternal and neonatal health will require stronger advocacy within circles that have not traditionally included nutritionists. Successful implementation will require greater attention to antenatal care for pregnancy women and prioritization of iron-promoting actions (including iron supplementation and deworming) within that platform.

**Essential Delivery Care Practices for Maternal and Newborn Health and Nutrition**

The first minutes after birth are a very vulnerable period for both mother and newborn. The care that is provided during this time is critical to ensure not only their immediate survival but also to improve their longer-term health and nutrition. Active management of the third stage of labor (AMTSL), the optimal timing of umbilical cord clamping, early skin-to-skin contact between mother and newborn, and early breastfeeding initiation are safe, effective, feasible and evidence-based care practices that should be offered by a skilled birth attendant to all mothers and their infants in the continuum of maternal-neonatal care.

**Further Evidence of the Effects of Preceding Birth Intervals on Neonatal, Infant, and Under-Five-Years Mortality and Nutritional Status in Developing Countries: Evidence from the Demographic and Health Surveys**

In general, the findings of this study confirm those of the author’s preceding study on 17 DHS surveys. While the excess risk of mortality is highest for very short intervals (less than 12 months birth to pregnancy), there are relatively few children conceived at such short intervals (14 percent). Combining both the increased risk of death for children conceived between 12 and 35 months with the great number of children with such intervals (42 percent) results in substantial declines in mortality by avoiding these intervals. The population attributable risk (PAR) for under-five mortality for avoiding conceptions at less than 24 months after a birth is 0.134. In other words, if all women would wait at least 24 months to conceive again, under-five deaths would fall by 13 percent. The effect of waiting 36 months to conceive again would avoid 25 percent of under-five deaths. The impact of avoiding these high risk intervals (less than 36 months) would be a total of 1,836,000 deaths avoided annually in less developed countries, excluding China (where there is a one child policy). Thus, parents who want their children to survive and thrive would do well to wait at least 30 months after a birth to conceive.
another child.

- **Effect of Timing of Umbilical Cord Clamping of Term Infants on Maternal and Neonatal Outcomes.**

At the time of birth, the infant is still attached to the mother via the umbilical cord, which is part of the placenta. The infant is usually separated from the placenta by clamping the cord. The timing of this clamping is one part of the third stage of labour (the time from birth until delivery of the placenta) which can vary according to clinical policy and practice. Early cord clamping is believed to lead to a reduced risk of bleeding after birth (postpartum haemorrhage). This review of 11 trials showed no significant difference in postpartum haemorrhage rates when early and late cord clamping were compared. For neonatal outcomes it is important to weigh the growing evidence that delayed cord clamping confers improved iron status in infants up to six months after birth, with a possible additional risk of jaundice that requires phototherapy.

- **Beyond Survival: Integrated Delivery Care Practices for Long-Term Maternal and Infant Nutrition, Health and Development**

This document by WHO PAHO focuses on 3 key practices for continuum of maternal newborn care at the community level ? delayed cord clamping, skin-to-skin contact, and early initiation of exclusive breastfeeding. It reviews the current evidence on the nutritional and health benefits of these interventions followed by discussion on the feasibility of their implementation.

- **Late vs. Early Clamping of the Umbilical Cord in Full-Term Neonates: Systematic Review and Meta-Analysis of Controlled Trials**

**Context:** With few exceptions, the umbilical cord of every newborn is clamped and cut at birth, yet the optimal timing for this intervention remains controversial.

**Objective:** To compare the potential benefits and harms of late vs. early clamping in term infants.

**Data Sources:** Search of 6 electronic databases (on November 15, 2006, starting from the
beginning of each): the Cochrane Pregnancy and CHildbirth Group trials register, the Cochrane Neonatal Group trials register, the Cochrane Library, MEDLINE, EMBASE, and CINHAL; hand search of secondary references in relevant studies; and contact of investigators about relevant published research.

**Study Selection:** Controlled trials comparing late vs. early cord clamping following birth in infants born at 37 or more weeks' gestation.

**Data Extraction:** Two reviewers independently assessed eligibility and quality of trials and extracted data for outcomes of interest: infant hematologic status; iron status; and risk of adverse events such as jaundice, polycythemia, and respiratory distress.

**Data Synthesis:** The meta-analysis included 15 controlled trials (1912 newborns). Late cord clamping was delayed for at least 2 minutes (n = 1001 newborns), while early clamping in most trials (n = 911 newborns) was performed immediately after birth. Benefits over ages 2 to 6 months associated with late cord clamping include improved hematologic status measured as hematocrit (weighted mean difference [WMD], 3.70%; 95% confidence interval [CI], 2.00%-5.40%); iron status as measured by ferritin concentration (WMD, 17.89; 95% CI, 16.58-19.21) and stored iron (WMD, 19.90; 95% CI, 7.67-32.13); and a clinically important reduction in the risk of anemia (relative risk (RR), 0.53; 95% CI, 0.40-0.70). Neonates with late clamping were at increased risk of experiencing asymptomatic polycythemia (7 studies [403 neonates]: RR, 3.82; 95% CI, 1.11-13.21; 2 high-quality studies only [281 infants]: RR, 3.91; 95% CI, 1.00-15.36).

**Conclusions:** Delaying clamping of the umbilical cord in full-term neonates for a minimum of 2 minutes following birth is beneficial to the newborn, extending into infancy. Although there was an increase in polycythemia among infants in whom cord clamping was delayed, this condition appeared to be benign.

**A Review: Birth Spacing and Risk of Adverse Perinatal Outcomes**

**Context:** Both short and long interpregnancy intervals have been associated with an increased risk of adverse perinatal outcomes. However, whether this possible association is confounded by maternal characteristics or socioeconomic status is uncertain.

**Objective:** To examine the association between birth spacing and relative risk of adverse perinatal outcomes.

**Study Selection:** Included studies were cohort, cross-sectional, and case-control studies with results adjusted for at least maternal age and socioeconomic status, reporting risk estimates and 95% confidence intervals (or data to calculate them) of birth spacing and perinatal outcomes. Of 130 articles identified in the search, 67 (52%) were included.
**Data Extraction:** Information on study design, participant characteristics, measure of birth spacing used, measures of outcome, control for potential confounding factors, and risk estimates was abstracted independently by 2 investigators using a standardized protocol.

**Data Synthesis:** A random-effects model and meta-regression analyses were used to pool data from individual studies. Compared with interpregnancy intervals of 18 to 23 months, interpregnancy intervals shorter than 6 months were associated with increased risks of preterm birth, low birth weight, and small for gestational age (pooled adjusted odds ratios [95% confidence intervals]: 1.40 [1.24-1.58], 1.61 [1.39-1.86], and 1.26 [1.18-1.33], respectively). Intervals of 6 to 17 months and longer than 59 months were also associated with a significantly greater risk for the 3 adverse perinatal outcomes.

**Conclusions:** Interpregnancy intervals shorter than 18 months and longer than 59 months are significantly associated with increased risk of adverse perinatal outcomes. These data suggest that spacing pregnancies appropriately could help prevent such adverse perinatal outcomes.

**Short Interpregnancy Intervals and Unfavourable Pregnancy: Role of Folate Depletion**

There is no generally accepted explanation for the excess risk of adverse pregnancy outcome after short interpregnancy intervals. In this paper, we present a hypothesis that is both biologically plausible, empirically testable, and able to explain many observations. Maternal serum and erythrocyte concentrations of folate decrease from the fifth month of pregnancy onwards and remain low for a fairly long time after delivery. Women who become pregnant before folate restoration is complete have a raised risk of folate insufficiency at the time of conception and during pregnancy. As a consequence, their offspring have higher risks of neural tube defects, intrauterine growth retardation, and preterm birth. We make several predictions based on our hypothesis and suggest ways of testing them empirically. The proposed mechanism implies, among other things, that postpartum supplementation with folic acid might prevent excess risk of unfavourable pregnancy outcome in women with short interpregnancy intervals.

**Prevention and Control of Anemia: Thailand Experiences**

Thailand has addressed nutrition in national development policy since the mid-1970s, including efforts to reduce iron deficiency anemia. Nutritional improvement has been implemented as an integral part of primary health care and community development extending beyond government services to include community participation. Utilization of village health volunteers has been a crucial feature of the program. Available data indicate
that anemia rates have declined among pregnant women and preschool children, although there has been no formal evaluation of the program effect. Universal iron supplementation has been the major strategy for pregnant women, using village health volunteers to encourage continuation of the antenatal care schedule and encouraging a preventive approach by health service providers. Program obstacles have included lack of access to iron tablets by some populations and lack of understanding of the importance of anemia. Women's compliance was complicated by fear of having a large fetus, forgetfulness and side effects. Weekly iron supplementation of school children was piloted in 2000, and is now being extended. Other strategies utilized to address iron deficiency include food fortification, dietary improvement and complementary public health measures. Program monitoring and evaluation require strengthening to assess the effectiveness of intervention strategies and provide proper data for decision-making.

• The Impact of Short Interpregnancy Intervals on Pregnancy Outcomes in a Low-Income Setting

Objectives: The objective of this study was to determine whether the length of the interval between pregnancies was associated with either preterm birth or intrauterine growth retardation in a low-income, largely Black population.

Methods: The study population consisted of 4400 women who had received prenatal care in county clinics and had two consecutive singleton births between 1980 and 1990.

Results: Interpregnancy intervals were positively associated with age and negatively associated with the trimester in which care was initiated in the second pregnancy. Whites had shorter intervals than non-Whites. The percentage of preterm births increased as the length of the interpregnancy interval decreased, but only for women who had not had a previous preterm birth. The association between interval and preterm birth was maintained when other factors associated with preterm birth were controlled. There was no significant relationship between intrauterine growth retardation and interpregnancy interval.

Conclusions: Women, particularly those who are poor and young, should be advised of the potential harm to their infants of short interpregnancy intervals.

• A New Definition of Maternal Depletion Syndrome
**Background:** Although the term "maternal depletion syndrome" has been commonly used to explain poor maternal and infant health, whether such a syndrome actually exists remains unclear. This uncertainty may be due to the lack of a clear definition of the syndrome and the absence of theoretical frameworks that account for the many factors related to reproductive nutrition.

**Methods:** We propose a new definition of maternal depletion syndrome within a framework that accounts for potential confounding factors.

**Results:** Our conceptual framework distinguishes between childbearing pattern and inadequate diet as causes of poor maternal health; hence, our definition of maternal depletion syndrome has both biological and practical meaning. The new definition is based on overall change in maternal nutritional status over one reproductive cycle in relation to possible depletion and repletion phases and in relation to initial nutritional status.

**Conclusions:** The empirical application of this approach should permit the testing of the existence of maternal depletion syndrome in the developing world, and the distinction between populations where family planning will alleviate maternal depletion and those in which an improved diet is also necessary.

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**Major Causes of Anemia by Region**

![Causes of Anemia](image)


**Resources:**

- The Proportion of Anemia Associated with Iron Deficiency in Low, Medium, and High Human
Development Index Countries: A Systematic Analysis of National Surveys

Iron deficiency is commonly assumed to cause half of all cases of anemias, with hereditary blood disorders and infections such as hookworm and malaria being the other major causes. In countries ranked as low, medium, and high by the Human Development Index, we conducted a systematic review of nationally representative surveys that reported the prevalence of iron deficiency, iron deficiency anemia, and anemia among pre-school children and non-pregnant women of reproductive age. Using random effects meta-analyses techniques, data from 23 countries for pre-school children and non-pregnant women of reproductive age was pooled, and the proportion of anemia attributable to iron deficiency was estimated by region, inflammation exposure, anemia prevalence, and urban/rural setting. For pre-school children and non-pregnant women of reproductive age, the proportion of anemia associated with iron deficiency was 25.0% (95% CI: 18.0, 32.0) and 37.0% (95% CI: 28.0, 46.0), respectively. The proportion of anemia associated with iron deficiency was lower in countries where anemia prevalence was >40%, especially in rural populations (14% for pre-school children; 16% for non-pregnant women of reproductive age), and in countries with very high inflammation exposure (20% for pre-school children; 25% for non-pregnant women of reproductive age). Despite large heterogeneity, our analyses suggest that the proportion of anemia associated with iron deficiency is lower than the previously assumed 50% in countries with low, medium, or high Human Development Index ranking. Anemia-reduction strategies and programs should be based on an analysis of country-specific data, as iron deficiency may not always be the key determinant of anemia.

Anemia and the Integrated Package
Food-Based Approaches

This toolkit advocates for a diverse diet that would provide adequate sources of all essential nutrients as well as chemicals, often called phyto-chemicals, in foods that have benefits for health. Because of the central role of iron in red blood cell production, the Toolkit will focus on food-based approaches to improve dietary intake of iron, although it recognizes the importance of food and a diverse diet to ensure adequate health and nutrition in general.

There are several micronutrients in addition to iron that are involved in red cell production and function. These include vitamins (A, B-12, folic acid, and possibly B-6, C, and riboflavin) and copper. A non-diverse diet increases the risk of micronutrient deficiencies including iron deficiency (Arimond, et. al., 2010). A recent paper (Lee, et al., 2012) on dietary takes in low- and middle-income country found the diets of pregnant were predominantly cereal-based and iron and folic acid intakes were lower than Estimated Average Requirements, followed by calcium and zinc. A 2010 publication on the Global Burden of Disease demonstrated that inadequate intake of nutritious foods (i.e., fruits, nuts and seeds, whole grains, vegetables, omega-3 fatty acids, and fiber) and excessive intake of high processed meat accounted for 20% (or 7 out of 33 risk factors) contributing to the global burden of disease.

Iron types, Requirements, and Bioavailability

There are two forms of iron, heme and non-heme iron, in food. One form of iron is called ?non-heme? iron, and it is present in a number of plants including some cereals, pulses, and vegetables. Non-heme iron is not well-absorbed because there are other substances in these foods, often called iron inhibitors, which decrease non-heme iron?fs bioavailability. Only 5-12% of non-heme iron is absorbed from the diet. Reducing inhibitors and increasing enhancers of non-heme iron absorption also will determine absolute iron take in the deficient individual. Click here for the recommended iron intake based on varying dietary iron bioavailability. Some types of food processing techniques decrease the inhibitors of non-heme iron in food. These methods include thermal processing, mechanical processing, soaking, fermentation, and germination/malting and a combination of these methods has been found to improve iron status (Hotz and Gibson, 2007). Animal flesh (meat including organs) and vitamin C in fruits and vegetables also improves the bioavailability of non-heme iron.

The other form of iron is called ?heme? iron which is present only in animal flesh and organs and fish. Heme iron is more bioavailable with 15% to 35% of heme iron absorbed. In many countries, meat is expensive and consumed in only on special occasions, if at all. Women and children,
who have the highest requirements, may not have access to these foods when they are available to the family. Even small amounts of the heme iron in meat increases the absorption of non-heme iron. Click here to view the enhancers and inhibitors of iron absorption. Click here for more information about the bioavailability of iron in foods.

The main determinant of iron absorption, however, is the iron status of the individual. Iron absorption increases when the body needs iron. The highest absorption occurs when an individual’s iron requirements increase (e.g., pregnancy or growth in young children) or the individual is severely iron deficient. When an individual has enough iron (is iron replete), little is absorbed because the body regulates the absorption of iron tightly because, unlike other minerals, the body has no mechanism for iron excretion (Hurrell and Egli, 2010).

Food-based approaches covered in this Toolkit include Agriculture Production and Markets and Fortification and Bioavailability.

**Behavior Change Communication**

All food-based approaches need complementary behavior change communications to ensure each approach is effective. Consumers need to be educated to use and purchase available nutrient-rich foods and food products. Mothers and families need to prioritize giving these foods to young children and ensure they consume them, when they are available. In many cultures, feeding children animal products is delayed until children are older than one year of age or until they have their first set of teeth. There also is a belief that young children do not need these foods when, in fact, children 6-12 months of age have the highest requirements for iron per body weight. A program in Mozambique which combined promoting and supporting the production of orange-flesh sweet potato (OFSP) with nutrition education about infant and young child feeding increased intakes of OFSWP and beta-carotene and increased serum retinol values in children involved in the program (Low, et al., 2007). For more information about infant and young child feeding click on the following: WHO, IYCN, and Alive and Thrive.

**Resources:**

- **Iron Pots for the Prevention and Treatment of Anemia in Preschoolers**

  **Objective:** To assess the effect of food cooked in iron pots for the prevention and treatment of iron deficiency anemia.
**Methods:** In this cluster randomized clinical trial, authors evaluated preschoolers aged 4?5 y for 16 wk. Children were cluster randomized to either eating from iron pots (Group A) or aluminum pots (Group B). Primary outcome variables were change in hemoglobin concentration and anemia prevalence. Two biochemical evaluations were performed, to determine Hb concentrations, before and after intervention. This study was conducted in two public preschools, located in the municipality of Mucambo, Ceará, in the northeast of Brazil.

**Results:** At baseline, for group A, mean hemoglobin concentration was 12.26±0.95 g/dL and 12.29±0.95 g/dL after intervention, p=0.78. In group B, mean baseline hemoglobin was 12.34±1.04 g/dL, and 12.13±0.86 g/dL after intervention, p=0.07. All ten participants, who were anemic at baseline, were no longer anemic after intervention.

**Conclusions:** Using iron cooking pots in developing countries could provide an innovative strategy to prevent and treat iron deficiency anemia.

- **Efficacy of Iron-Supplement Bars to Reduce Anemia in Urban Indian Women: A Cluster-Randomized Controlled Trial**

**Background:** India’s high prevalence of iron-deficiency anemia has largely been attributed to the local diet consisting of nonheme iron, which has lower absorption than that of heme iron.

**Objective:** We assessed the efficacy of the consumption of iron-supplement bars in raising hemoglobin concentrations and hematocrit percentages in anemic (hemoglobin concentration <12 g/dL) Indian women of reproductive age.

**Design:** The Let’s be Well Red study was a 90-d, pair-matched, cluster-randomized controlled trial. A total of 361 nonpregnant women (age 18-35 y) were recruited from 10 sites within Mumbai and Navi Mumbai, India. All participants received anemia education and a complete blood count (CBC). Random assignment of anemic participants to intervention and control arms occurred within 5 matched site-pairs. Intervention participants received 1 iron-supplement bar (containing 14 mg Fe)/d for 90 d, whereas control subjects received nothing. CBC tests were given at days 15, 45, and 90. Primary outcomes were 90-d changes from baseline in hemoglobin concentrations and hematocrit percentages. Linear mixed models and generalized estimating equations were used to model continuous and binary outcomes, respectively.
Results: Of 179 anemic participants, 136 (76.0%) completed all follow-up assessments (65 intervention and 71 control participants). Baseline characteristics were comparable by arm. Mean hemoglobin and hematocrit increases after 90 d were greater for intervention than for control participants [1.4 g/dL (95% CI: 1.3, 1.6 g/dL) and 2.7% (95% CI: 2.2%, 3.2%), respectively]. The anemia prevalence at 90 d was lower for intervention (29.2%) than for control participants (98.6%) (OR: 0.007; 95% CI: 0.001, 0.04).

Conclusions: The daily consumption of an iron-supplement bar leads to increased hemoglobin concentrations and hematocrit percentages and to a lower anemia prevalence in the target population with no reported side effects. This intervention is an attractive option to combat anemia in India.

An Animal-Source Food Supplement Increases Micronutrient Intakes and Iron Status Among Reproductive-Age Women in Rural Vietnam

Background: Few studies have examined the impact of local animal-source foods (ASFs) on the nutritional status of reproductive-age women in developing countries.

Objective: We hypothesized that a midmorning snack of local ASF for 6 mo would reduce dietary micronutrient deficiencies [usual intake less than the estimated average requirement (EAR)] and improve blood biomarkers of iron, zinc, and vitamins A and B-12 status among nonpregnant, reproductive-age women in rural Vietnam.

Methods: One hundred seventeen women, 18-30 y old, were randomly assigned to receive either an ASF (mean: 144 kcal, 8.9 mg Fe, 2.7 mg Zn, 1050 µg retinoic acid equivalent vitamin A, and 5.5 µg vitamin B-12) or a control snack (mean: 150 kcal, 2.0 mg Fe, 0.9 mg Zn, 0 µg retinoic acid equivalent vitamin A, and 0 µg vitamin B-12) 5 d/wk for 6 mo. Usual nutrient intakes were estimated by repeated 24-h dietary recalls. Blood samples were collected at baseline and 3 and 6 mo. Because of the relation between nutritional status and inflammation, serum C-reactive protein, ?-1-acid-glycoprotein, and urinary tract infections (UTIs) were also monitored.

Results: Eighty-nine women (47 in the ASF group and 42 controls) completed the study. In the ASF group, intakes of iron and vitamins A and B-12 below the EAR were eliminated, and the prevalence of a low zinc intake was reduced to 9.6% compared with 64.7% in controls (P

Conclusions: Adding a small amount of locally produced ASF to the diets of reproductive-age Vietnamese women improved micronutrient intakes and iron status. However, the increased UTI incidence in women in the ASF group with initially lower iron stores warrants further investigation.
Randomized Controlled Trial Assessing the Efficacy of a Reusable Fish-Shaped Iron Ingot to Increase Hemoglobin Concentration in Anemic, Rural Cambodian Women

**Background:** Anemia affects 45% of women of childbearing age in Cambodia. Iron supplementation is recommended in populations in which anemia prevalence is high. However, there are issues of cost, distribution, and adherence. A potential alternative is a reusable fish-shaped iron ingot, which, when added to the cooking pot, leaches iron into the fluid in which it is prepared.

**Objective:** We sought to determine whether there was a difference in hemoglobin concentrations in rural Cambodian anemic women (aged 18-49 y) who cooked with the iron ingot or consumed a daily iron supplement compared with a control after 1 y.

**Design:** In Preah Vihear, 340 women with mild or moderate anemia were randomly assigned to 1) an iron-ingot group, 2) an iron-supplement (18 mg/d) group, or 3) a nonplacebo control group. A venous blood sample was taken at baseline and at 6 and 12 mo. Blood was analyzed for hemoglobin, serum ferritin, and serum transferrin receptor. Hemoglobin electrophoresis was used to detect structural hemoglobin variants.

**Results:** Anemia prevalence was 44% with the use of a portable hemoglobinometer during screening. At baseline, prevalence of iron deficiency was 9% on the basis of a low serum ferritin concentration. There was no significant difference in mean hemoglobin concentrations between the iron-ingot group (115 g/L; 95% CI: 113, 118 g/L; P = 0.850) or iron-supplement group (115 g/L; 95% CI: 113, 117 g/L; P = 0.998) compared with the control group (115 g/L; 95% CI: 113, 117 g/L) at 12 mo. Serum ferritin was significantly higher in the iron-supplement group (73 ?g/L; 95% CI: 64, 82 ?g/L; P = 0.002) than in the control group at 6 mo; however, this significance was not maintained at 12 mo (73 ?g/L; 95% CI: 58, 91 ?g/L; P = 0.176).

**Conclusions:** Neither the iron ingot nor iron supplements increased hemoglobin concentrations in this population at 6 or 12 mo. We do not recommend the use of the fish-shaped iron ingot in Cambodia or in countries where the prevalence of iron deficiency is low and genetic hemoglobin disorders are high.

**Point-of-Use Fortification of Foods with Micronutrient Powders Containing Iron in Children of Preschool and School-Age**

**Background:** Approximately 600 million children of preschool and school age are anaemic worldwide. It is estimated that at least half of the cases are due to iron deficiency. Point-of-
use fortification of foods with micronutrient powders (MNP) has been proposed as a feasible intervention to prevent and treat anaemia. It refers to the addition of iron alone or in combination with other vitamins and minerals in powder form, to energyContaining foods (excluding beverages) at home or in any other place where meals are to be consumed. MNPs can be added to foods either during or after cooking or immediately before consumption without the explicit purpose of improving the flavour or colour.

**Objectives:** To assess the effects of point-of-use fortification of foods with iron-containing MNP alone, or in combination with other vitamins and minerals on nutrition, health and development among children at preschool (24 to 59 months) and school (five to 12 years) age, compared with no intervention, a placebo or iron-containing supplements.

**Search Methods:** In December 2016, we searched the following databases: CENTRAL, MEDLINE, Embase, BIOSIS, Science Citation Index, Social Science Citation Index, CINAHL, LILACS, IBECS, Popline and SciELO. We also searched two trials registers in April 2017, and contacted relevant organisations to identify ongoing and unpublished trials.

**Selection Criteria:** Randomised controlled trials (RCTs) and quasi-RCTs trials with either individual or cluster randomisation. Participants were children aged between 24 months and 12 years at the time of intervention. For trials with children outside this age range, we included studies where we were able to disaggregate the data for children aged 24 months to 12 years, or when more than half of the participants were within the requisite age range. We included trials with apparently healthy children; however, we included studies carried out in settings where anaemia and iron deficiency are prevalent, and thus participants may have had these conditions at baseline.

**Data Collection and Analysis:** Two review authors independently assessed the eligibility of trials against the inclusion criteria, extracted data from included trials, assessed the risk of bias of the included trials and graded the quality of the evidence.

**Main Results:** We included 13 studies involving 5810 participants from Latin America, Africa and Asia. We excluded 38 studies and identified six ongoing/unpublished trials. All trials compared the provision of MNP for point-of-use fortification with no intervention or placebo. No trials compared the effects of MNP versus iron-containing supplements (as drops, tablets or syrup). The sample sizes in the included trials ranged from 90 to 2193 participants. Six trials included participants younger than 59 months of age only, four included only children aged 60 months or older, and three trials included children both younger and older than 59 months of age. MNPs contained from two to 18 vitamins and minerals. The iron doses varied from 2.5 mg to 30 mg of elemental iron. Four trials reported giving 10 mg of elemental iron as sodium iron ethylenediaminetetraacetic acid (NaFeEDTA), chelated ferrous sulphate or microencapsulated ferrous fumarate. Three trials gave 12.5 mg of elemental iron as microencapsulated ferrous fumarate. Three trials gave 2.5 mg or 2.86 mg of elemental iron as NaFeEDTA. One trial gave 30 mg and one trial provided 14 mg of elemental iron as microencapsulated ferrous fumarate, while one trial gave 28 mg of iron as ferrous glycine phosphate. In comparison with receiving no intervention or a placebo, children receiving iron-containing MNP for point-of-use fortification of foods had lower risk of anaemia prevalence ratio (PR) 0.66, 95% confidence interval (CI) 0.49 to 0.88, 10 trials, 2448 children; moderate-
quality evidence) and iron deficiency (PR 0.35, 95% CI 0.27 to 0.47, 5 trials, 1364 children; moderate-quality evidence) and had higher haemoglobin (mean difference (MD) 3.37 g/L, 95% CI 0.94 to 5.80, 11 trials, 2746 children; low-quality evidence). Only one trial with 115 children reported on all-cause mortality (zero cases; low-quality evidence). There was no effect on diarrhoea (risk ratio (RR) 0.97, 95% CI 0.53 to 1.78, 2 trials, 366 children; low-quality evidence).

Authors’ Conclusions: Point-of-use fortification of foods with MNPs containing iron reduces anaemia and iron deficiency in preschool- and school-age children. However, information on mortality, morbidity, developmental outcomes and adverse effects is still scarce.

Consuming Iron Biofortified Beans Increases Iron Status in Rwandan Women after 128 Days in a Randomized Controlled Feeding Trial

Background: Food-based strategies to reduce nutritional iron deficiency have not been universally successful. Biofortification has the potential to become a sustainable, inexpensive, and effective solution.

Objective: This randomized controlled trial was conducted to determine the efficacy of iron-biofortified beans (Fe-Beans) to improve iron status in Rwandan women.

Methods: A total of 195 women (aged 18-27 y) with serum ferritin <20 µg/L were randomly assigned to receive either Fe-Beans, with 86 mg Fe/kg, or standard unfortified beans (Control-Beans), with 50 mg Fe/kg, 2 times/d for 128 d in Huye, Rwanda. Iron status was assessed by hemoglobin, serum ferritin, soluble transferrin receptor (sTfR), and body iron (BI); inflammation was assessed by serum C-reactive protein (CRP) and serum 1-acid glycoprotein (AGP). Anthropometric measurements were performed at baseline and at end line. Random weekly serial sampling was used to collect blood during the middle 8 wk of the feeding trial. Mixed-effects regression analysis with repeated measurements was used to evaluate the effect of Fe-Beans compared with Control-Beans on iron biomarkers throughout the course of the study.

Results: At baseline, 86% of subjects were iron-deficient (serum ferritin <15 mg/L) and 37% were anemic (hemoglobin <120 g/L). Both groups consumed an average of 336 g wet beans/d. The Fe-Beans group consumed 14.5 ± 1.6 mg Fe/d from biofortified beans, whereas the Control-Beans group consumed 8.6 ± 0.8 mg Fe/d from standard beans (P < 0.05). Repeated-measures analyses showed significant time-by-treatment interactions for hemoglobin, log serum ferritin, and BI (P < 0.05). The Fe-Beans group had significantly greater increases in hemoglobin (3.8 g/L), log serum ferritin (0.1 log mg/L), and BI (0.5 mg/kg) than did controls after 128 d. For every 1 g Fe consumed from beans over the 128 study days, there was a significant 4.2-g/L increase in hemoglobin (P < 0.05).
Conclusions: The consumption of iron-biofortified beans significantly improved iron status in Rwandan women. This trial was registered at clinicaltrials.gov as NCT01594359.

Combining Home Garden, Poultry, and Nutrition Education Program Targeted to Families with Young Children Improved Anemia Among Children and Anemia and Underweight Among Nonpregnant Women in Nepal

Background: The impact of food-based interventions on child and maternal anthropometry and anemia has not been adequately studied.

Objective: This study tested the effect of an enhanced homestead food production (EHFP) program consisting of home garden, poultry raising, and nutrition education implemented over 2.5 years versus control (no intervention) on anthropometry and anemia among children (12-48 months) and their mothers.

Methods: An unblinded cluster-randomized controlled trial involving pre- and post-surveys with independent samples was conducted in rural areas of Baitadi District, Nepal. Data (including weight, height/length, and hemoglobin) were obtained from 2106 and 2614 mother-child pairs at baseline and follow-up, respectively. Changes in outcome variables (stunting, underweight, wasting, and anemia among children and underweight and anemia among mothers) were compared between the study groups using mixed-effects logistic regression models.

Results: A follow-up, anemia was significantly lower among children (odds ratio, OR [95% confidence interval, CI]: 0.76 [0.59-0.98]) and mothers (OR [95% CI]: 0.62 [0.48-0.82]) in the treatment group compared to the control. Underweight was lower among mothers in the treatment group compared to the control (OR [95% CI]: 0.61 [0.46-0.82]). There was no impact on child anthropometry.

Conclusion: The EHFP intervention improved anemia among children aged 12-48 months and their mothers in Baitadi District of Nepal. The intervention also reduced underweight among these women, but had no impact on child growth, in this district.

Fortified Snack Reduced Anemia in Rural School-Aged Children of Haiti: A Cluster-Randomized, Controlled Trial

Background: Nutrition in the school-aged child matters for brain development and public policy investments globally. Our group previously conducted a trial in urban schools of Haiti to examine the effects of a fortified peanut butter snack, Vita Mamba, with limited findings for
anemia.

**Objective:** We aimed to test the hypothesis that Vita Mamba, with systematic deworming in both study arms, would significantly reduce anemia among rural, school-aged children.

**Methods:** A cluster-randomized, longitudinal study was conducted in two rural communities of the North-East Department of Haiti, 2014-2015. Healthy children ages 3-16 years were enrolled (n=321) and assigned by school to intervention (Vita Mamba and deworming) and control (deworming). Vita Mamba contains 260 kcal and meets >75% of the Recommended Dietary Allowance for critical micronutrients. Multivariate regression analyses including propensity score matching techniques to correct for potential group imbalance (Kernel-based Matching and Propensity Score Weighting) were applied to examine difference-in-difference intervention effects.

**Results:** At baseline, 51% of the children were anemic with no significant differences between study groups. Vita Mamba supplementation showed a consistent, positive effect across regression models on increasing Hb concentration and reducing the odds of anemia compared to the control group after adjusting for child age, vitamin A supplementation, milk consumption, and height-for-age z score. The average treatment effect for the treated in the Propensity Score Weighting models was 0.62±0.27 grams per 100 milliliters (g/dL) for Hb concentration (F = 4.64, P = 0.001), and the odds of anemia were reduced by 88% (Wald ? = 9.77, P = 0.02). No differences in change in anthropometric markers were evident.

**Conclusions:** School feeding programs that integrate fortified foods with deworming could reduce anemia burden with important implications for learning, health, and well-being. The rural-urban differences in anemia require further study.

- **Kenya's Applied Basic Agri-Nutrition Resource Manual for Trainers**

  This training-of-trainers (TOT) manual along with the toolkit were developed to provide the trainer with further knowledge on applied nutrition in order to educate and inform members of the general public on the importance of nutrition in their day-to-day lives.

- **Kenya's Applied Basic Agri-Nutrition Resource Toolkit for Trainers**

  This toolkit along with the training manual were developed to provide the trainer with further knowledge on applied nutrition in order to educate and inform the general public on the importance of nutrition in their day to day lives.
Iron Interventions for Women and Children in Low-Income Countries

The WHO estimates that 41% of women and 27% of children suffer from anemia due to iron deficiency. The consequences of iron deficiency anemia include suboptimal mental and motor development in young children, increased risk of maternal mortality, and decreased economic productivity of adults. Recent research also provides evidence that maternal iron deficiency in pregnancy increases neonatal morbidity and mortality. This short review briefly highlights how iron interventions might be positioned within 4 global health initiatives: making pregnancy safer, saving newborn lives, infant and young child feeding, and fortification. The importance of iron nutrition is recognized in the context of child nutrition, fortification, and biofortification, and it is likely that meaningful advances will be made through these initiatives in the coming decade. However, iron nutrition is not yet well integrated into the programmatic agendas for reducing morbidity and mortality of pregnant women and neonates. Iron supplementation in pregnancy has been advocated for decades as a means of controlling anemia, but this outcome has not been sufficient to motivate strong programs and policies, and the evidence base is still sparse for high-priority clinical outcomes. To act on the current evidence for maternal and neonatal health will require stronger advocacy within circles that have not traditionally included nutritionists. Successful implementation will require greater attention to antenatal care for pregnancy women and prioritization of iron-promoting actions (including iron supplementation and deworming) within that platform.

Nutrient Biofortification of Food Crops

Plant-based foods offer an array of nutrients that are essential for human nutrition and promote good health. However, the major staple crops of the world are often deficient in some of these nutrients. Traditional agricultural approaches can marginally enhance the nutritional value of some foods, but the advances in molecular biology are rapidly being exploited to engineer crops with enhanced key nutrients. Nutritional targets include elevated mineral content, improved fatty acid composition, increased amino acid levels, and heightened antioxidant levels. Unfortunately, in many cases the benefits of these "biofortified" crops to human nutrition have not been demonstrated.

The Importance and Limitation of Food Fortification for the Management of Nutritional Anemia
This brief document focuses on food fortification to address nutritional anemia in women of reproductive age and school age children.

**Anaemia Prevention Badge Project**

**Background:** FANTA and the Regional Center for Quality of Health Care (RCQHC), in partnership with the African Regional Office of the World Association of Girl Guides and Girl Scouts (WAGGGS), designed the Girl Guides Anemia Prevention Badge Project, a program to reach adolescent girls in East and Southern Africa with information and activities on anemia prevention and control.

**Methods:** Under the program, Girl Guides (ages 7-18) can earn a badge in anemia prevention through educational programs and community involvement in anemia control. FANTA and RCQHC developed an Anemia Prevention Badge Handbook and Workbook for the Girl Guides as well as a training manual for Girl Guide leaders.

**Results:** Anemia and iron deficiency remain at epidemic levels among women and children in many nations. Iron deficiency anemia (IDA) is associated with 22% of maternal deaths and 24% of perinatal deaths, according to a recent meta-analysis.

**Conclusions:** Correcting anemia of any severity reduces the risk of death, the analysis also showed. These estimates of the maternal and perinatal deaths associated with IDA underscore the importance of implementing a package of interventions, such as the Girl Guides badge project, to address the multiple causes of anemia.

Both the English and French versions are available for download via the link below. Due to file size, the English version of the Guiders’ Training Manual is also available for download by section.

**Guidelines on Food Fortification with Micronutrients**

The document is organized into four complementary sections. Part I introduces the concept of food fortification as a potential strategy for the control of micronutrient malnutrition. Part II summarizes the prevalence, causes and consequences of micronutrient deficiencies, and the public health benefits of micronutrient malnutrition control. It lays the groundwork for public health personnel to assess the magnitude of the problem, and the potential benefits of fortification, in their particular situation. Part III provides technical information on the various chemical forms of micronutrients that can be used to fortify foods, and reviews experience of their use in specific food vehicles. Part IV describes the key steps involved in designing, implementing and sustaining fortification programmes, starting with the determination of the amount of nutrients to be added to foods, followed by the implementation of monitoring
and evaluating systems, including quality control/quality assurance procedures, before moving on to the estimation of cost-effectiveness and cost?benefit ratios. The importance of, and strategies for, regulation and international harmonization, communication, advocacy, consumer marketing and public education are also explained in some detail.

Iron-Biofortified Rice Improves the Iron Stores of Non-Anemic Filipino Women

Iron deficiency is endemic in much of the world, and food system-based approaches to eradication may be viable with new plant breeding approaches to increase the micronutrient content in staple crops. It is thought that conventional plant breeding approaches provide varieties of rice that have 400?500% higher iron contents than varieties commonly consumed in much of Asia. The efficacy of consuming high-iron rice was tested during a 9-mo feeding trial with a double-blind dietary intervention in 192 religious sisters living in 10 convents around metro Manila, the Philippines. Subjects were randomly assigned to consume either high-iron rice (3.21 mg/kg Fe) or a local variety of control rice (0.57 mg/kg Fe), and daily food consumption was monitored. The high-iron rice contributed 1.79 mg Fe/d to the diet in contrast to 0.37 mg Fe/d from the control rice. The 17% difference in total dietary iron consumption compared with controls (10.16 ± 1.06 vs. 8.44 ± 1.82 mg/d) resulted in a modest increase in serum ferritin ($P = 0.10$) and total body iron ($P = 0.06$) and no increase in hemoglobin ($P = 0.59$). However, the response was greater in nonanemic subjects for ferritin ($P = 0.02$) and body iron ($P = 0.05$), representing a 20% increase after controlling for baseline values and daily rice consumption. The greatest improvements in iron status were seen in those nonanemic women who had the lowest baseline iron status and in those who consumed the most iron from rice. Consumption of biofortified rice, without any other changes in diet, is efficacious in improving iron stores of women with iron-poor diets in the developing world.

Prediction of Dietary Iron Absorption: An Algorithm for Calculating Absorption and Bioavailability of Dietary Iron

**Background:** Dietary iron absorption from a meal is determined by iron status, heme- and nonheme-iron contents, and amounts of various dietary factors that influence iron absorption. Limited information is available about the net effect of these factors.

**Objective:** The objective was to develop an algorithm for predicting the effects of factors known to influence heme- and nonheme-iron absorption from meals and diets.

**Design:** The basis for the algorithm was the absorption of iron from a wheat roll ($22.1 ± 0.18\%$) containing no known inhibitors or enhancers of iron absorption and adjusted to a reference dose absorption of 40%. This basal absorption was multiplied by the expected
effect of different amounts of dietary factors known to influence iron absorption: phytate, polyphenols, ascorbic acid, meat, fish and seafood, calcium, egg, soy protein, and alcohol. For each factor, an equation describing the dose-effect relation was developed. Special considerations were made for interactions between individual factors.

**Results:** Good agreement was seen when measurements of iron absorption from 24 complete meals were compared with results from use of the algorithm \( r^2 = 0.987 \) and when mean iron absorption in 31 subjects served a varied whole diet labeled with heme- and nonheme-iron tracers over a period of 5 d was compared with the mean total iron absorption calculated by using the algorithm \( P = 0.958 \).

**Conclusions:** This algorithm has several applications. It can be used to predict iron absorption from various diets, to estimate the effects expected by dietary modification, and to translate physiologic into dietary iron requirements from different types of diets. *Am J Clin Nutr* 2000;71:1147–60.

**Iron Nutrition and Absorption: Dietary Factors which Impact Iron Bioavailability**

Iron deficiency is widely observed worldwide, yet, paradoxically, iron is the most plentiful heavy metal in the earth’s crust. Although absorption of iron from the gastrointestinal tract is strictly controlled, excretion is limited to iron lost from exfoliation of skin and gastrointestinal cells, customary and abnormal blood loss, and menses. Individuals highly vulnerable to iron deficiency have high iron needs, as during growth or pregnancy; high iron loss, as during marked hemorrhage or excessive and/or frequent menstrual losses; or diets with low iron content or bioavailability. Food iron is classified as heme or nonheme. Approximately half of the iron in meat, fish, and poultry is heme iron. Depending on an individual's iron stores, 15% to 35% of heme iron is absorbed. Food contains more nonheme iron and, thus, it makes the larger contribution to the body’s iron pool despite its lower absorption rate of 2% to 20%. Absorption of nonheme iron is markedly influenced by the levels of iron stores and by concomitantly consumed dietary components. Enhancing factors, such as ascorbic acid and meat/fish/poultry, may increase nonheme iron bioavailability fourfold.

**Recommended Dietary Iron Intake Based on Varying Bioavailability of Iron**
Inhibitors and Enhancers of Iron Supplementation

Agriculture Production and Markets

Agriculture Production of Nutrient-Rich Foods

Because livestock, whole fish, and pulses are good sources of iron, increasing the production...
decreasing anemia. Most cultures desire animal products in their diets and as income increases, the proportion of the food budget spent on meat increases. Lower cost sources of iron need to be available for poorer families. In many countries legumes provide a good source of iron for the poor. While the availability per capita of meat has increased worldwide by 72% from 1963 to 2009 (with an almost 400% increase in Asia and a 100% increase in Latin America (Figure 1), over the same period the availability of pulses has decreased by 30% worldwide with much of the decline in the Asia region (a 48% decline) (Figure 2).

There is some evidence from studies and small programs that agriculture including livestock projects can improve food intake of certain micronutrients and nutrition status (Allen, 2003; Murphy, et al., 2003) although a more recent analysis of 23 agriculture and nutrition studies found no effect of the interventions on the absorption of iron but there was some evidence for an improvement in vitamin A absorption (Masset, et al., 2012).

Livestock value chains could be used to improve the iron status in the people and their families who participate in them, if some of the livestock is consumed at home or the income earned is used to buy iron-rich foods. The people involved in agriculture value chains are not always the most vulnerable families, however. It has not yet been well-documented of the effect of agriculture value chains on food intake or nutritional status. Authors of a review of the subject suggest that in order to obtain nutrition outcomes from agricultural value change, there will need to be specific nutrition goals and a clearly defined nutrition problem, among other considerations. Click here and here to view the publications.

Creating Healthy Markets and Controlling Food Prices

In order to decrease anemia through increased food production including livestock, legumes, and even good sources of vitamin C which improves the absorption of non-heme iron, there need to be supportive policies and actions that will ensure these foods are produced by those who need them or are available to purchase in markets. The availability of micronutrient-rich foods is often seasonal and a steady, year-round supply may not be possible. Government intervention may be needed to increase the production of fruits and vegetables for consumption by lower income groups. Subsidies are often relegated to staple crops. Agriculture subsidies could be used to increase the availability of a number of nutritious foods which have potential for improving the nutritional status of the population. Social safety nets and control food prices during financial insecurity could buffer a crisis. An analysis from one country found a 50% increase in food prices
in one country decreased iron intake by 10% to 30% which was estimated to translate to a 25 percentage point increase in the proportion of women not meeting their iron requirements (Bouis, et al., 2011).

Resources:

- Assessing the Impact of Livestock Husbandry on Anemia in Women and Children: A Systematic Review

Anemia is a major public health concern among women and children in low- and middle-income countries (LMICs) and can result from both micronutrient deficiencies (nutritional anemia) and infection (anemia of inflammation). Livestock husbandry may positively impact anemia through provision of animal-source foods (ASF) and income, but may also contribute to the development of anemia through infectious disease. Sustainable livestock production and management interventions may thus provide an avenue to address preventable causes of anemia. The objective of this review is to assess the impact of livestock husbandry on anemia in women and children and to identify the mechanisms underlying this relation including diet, micronutrient status, and infection. Using a priori exclusion criteria and a systematic search of databases of indexed literature, we identified fourteen observational and two experimental studies that empirically measured the association of livestock husbandry with anemia or its potential determinants. Out of the thirteen studies that reported measures of anemia or iron status, seven observed a lower prevalence of anemia with exposure to or increased production of livestock. Six studies examined pastoral populations and four of these found a higher prevalence of anemia in pastoral populations as compared to settled or farming populations. Some authors hypothesized that this higher prevalence of anemia may be due to a greater burden of infection among pastoralists. This livestock-pathogen interface is supported by findings of increased hookworm and S. stercoralis in children living in households owning livestock, and of a higher incidence of human illness with increasing animal illness or death. No studies assessed sub-clinical infection associated with environmental enteric dysfunction. Although livestock rearing may increase exposure to infection, it may also increase access to nutrient-rich ASFs. Of the five studies that assessed ASF consumption, two found a positive association between animal ownership and consumption of those animals, and three found positive associations of ASF consumption with anemia. Of the two identified experimental studies that randomly assigned households to receive a poultry production intervention, only one observed a significant reduction in anemia among infants. This result was dependent on the type of educational platform that households received in concert with the poultry production intervention. Although livestock ownership and rearing is associated with a lower prevalence of anemia among women and children in some contexts, particularly among those with greater ASF consumption, a high risk of infection from livestock exposure may detract from these potential benefits in other contexts. The evidence base to assess this relation and its mechanisms would benefit from
additional experimental studies that distinguish nutritional anemia from anemia of inflammation and further consider how livestock management and increased animal production may influence determinants of anemia in the long-term.

- Mapping the Global Reach of Biofortified Crops

The number of countries that have adopted biofortified crops continues to grow around the world. Since September 2015, several additional countries have released or tested these nutritious crops. They include Afghanistan, Eritrea, Chad, Gabon, Gambia, Morocco, Lebanon, South Sudan, and Tunisia. More than 50 countries in total have now embraced biofortification.

Fortification and Bioavailability

Food Fortification

Food fortification is the addition of vitamins and minerals to foods and water and has been the most direct policy intervention to improve nutrition in Western countries (World Bank, 1994). This includes food enrichment in which nutrients are added at the level that existed before food processing (e.g., adding the iron back that was lost during the milling of wheat flour) or fortification in which nutrients are added at levels higher than exist in foods (e.g., iodine in salt). Food fortification, instead of enrichment, is the approach in most developing countries because dietary intake of a number of micronutrients is inadequate. Fortification of flour with iron in many Western countries has been attributed to a reduction in anemia. Fortifying a food consumed by the entire population with any nutrient needs to be safe for the entire population and will not meet the entire nutrient requirements of the vulnerable groups.

Specific foods that are only consumed by vulnerable groups also have been fortified to meet higher requirements of these groups. Examples of these include fortifying baby cereals with iron in some Western countries which reduced iron deficiency in these countries. Fortified complementary foods are being developed and introduced in developing countries to provide more micronutrients to young children. Foods, often called ?vehicles? for fortification, which have been used for food fortification are displayed in the table below.
The private food industry is responsible for food fortification but in many countries, the public health sector works in partnership with the food industry to fortify foods or makes fortification mandatory. There is a price differential between fortified and unfortified foods which can be a deterrent to the food industry fortifying a food and consumers buying it, if the cost is passed onto the consumer. The "fortificant" used to fortify the food may be taxed at the point of importation which also increases the cost of the food. In countries where consumers demand fortified foods, the private sector is motivated to voluntarily fortify foods. Where consumers do not know about the benefits of a fortified and are not motivated to buy it, a single food company may not be motivated to voluntarily fortify a product. The food industry in developing countries may not have the resources to market the product and thus are competing with products which are less expensive. Mandatory food fortification (requiring all companies to fortify foods with specific nutrients) can "level the playing field" for companies that are interested in fortification. When there are many small companies producing a food production (e.g., salt), it makes it more difficult to enforce mandatory fortification. In countries with fluid borders, unfortified foods from other countries may reduce the effectiveness of a food fortification program.

Fortificants (or the form of the micronutrient used to fortify foods) vary widely in cost, bioavailability, and their appearance in foods. Fortified foods need to be tested during the development phase to ensure these foods can be manufactured easily and consumers like them. Price, taste, appearance and other considerations need to be assessed. Marketing these foods to the relevant target groups is needed for most fortified foods. For example, consumers may be wary of adding something to their food. Mothers need to have information about how to use a fortified complementary food appropriately in their children's diet. The fortified complementary food may not have much impact if the child is not eating it. Click here for a comprehensive manual on food fortification.

**Biofortification**

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Food Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine</td>
<td>Salt, Bread, Water</td>
</tr>
<tr>
<td>Iron</td>
<td>Wheat flour, Cornmeal, Rice, Salt, Condiments, Milk, Infant cereals, Processed food</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Sugar, Cooking fat, Margarine, Vegetable oils, MSG, Tea</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>Wheat flour</td>
</tr>
</tbody>
</table>

Biofortification uses plant breeding and/or modern technology to enhance the nutrient content of commonly consumed food staple crops. Micronutrient rich traits can be identified within most of the staple crops which would significantly improve the nutrient status (for iron, for example) of the populations who consume them and will reach remote populations that do not have access to centrally-fortified foods and supplements (Bouis, 2003). Decreasing the content of inhibitors of iron absorption may also be possible as long as it does not reduce crop yield. (Welch, 2002). This approach is highly sustainable. After the investments are made to develop new seeds for crops with higher nutrient content, the current costs and germplasm can be shared internationally (Bouis, 2003). Some examples of nutrients and crops that are being developed and relevant to reducing anemia include:

- Iron biofortification of rice, beans, and sweet potato
- Beta-carotene (the precursor of vitamin A) biofortification of sweet potato, maize, and cassava.

Click here and here for additional information on biofortification.

Resources:

- **Effect of Iron Fortified Wheat Flour Consumption on the Hemoglobin Status of Adolescent Girls in District Buner**

Food fortification has been defined as the addition of one or more essential nutrients to a food whether or not it is normally contained in the food. Iron acts as an integral part of hemoglobin and is required for the transport of oxygen and carbon dioxide in the blood. Cereal foods can be successfully fortified with iron. Among the cereals, wheat has additional advantage to be used as vehicle. The bioavailability of iron added to wheat is several times greater than other staples such as maize and rice. Ferrous sulphate has excellent bioavailability. It is the fortificant of choice when used in wheat flour and is the best iron source because of its high bioavailability and low cost. In this study the effect of ferrous sulphate fortified wheat flour on the hemoglobin status of adolescent girls was examined in district Buner. A total of 200 adolescent girls were randomly selected and divided into two groups, study and control each group having 100 girls. The subjects of the study group were fed with ferrous sulphate fortified wheat flour while the control group were fed with non-fortified wheat flour as a placebo. The hemoglobin level of both groups was determined 4 times, prior to intervention, after 1st, 2nd and 3rd month of consuming ferrous sulphate fortified wheat flour with the help of Hemo Cue. The mean (± S.D) Hb values (g/dl) of control and study groups prior to
intervention, after 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} month were \((11.878 \pm 0.46, 11.754 \pm 0.61)\), \((11.91 \pm 0.50, 11.837 \pm 0.60)\), \((11.88 \pm 0.53, 11.93 \pm 0.65)\), \((11.87 \pm 0.66, 12.107 \pm 0.63)\) respectively. The results showed no significant difference between study and control groups by comparing baseline data with the 1\textsuperscript{st} month while showed significant difference by comparing baseline data with 2\textsuperscript{nd} and 3\textsuperscript{rd} month of intervention. The study suggests that the hemoglobin status of adolescent girls was significantly improved by consuming wheat flour fortified with ferrous sulphate.

\section*{Delivery of Iron-Fortified Yoghurt, Through a Dairy Value Chain Program, Increases Hemoglobin Concentration Among Children 24 to 59 Months Old in Northern Senegal: A Cluster-Randomized Control Trial}

\textbf{Background:} Innovative strategies are needed to enhance the nutritional impact of agriculture. Value chain approaches, which use supply chains to add value (usually economic) to products as they move from producers to consumers, can be used to increase access to nutritious foods and improve nutritional status. This study tested whether a dairy value chain could be used to distribute a micronutrient-fortified yoghurt (MNFY) (conditional upon the producer supplying a minimum amount of cow milk/day) to improve hemoglobin and reduce anemia among preschool children in a remote area in Northern Senegal.

\textbf{Methods:} A cluster randomized control trial was used to compare 204 children (24 to 59 months of age at baseline) from households who received the MNFY coupled to a behavior change communication (BCC) campaign focusing on anemia prevention to 245 children from a control group (receiving BCC only) after one year. Randomization was done at the level of the family concession (households from the same family) \((n = 321)\). Eligible households had a child of the target age and were willing to deliver milk to the dairy factory. Changes in anemia and hemoglobin between groups were assessed using mixed regression models.

\textbf{Key Findings:} Anemia prevalence was very high at baseline (80\%) and dropped to close to 60\% at endline, with no differences between intervention groups. Hemoglobin increased by 0.55 g/dL, 95\%CI (0.27; 0.84) more in the intervention compared to the control group after one year, in models that controlled for potentially confounding factors. The impact was greater (0.72 g/dL, 95\%CI (0.34; 1.12)) for boys, compared to girls (0.38 g/dL, 95\%CI (-0.03; 0.80)).

\textbf{Conclusion:} The dairy value chain was a successful strategy to distribute MNFY among pastoralists in Northern Senegal, and increase Hb concentrations among their children. This study is one of the first proofs of concept showing that a nutrition-sensitive agriculture value chain approach can contribute to improved child nutrition in a remote pastoralist population.
Impact of Home Fortification of Complementary Foods Program on Child Anemia and Stunting in Bihar, India

Home fortification of complementary foods with multiple micronutrient powders (MMP) is recommended to reduce child anemia in resource-poor settings. However, there is a lack of program effectiveness data in Bihar, India to guide policies. We conducted a cluster randomized effectiveness trial in West Champaran, Bihar in over 4000 children aged 6?18 months for a duration of one year, within the context of an ongoing program (CARE, India: Integrated Family Health Initiative) delivered by community front line workers. 70 health sub-centers were randomized to intervention (MMPs and Infant and Young Child Feeding (IYCF) counseling) or control (only IYCF counseling). The MMPs included a daily RDA of iron, zinc, iodine, folic acid, and vitamins A, C and B12, for children. The study aimed to determine impact on measures of nutritional status (anemia, stunting, underweight and wasting) and child feeding practices and inform potential statewide scale-up. A secondary objective was to examine potentially adverse outcomes (diarrhea, hospitalization and fever). We used a difference in difference approach using cross-sectional baseline and endline surveys to evaluate impact and adjusted for caste, socioeconomic status, age, gender, maternal education, young mother status, and religion. The duration of the intervention was one year and at baseline, 72% of children were anemic and 33% were stunted. Although 86% of caretakers indicated that they would like to continue using the powders, only 38% of children had consumed MMPs in the last month and 24% were currently consuming MMP at endline. Anemia declined significantly by 7.8% (6.7% in adjusted models; p<0.05) with a greater decline among children 12?18 months (9.3%, p<0.05). There were no overall effects on the prevalence of stunting, underweight or wasting but there was a significant decline of 8.4% in stunting for children aged 12?18 months (7.2% in adjusted models; p<0.05). There were no significant differences in IYCF (age of initiation of complementary feeding, feeding frequency, dietary diversity or minimum acceptable diet). There were no differences in severe morbidity (bloody diarrhea, severe diarrhea, persistent diarrhea, hospitalizations or fever) and there was a significant 4% decrease in the prevalence of any diarrhea self-reported in past 2 weeks in the intervention communities. In conclusion, home fortification of complementary foods is a promising intervention associated with modest improvements in anemia and possibly stunting within the existing government run program context in Bihar, India.

Iron, Zinc, Folate, and Vitamin B-12 Status Increased Among Women and Children in Yaoundé and Douala, Cameroon, 1 Year After Introducing Fortified Wheat Flour

Background: Few data are available on the effectiveness of large-scale food fortification programs.
Objective: We assessed the impact of mandatory wheat flour fortification on micronutrient status in Yaoundé and Douala, Cameroon.

Methods: We conducted representative surveys 2 y before and 1 y after the introduction of fortified wheat flour. In each survey, 10 households were selected within each of the same 30 clusters (n = ?300 households). Indicators of inflammation, malaria, anemia, and micronutrient status [plasma ferritin, soluble transferrin receptor (sTfR), zinc, folate, and vitamin B-12] were assessed among women aged 15?49 y and children 12?59 mo of age.

Results: Wheat flour was consumed in the past 7 d by ?90% of participants. Postfortification, mean total iron and zinc concentrations of flour samples were 46.2 and 73.6 mg/kg (target added amounts were 60 and 95 mg/kg, respectively). Maternal anemia prevalence was significantly lower postfortification (46.7% compared with 39.1%; adjusted P = 0.01), but mean hemoglobin concentrations and child anemia prevalence did not differ. For both women and children postfortification, mean plasma concentrations were greater for ferritin and lower for sTfR after adjustments for potential confounders. Mean plasma zinc concentrations were greater postfortification and the prevalence of low plasma zinc concentration in women after fortification (21%) was lower than before fortification (39%, P 50% greater postfortification.

Conclusion: Although the pre-post survey design limits causal inference, iron, zinc, folate, and vitamin B-12 status increased among women and children in urban Cameroon after mandatory wheat flour fortification.

**The Effect of a Micronutrient Powder Home Fortification Program on Anemia and Cognitive Outcomes Among Young Children in Rural China: A Cluster Randomized Trial**

Background: Anemia early in life has been associated with delayed cognitive and motor development. The WHO recommends home fortification using multiple micronutrient powders (MNPs) containing iron as a strategy to address anemia in children under two. We evaluated the effects of a program freely distributing MNP sachets to caregivers of infants in rural China.

Methods: We conducted a cluster-randomized controlled trial in Shaanxi province, enrolling all children aged 6?11 months in target villages. Following a baseline survey, investigators randomly assigned each village/cluster to a control or treatment group. In the treatment group, caregivers were instructed to give MNPs daily. Follow-up was after 6, 12, and 18 months of intervention. Primary outcomes were hemoglobin concentrations and scores on the Bayley Scales of Infant Development.

Results: One thousand, eight hundred and-two eligible children and their caregivers were
enrolled. At baseline 48% (870) of children were anemic and 29% (529) were developmentally delayed. Six hundred and ten children (117 villages) were assigned to the control group and 1192 children (234 villages) were assigned to the treatment group. Assignment to the treatment group was associated with an improvement in hemoglobin levels (marginal effect 1.77 g/L, 95% CI 0.017?3.520, p-value = 0.048) and cognitive development (marginal effect 2.23 points, 95% CI 0.061?4.399, p-value = 0.044) after 6 months but not thereafter. There were no significant effects on motor development. Zero effects after the first 6 months were not due to low compliance, low statistical power, or changes in feeding behavior. Hemoglobin concentrations improved in both the treatment and control groups over the course of the study; however, 22% (325) of children remained anemic at endline, and 48% (721) were cognitively delayed.

**Conclusions:** Providing caregivers with MNP sachets modestly hastened improvement in hemoglobin levels that was occurring absent intervention; however, this improvement did not translate into improved developmental outcomes at endline.

- **Iron Retention in Iron-Fortified Rice and Use of Iron-Fortified Rice to Treat Women with Iron Deficiency: A Pilot Study**

**Objectives:** 1. Evaluate the effect of washing and cooking iron-fortified rice on iron retention and bioavailability. 2. Evaluate the effect of iron-fortified rice on women with iron deficiency anemia.

**Methods:** 1. Iron-fortified rice (18 mg/100 g as FeSO4) was cooked in Baton Rouge, Louisiana (C), rinsed and cooked (RC), fried and cooked (FC), cooked with extra water (CW), or soaked and cooked with extra water (SCW), and iron retention was determined. 2. Rice samples were cooked in Kampala, Uganda in a lab (C-Uganda) and households using traditional cooking method (TC-Uganda) and iron retention were determined. 3. Seventeen women with iron deficiency (low iron and/or low ferritin) anemia were randomized to 100 g/d of rice (two cooked 0.75 cup servings) for two weeks containing 18 mg/d iron (supplemented) or 0.5 mg/d iron (un-supplemented). Hemoglobin and hematocrit were evaluated at baseline and 2 weeks with other measures of iron metabolism.

**Results:** 1. Iron retention, from highest to lowest, was (C), (RC), (FC), (C-Uganda), (CW), (SCW), and (TC-Uganda). 2. Seventeen women were randomized and 15 completed the study (hemoglobin ± 1.6 g, hematocrit 33.7 ± 4.1%), 9 in the iron-fortified rice group and 6 in the un-fortified rice group. The iron-fortified group had a greater increase in hemoglobin (0.82, p = 0.0035) and hematocrit (1.83%, p = 0.0248) with directional differences in other measures of iron metabolism favoring the iron-fortified group.

**Conclusions:** Iron-fortified rice increased hemoglobin and hematocrit in women with iron-deficient anemia. Iron deficiency and anemia are widespread in Southeast Asia and Africa.
and undermine development in these regions.

Effect of the Brazilian Iron Fortification of Wheat and Corn Flour on the Nutritional Iron Status in Adolescents, 6 Years After Its Implementation

**Background:** As it is difficult to know the content of iron added in the Brazilian iron fortification of wheat and corn flour, and if the compound has good or poor bioavailability, the objective was to assess the effect of the Brazilian iron fortification program, as it was carried out, on iron nutritional status of adolescents, 6 years after its implementation.

**Methods:** A cross-sectional retrospective study was conducted with adolescents aged 10 to 17 years, both sexes, treated at a primary health care center. Data were collected from medical records of patients and compared with those of a previous survey conducted at the same center in 2004. Anthropometry, iron biochemical indicators, food intake, pubertal stage, and transferrin saturation were assessed, with pubertal stage and transferrin saturation being the last two variables compared between 2004 and 2010. Mann-Whitney and chi-square tests were also used.

**Results:** In 2010, mean hemoglobin values and serum ferritin levels were within normal ranges for both sexes, and adolescents who consumed diets with low iron bioavailability constituted more than half of the sample (52.7%). In 2004, a 10.3 and 18.6% prevalence of iron deficiency was observed, based on low transferrin saturation, in females and males, respectively. It was noted that during the 6-year period, this prevalence decreased significantly, 4 and 10.4%.

**Conclusions:** Anemia and iron deficiency are not prevalent in this population, probably due to the implementation of flour fortification with iron; it is not possible, however, to attribute such a result only to the implementation of this strategy.

Uganda Releases Biofortified Beans to Address Iron Deficiency Anemia

The Government of Uganda released the first five high iron bean varieties that will provide more iron in the diets of millions of Ugandans who eat beans almost every day. Three of the released varieties are bush beans and two are climbers.
WHO Guideline: Use of Multiple Micronutrient Powders for Point-of-Use Fortification of Foods Consumed by Infants and Young Children Aged 6-23 Months and Children Aged 2-12 Years

Member States have requested guidance from WHO on the effects and safety of the use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6-23 months and children aged 2-12 years. Point-of-use fortification is often referred to as "home fortification;" the word "home" has been substituted by "point-of-use," to reflect the variety of settings where this intervention may take place. This guideline is intended to help Member States and their partners in their efforts to make evidence-informed decisions on the appropriate nutrition actions to improve the nutritional status of infants and children aged 6 months to 12 years. It will also support their efforts to achieve the Sustainable Development Goals, the global targets set by the Comprehensive implementation plan on maternal, infant and young child nutrition, and the Global strategy for women?s, children?s and adolescents? health 2016-2030.

The guideline is intended for a wide audience, including governments, nongovernmental organizations, health-care workers, scientists and donors involved in the design and implementation of micronutrient programmes and their integration into national and subnational public health strategies and programmes.

The guideline is an update of the 2011 WHO guideline on Use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6-23 months of age. The present guideline supersedes the previous one for infants and young children aged 6-23 months and provides new recommendations for children aged 2-12 years.

Iron Content in Common Foods
Iron-Folic Acid Supplementation

Iron deficiency is caused by inadequate iron intake to meet normal requirements or increased requirements due to excessive blood loss and reproduction. Anemia is a good predictor of iron deficiency when iron deficiency is the main cause of anemia. There are specific tests to measure iron deficiency such as serum ferritin but these tests are not described here because they are not available in most developing countries. In addition, the interpretation of some of the tests will differ based on presence of infection in a population. Click here for more information on tests for iron deficiency.

Giving iron and folic acid (IFA) supplements to pregnant women to prevent and treat anemia is a policy in most developing countries. All pregnant women need iron because a woman will become iron deficient with or without anemia by the end of her pregnancy, if she does not take iron supplements (Lynch, 2000). IFA supplementation should be integrated with other effective anemia control interventions in pregnancy such as IPTp, ITNs, and deworming (visit the sub-tabs

<table>
<thead>
<tr>
<th>Food type</th>
<th>Iron content (mg) per 100 grams of cooked food</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals</td>
<td></td>
</tr>
<tr>
<td>Maize porridge, cooked, plain</td>
<td>0.1</td>
</tr>
<tr>
<td>Millet porridge, cooked, plain</td>
<td>0.3</td>
</tr>
<tr>
<td>Rice, boiled</td>
<td>0.2</td>
</tr>
<tr>
<td>Pulses and Seeds</td>
<td></td>
</tr>
<tr>
<td>Soybeans, mature, cooked</td>
<td>5-16</td>
</tr>
<tr>
<td>Kidneys, mature, cooked</td>
<td>3</td>
</tr>
<tr>
<td>Lentils, mature, cooked</td>
<td>3-9</td>
</tr>
<tr>
<td>Chickpeas, mature, cooked</td>
<td>3</td>
</tr>
<tr>
<td>Pumpkin seeds, dried</td>
<td>6</td>
</tr>
<tr>
<td>Beef, beef liver, fish</td>
<td></td>
</tr>
<tr>
<td>Beef, cooked, medium fat</td>
<td>2</td>
</tr>
<tr>
<td>Beef, cooked, lean</td>
<td>3</td>
</tr>
<tr>
<td>Beef liver, braised</td>
<td>6-7</td>
</tr>
<tr>
<td>Fish, smelt, whole, cooked</td>
<td>1</td>
</tr>
<tr>
<td>Fish, tilapia, cooked</td>
<td>1</td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
</tr>
<tr>
<td>Spinach, cooked</td>
<td>4</td>
</tr>
</tbody>
</table>

Source: United States Department of Agriculture Food Composition Database: Tanzania Food Composition Tables (2008), Muhimbili University and Tanzania Food and Nutrition Centre (TFNC), Dar es Salaam, Tanzania; Harvard School of Public Health, Boston, MA, USA.
on helminths, malaria and program guidance for more information). Giving iron supplementation to children younger than five years of age is not a policy in all countries, a few countries are continuing the practice of supplementing with iron and have taken it to scale. Premature and low-birth-weight infants need additional iron starting at two months of age.

**The Impact of Giving Iron-Folic Acid (IFA) Supplements**

Giving IFA is effective in increasing hemoglobin values and reducing anemia prevalence (Peña-Rosa, et al., 2012). Recent studies have shown that antenatal iron and folic acid given during pregnancy reduces rates of low birth weight and preterm birth, and anemia which is associated with increased risk of perinatal and maternal mortality. Emerging evidence finds that iron and folic acid supplementation during pregnancy significantly reduces the risk of early neonatal death and child mortality in Indonesia.

**Giving Iron-Folic Acid (IFA) Supplements to Children in Malaria-Endemic Areas**

The World Health Organization recommends giving iron-folic acid supplements to young children in areas of high malaria transmission along with malaria programs and surveillance. Click here for information about giving IFA to children in malaria endemic areas.

**The Dose of Iron-Folic Acid (IFA) Supplements**

WHO recommends both preventive and treatment doses of IFA. Click here to view IFA preventive and treatment doses and duration.

Some women will not be able to take all 180 IFA supplements during pregnancy, either because supplies are not available or women do not visit ANC early or frequently enough to receive all their IFA supplements. These women should continue to take IFA after delivery until they have taken 180 IFA supplements. In countries, where anemia prevalence is less than 20%, non-anemic pregnant women can be offered a weekly dose of iron (WHO, 2011). Other groups that can be offered a weekly dose are school-age children, adolescent girls or all reproductive age women, the elderly, and men who are exposed to helminths or engage in heavy labor. The cost of providing weekly doses of IFA to many different groups should be considered when additional funding is available. Pregnant women and children younger than two years of age should
continue to receive the highest priority.

In most countries, a combined iron-folic acid supplement is given to pregnant women containing 60 mg of iron and 400 mcg of folic acid. This dose of folic acid helps meet the requirement of the mother for additional folic acid during pregnancy. However, in some countries large doses of 5 mg of folic acid are given as a separate supplement. These large doses of folic acid are not needed and interfere with the treatment of malaria using sulphadoxine-pyrimethamine (SP). The World Health Organization recommends giving folic acid at a dose of less than 5 mg (WHO, 2012).

Coverage of Iron-Folic Acid (IFA) Supplementation

IFA supplementation programs for pregnant women and young children have not reached public health coverage as defined by 80% of the target population receiving the recommended dose of IFA. The coverage of IFA supplements for pregnant women is higher than coverage for children. Click here to view the IFA coverage for pregnant women for USAID priority countries. No country has achieved 80% coverage, and only two (Nepal and Senegal) have achieved coverage of greater than 50% of women receiving IFA supplements during pregnancy.

Types of Supplements

In most countries, IFA is given as one tablet to pregnant women, although iron syrups also may be given. Some countries have not transitioned to a combined IFA supplement and give iron and folic acid supplements separately and may give other micronutrients such as the B-vitamins separately as well. Some countries recommend giving children iron drops or syrup, but many countries are piloting micronutrient powders that contain iron and can be sprinkled on the child’s porridge. There is no evidence that giving iron to pregnant women in the form of micronutrient powders has a comparative advantage over IFA supplements. As a result, the World Health organization does not recommend multi-micronutrient powders during pregnancy (WHO, 2011). Click Program Guidance for information about the types of IFA supplements women prefer.

Giving Multi-Micronutrient (MMN) Supplements Instead of Iron-Folic Acid (IFA)

WHO’s policy still supports giving women IFA supplements during pregnancy. Replacing IFA
with multi-micronutrient (MMN) supplements will need to be balanced with the benefits of MMN over IFA and the costs. MMN supplements are three times more expensive than IFA supplements. See the Questions and Answers section for more information on giving MMN supplements instead of IFA.

Visit the UNICEF Supply Catalogue to view the costs of all commodities including IFA and MMN. Click on ?Pharmaceuticals? on the left to access cost information for both IFA and MMN. For IFA click on ?affecting blood? and then ?antianaemias.? For MMN click on ?minerals and vitamins.? Click here for information on how to improve IFA supplementation programs and integrate with other components of the integrated package to address anemia.

Resources:

- How Non Consumers Differ from Consumers: A Qualitative Approach to Synthesize the Attributes of Iron Folic Acid End Users

Introduction: Anaemia continues to be a major hurdle to achieve optimum health in Indian population context. Although government continues to promote Iron Folic Acid (IFA) supplementation as one of the key strategies to combat with burden of anaemia, the expected level of IFA consumption and subsequent anaemia reduction could not be achieved. This study tries to investigate those influences, concerns, experiences and behaviour from an end user perspective through a qualitative methodology which may affect the IFA consumption ambi-directionally.

Aim: To explore and understand the several aspects related with anaemia and IFA supplementation with special emphasis to reveal the contributory factors behind low level of IFA consumption at consumer end.

Materials and Methods: A community based qualitative study was conducted in clusters identified through multileveled stratification from a state of central India. A conceptual construct was made in priory for this study. As the research question was related with policy, this study adapted a framework technique for making interview topic guides. Two consumers and two non consumers from each identified cluster were interviewed in depth. The data obtained through 160 in depth interviews (from 80 consumers and 80 non consumers) was utilized for thematic framework, linkage association and to typify the phenomenon.

Results: Ignorance, difficult intake, meaninglessness, misconceptions and discontentment with the system were the major dimensions (sub themes) associated with discontinuation. All these sub themes were further converged into major theme of informational discontinuity. Investigators further typified the users/non users into persistent user, potential defaulters, impending defaulters and absolute non users.
Conclusion: Informational gap seems to be the fundamental factor behind sub optimum IFA consumption. On a policy perspective, all the attempts should be done to instigate arise felt need among target groups for IFA consumption.

Iron Supplementation in Predominantly Iron-Replete Populations: Is There an Emerging Concern?

The efficacy and safety of iron supplementation probably varies by population and context, and also depending on the proportion of anemia that is due to iron deficiency rather than other causes. Recent surveys showing a low prevalence of iron deficiency among non-pregnant WRA warrants further attention to the potential risks of iron supplementation in predominantly iron-replete populations.

Impact of Preconception Micronutrient Supplementation on Anemia and Iron Status during Pregnancy and Postpartum: A Randomized Controlled Trial in Rural Vietnam

Objective: Preconception micronutrient interventions may be a promising approach to reduce anemia and iron deficiency during pregnancy, but currently we have limited data to inform policies. We evaluated whether providing additional pre-pregnancy weekly iron-folic acid (IFA) or multiple micronutrient (MM) supplements compared to only folic acid (FA) improves iron status and anemia during pregnancy and early postpartum.

Methods: We conducted a double blind randomized controlled trial in which 5011 Vietnamese women were provided with weekly supplements containing either only 2800 ?g FA (control group), IFA (60 mg Fe and 2800 ?g FA) or MM (15 micronutrients with similar amounts of IFA). All women who became pregnant (n = 1813) in each of the 3 groups received daily IFA (60 mg Fe and 400 ?g FA) through delivery. Hematological indicators were assessed at baseline (pre-pregnancy), during pregnancy, 3 months post-partum, and in cord blood. Adjusted generalized linear models were applied to examine the impact of preconception supplementation on anemia and iron stores, using both intention to treat and per protocol analyses (women consumed supplements ? 26 weeks before conception).

Results: At baseline, 20% of women were anemic, but only 14% had low iron stores (ferritin <30 ?g/L) and 3% had iron deficiency (ferritin <12 ?g/L). The groups were balanced for baseline characteristics. Anemia prevalence increased during pregnancy and post-partum but was similar among intervention groups. In intention to treat analyses, prenatal ferritin was significantly higher among women receiving MM (geometric mean (?g/L) [95% CI]: 93.6
In per protocol analyses, women receiving MM or IFA had higher ferritin 3 months postpartum (MM 118.2 [109.3?127.8]), IFA 117.8 [108.7?127.7] vs control 101.5 [94.0?109.7]) and gave birth to infants with greater iron stores (MM 184.3 [176.1?192.9]), IFA 189.9 [181.6?198.3] vs control 175.1 [167.9?182.6]).

**Conclusion:** Preconception supplementation with MM or IFA resulted in modest increases in maternal and infant iron stores but did not impact anemia. Further research is needed to characterize the etiology of anemia in this population and identify effective interventions for reducing prenatal anemia.

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**Rang-Din Nutrition Study: Assessment of Participant Adherence to Lipid-Based Nutrient and Iron-Folic Acid Supplements among Pregnant and Lactating Women in the Context of a Study on the Effectiveness of Supplements in Bangladesh**

The Rang-Din Nutrition Study (RDNS) is a collaborative effort of the U.S. Agency for International Development (USAID)-funded Food and Nutrition Technical Assistance II and III Projects (FANTA); the University of California, Davis (UCD); the International Centre for Diarrhoeal Disease Research, Bangladesh (ICCDR,B); and the LAMB Project (formerly known as Lutheran Aid to Medicine in Bangladesh).

The objective of RDNS is to evaluate the effect of lipid-based nutrient supplements (LNS) provided to pregnant and lactating women (PLW) and their children on nutrition and health outcomes through a cluster-randomized, partially blinded effectiveness trial, which is being implemented in rural northwest Bangladesh. As part of the effectiveness trial, the research team is conducting a process evaluation (PE) to thoroughly evaluate the implementation of the community health and development program (CHDP) of LAMB. The CHDP provided PLW with either LNS designed for PLW (through 6 months postpartum), starting at the time the woman was identified as being pregnant (at or before 20 weeks gestation). The women’s children receive LNS-child, micronutrient powder (MNP), or no supplement, starting at 6 months of age and continuing until they are 24 months old.

According to the LAMB CHDP protocol, community health workers (CHWs) visited women monthly to distribute a month's supple of supplements. The CHWs provided standard messages regarding the supplements (Appendix 1). Women receiving LNS were advised to consume one supplement per day through 6 months postpartum and were told that it was best if they mixed it with rice. IFA recipients were advised to consume one tablet per day throughout pregnancy and one tablet every other day after the child was born until 3 months postpartum and were told to consume it with water between meals.
This report presents a summary of the findings of the RDNS process evaluation participant adherence among pregnant and lactating women (PEPA-PLW) assessment. The PEPA-PLW assessment aimed to evaluate several aspects of the LAMB CHDP supplement distribution to PLW, and specifically to assess adherence to the formulation of LNS being distributed at the time of the interview (LNS-regular) and IFA among women participating in the LAMB CHDP, with particular interest in assessing whether the type of supplement (LNS versus IFA) affects adherence and whether adherence to LNS is sustained through 6 months postpartum.

- **Kenya's Regional Community Health Worker Iron Folic Acid Supplementation Counseling Guides**

  This counseling guide is targeted to community health workers providing anemia prevention counseling to pregnant women and family members at the household level. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout their pregnancy. An English version is not available here, but you can refer to the English versions of "Kenya's IFA Supplementation Participant's Manual for Health Care Providers;" "Kenya's IFA Supplementation Trainer's Guide for Health Care Providers;" and "Kenya's Regional Health Care Provider IFA Supplementation Counseling Guides" to get an idea of the messages that are provided in this guide.

- **Kenya's Algorithm or Flow Chart for Counseling Women on Iron Folic Acid Supplementation**

  Algorithm or Flow Chart for Iron and Folic Acid Supplementation (IFAS) for pregnant and non pregnant women

- **Kenya's Regional Health Care Provider Iron Folic Acid Supplementation Counseling Guides**

  This dialogue guide or counseling guide is targeted to health care providers providing anemia prevention counseling to pregnant women and family members within a health facility. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout pregnancy. It is available here in three different versions representative of the three regions of Kenya (national, north eastern and the coast). For similar resources, see also "Kenya's IFA supplementation participants manual for health care providers" (in English); "Kenya's IFA supplementation trainer's guide for health care providers" (in English) and
Kenya's IFA supplementation counseling guide for community health workers" (in Kiswahili).

- **Kenya Poster 1: Promoting Iron Folic Acid Supplementation (Male Health Worker)**

  This poster was created for display in health facilities to help motivate health workers to "Give Complete and Accurate Information on Iron Folic Acid Supplements". This particular poster highlights four points a health worker should ensure they provide pregnant women regarding iron folic acid supplementation (IFAS): 1) Ensure that you counsel mothers on benefits of IFAS 2) Ensure you provide IFAS to all pregnant women regardless of their hb (hemoglobin) status 3) Ensure you provide complete dosage to be taken daily from conception to delivery and 4) Ensure you counsel pregnant mothers on managing side effects of IFAS.

- **Kenya Poster 2: Promoting Iron Folic Acid Supplementation (Female Health Worker)**

  This poster was created to help motivate health workers and for display in health facilities. The message is to "Be a champion; Give Pregnant Women the Chance to have a Healthy Pregnancy". It encourages the health worker to counsel and support pregnant women on the use of iron folic acid supplements (IFAS) and highlights the benefits of women taking them: 1) prevent anaemia 2) prevent risk of low birth weight 3) prevent unsafe pregnancy and complications during delivery.

- **Kenya Poster 3 (Regional): Promoting Iron Folic Acid Supplementation Targeting Pregnant Women (Kiswahili)**

  These three posters are targeted to pregnant women and intended to help raise awareness of the importance of pregnant women taking iron folic acid supplements (IFAS) during pregnancy. Each poster features a pregnant woman representative of one of three regions in Kenya (national, coastal and north east) and encourage pregnant women to take IFAS. Also attached is a word document with the English translation of these posters; all three posters include the same information.

The National Iron and Folic Acid Supplementation programme is guided by different Policy and National action frameworks. These policy documents include the Kenya Food and Nutrition Security Policy (2011) and the Kenya National Nutrition Action Plan (2011-2017). These documents provide a platform for National and County response to addressing Iron and Folic Acid deficiencies through, among other interventions, supplementation programmes. The Kenya National Health Policy (2012-2030) and the Kenya Health Sector Strategic Plan 2012-2017 provide clear policy objectives and strategies that are supportive of nutrition. The Constitution of Kenya guarantees that every person has the right to health, which includes healthcare services. The Government of Kenya developed the Vision 2030 as its new long-term development plan for the country. To improve the overall livelihoods of Kenyans, the country aims to provide an efficient integrated and high quality affordable health care system. Under the nutrition sector, the Health Strategy aims to strengthen collaboration in order to ensure adequate nutrition for the whole population, through avoiding and managing over or under nutrition and micronutrient deficiencies. Iron and Folic Acid Supplementation was made a flagship project under the MTP 11 under Vision 2030.

According to World Health Organization it is estimated that 41.8% of pregnant women worldwide are anaemic. In Kenya the most recent micronutrient survey in the country indicated the prevalence of anaemia among pregnant women to be 55.1% and 46.4% among non-pregnant women. Anaemia is the leading indirect cause of high maternal and neonatal deaths. Iron and Folic Acid Supplementation (IFAS) for pregnant women is one of the interventions that has been recommended by WHO and implemented by the Ministry of Health to reduce anaemia levels. IFAS has been implemented through Focused Antenatal Care (FANC) and although this is the case, there have been challenges which have resulted in sub-optimal IFAS coverage rates and very low adherence rates.

This strategy provides a road map that is aimed at improving ANC attendance and IFAS coverage and utilization rates among pregnant women in Kenya in alignment with National IFAS plan targets. We call upon all partners and stakeholders to collaborate and ensure good coordination in the implementation of IFAS interventions to improve the chances of maternal and child survival.

Kenya's Regional Iron Folic Acid Supplementation Calendars (Kiswahili)

Women report that forgetting to take IFA supplements is one of the main reasons they don’t take IFA. As part of its efforts to improve its IFA supplementation program and help women remember to take all their IFA, Kenya’s MOH has developed a calendar for pregnant women to record when they take IFA. These three iron folic acid (IFA) calendars each feature a pregnant woman representative of one of three regions in Kenya and aims to help remind women to take their IFA supplementation daily during their pregnancy. There is a calendar for each month of pregnancy as well as information reinforcing the importance of taking IFA supplements, coming regularly for ANC, sleeping under a mosquito net and eating a variety
of nutritious foods throughout pregnancy.

- **Kenya's Regional Pregnant Woman's Iron Folic Acid Information Leaflets (Kiswahili)**

  This informational booklet for pregnant women is offered in three versions representative of women from different regions of Kenya and is intended to guide pregnant women on iron folic acid supplementation (IFAS) during pregnancy. The leaflets are available in three versions: for national use, use in the coastal region of Kenya and in the north-eastern region of Kenya.

- **Kenya Poster 4: Promoting Iron Folic Acid Supplementation to Potential Mother (Kiswahili)**

  This poster is targeted to women of child-bearing age and features a young Kenyan woman. The message encourages women of child-bearing age to take folic acid before they become pregnant. A word document is attached for translation of these messages from Kiswahili into English.

- **Kenya Poster 5: Promoting Iron Folic Acid Supplementation for Healthy Families (Kiswahili)**

  This poster is primarily targeted to fathers or potential fathers as well as mothers and potential mothers. It features a healthy looking family of three and encourages pregnant women to take iron folic acid supplements (IFAS) during their pregnancy. Attached is a word document of the Kiswahili to English translation.


  IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focussed Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates. This training has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that
will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017. IFAS is one of the performance indicators for the Cabinet Secretary, Ministry of Health, with coverage targets set from a baseline of 8% to 25% improvement by June 2014. Therefore, this course is designed to be integrated into or be delivered as part of focused antenatal care training. It is designed for in service and refresher training, in continuing medical education sessions, on-job training and continuous professional development.

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About this Manual and Training Guide: IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focused Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates.

This manual is meant to go along with the IFAS Trainer's Guide and has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017.

Course Participants: This training is targeted to frontline ANC service providers, including health managers, nurses, nutritionists, and community strategy coordinators. The training module is competency-based and can be used to train health workers at a wide range of education levels such as diploma holders, certificate levels, degree holders, etc.

Training Approaches: This training approach is based on adult learning principles, that is, the belief that adults learn best in interactive sessions that include practice between the trainers and the trainees. Structured learning activities will be used including presentations, group discussions, demonstrations, role plays, and practical exercises.

The method of training recommended for use is Teach-back. This methodology is successful because it is based on adult learning principles, adults want training that is participatory, and they want to gain knowledge and skills applied to their jobs, they would like to share knowledge and experiences. The participants receive positive reinforcement and feedback about areas of weakness and practice teach-back training using the course content in a safe and supportive environment.

Instructions on Use: The IFAS course includes a Trainer's Guide and Participant Manual. The course follows a modular approach. It is divided into five independent modules that can stand alone or be combined into a 2 1/2 day package of instructional material, as needed. Each module is divided into sessions, which are further divided into topics. The learning objectives of each session are followed by materials needed, advance preparation, and
Anaemia, Prenatal Iron Use, and Risk of Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis

Objectives: To summarise evidence on the associations of maternal anaemia and prenatal iron use with maternal haemotological and adverse pregnancy outcomes; and to evaluate potential exposure relations of dose of iron, duration of use, and haemoglobin concentration in prenatal period with pregnancy outcomes.

Design: Systematic review and meta-analysis.

Data Sources: Searches of PubMed and Embase for studies published up to May 2012 and references of review articles.

Study Selection Criteria: Randomised trials of prenatal iron use and prospective cohort studies of prenatal anaemia; cross-sectional and case-control studies were excluded.

Results: 48 randomised trials (17,793 women) and 44 cohort studies (1,851,682 women) were included. Iron use increased maternal mean haemoglobin concentration by 4.59 (95% CI 3.72 to 5.46) g/L compared with controls and significantly reduced the risk of anaemia (relative risk 0.50, 0.42 to 0.59), iron deficiency (0.59, 0.46 to 0.79), iron deficiency anaemia (0.40, 0.26 to 0.60), and low birth weight (0.81, 0.71 to 0.93). The effect of iron on preterm birth was not significant (relative risk 0.84, 0.68 to 1.03). Analysis of cohort studies showed a significantly higher risk of low birth weight (adjusted odds ratio 1.29, 1.09 to 1.53) and preterm birth (1.21, 1.13 to 1.30) with anaemia in the first or second trimester. Exposure-response analysis indicated that for every 10 mg increase in iron dose/day, up to 66 mg/day, the relative risk of maternal anaemia was 0.88 (0.84 to 0.92) (P for linear trend<0.001). Duration of use was not significantly associated with the outcomes after adjustment for dose. Furthermore, for each 1 g/L increase in mean haemoglobin, birth weight increased by 14.0 (6.8 to 21.8) g (P for linear trend=0.002); however, mean haemoglobin was not associated with the risk of low birth weight and preterm birth. No evidence of a significant effect on duration of gestation, small for gestational age births, and birth length was noted.

Conclusions: Daily prenatal use of iron substantially improved birth weight in a linear dose-response fashion, probably leading to a reduction in risk of low birth weight. An improvement in prenatal mean haemoglobin concentration linearly increased birth weight.

Kenya's National Iron Folic Acid Policy Guideline
This is a poster size version of Kenya's National Policy Guideline on Combined Iron and Folic Acid (IFA) Supplementation for Pregnant Women in Kenya. This version of the policy is meant for display in a health care facility and serve as easy reference for health care providers. It includes information about the purpose of IFA supplementation, composition, dosage, duration, target group, administration, possible side effects and the recommended action to take if they occur.


The purpose of the 2012-2017 National Nutrition Action Plan (NNAP) is to provide a framework for coordinated implementation of nutrition intervention activities by the government and nutrition stakeholders. The Plan has been developed at a time when the government of Kenya is stepping up efforts to realize Millennium Development Goals through implementation of high impact Nutrition initiatives (HiNi). The HiNi include: exclusive breastfeeding, timely complementary feeding, iron folate, vitamin A and zinc supplementation, hand washing, deworming, food fortification and management of moderate and severe acute malnutrition. The NNAP was a collaborated effort of a task force through the supplementation sub-committee, compromised of members from the Division of Nutrition, Division of Child and Adolescent Health, Division of Reproductive Health, in the Ministry of Health (MoH) as well as multiple partners.

- **Relative Efficacy of Micronutrient Powders Versus Iron-Folic Acid Tablets in Controlling Anemia in Women in the Second Trimester of Pregnancy**

**Background:** Iron deficiency is a major cause of anemia and the most prevalent nutrient deficiency among pregnant women in developing countries. The use of iron and folic acid supplements to treat and prevent iron-deficiency anemia has limited effectiveness, mainly due to poor adherence. Home fortification with a micronutrient powder for pregnant women may be an effective and acceptable alternative to traditional drug models.

**Objective:** To determine whether home fortification with micronutrient powders is at least as efficacious as iron and folic acid tablets for improving hemoglobin concentration in pregnant women.

**Methods:** A cluster-randomized noninferiority trial was conducted in the rural subdistrict of Kaliganj in central Bangladesh. Pregnant women (gestational age 14-22 weeks, n=478), were recruited from 42 community-based Antenatal Care Centres. Each centre was randomly
allocated to receive either a micronutrient powder (containing iron, folic acid, vitamin C, and zinc) or iron and folic acid tablets. Changes in hemoglobin from baseline were compared across groups using a linear mixed-effects regression model.

**Results:** At enrollment, the overall prevalence of anemia was 45% (n = 213/478). After the intervention period, the mean hemoglobin concentrations among women receiving the micronutrient powder were not inferior to those among women receiving tablets (109.5 ± 12.9 vs. 112.0 ± 11.2 g/L; 95% CI, -0.757 to 5.716). Adherence to the micronutrient powder was lower than adherence to tablets (57.5 ± 22.5% vs. 76.0 ± 13.7%; 95% CI, -22.39 to -12.94); however, in both groups, increased adherence was positively correlated with hemoglobin concentration.

**Conclusions:** The micronutrient powder was at least as efficacious as the iron and folic acid tablets in controlling moderate to severe anemia during pregnancy.

- **Maternal Iron Status: Relation to Fetal Growth, Length of Gestation, and Iron Endowment of the Neonate**

  Anemia prevalence is highest in preschool children, women of reproductive age, and women who are pregnant. While the etiology of anemia is multifactorial, iron deficiency is the most commonly recognized nutritional cause. Observational studies imply that supplementation with iron or iron-folic acid should be started early in pregnancy, if not before, in order to prevent low-birth-weight and preterm delivery. Despite this, findings from clinical trials, even those conducted during early pregnancy, are equivocal. Recent follow-up studies of children born to women supplemented with iron-folic acid suggest that mortality is decreased and that the infant's iron endowment reflects the mother's iron status during pregnancy.

- **Oral Iron Supplements for Children in Malaria-Endemic Areas**

  Children commonly develop anaemia (low haemoglobin) after birth. Anaemia is associated with several ill effects, including hindering motor development and learning skills, and impaired immunity. Children are therefore commonly given iron supplements to prevent or treat anaemia. In countries where malaria is prevalent, it has been suggested that iron supplementation increases the risk of malaria and death. The high dose of iron which is given as medicine may result in free iron circulating in the blood and is made available to the malaria parasite, promoting its growth. We aimed to assess the effects of oral iron supplementation in children living in countries where malaria is prevalent. Iron did not increase the risk of malaria, indicated by fever and the presence of parasites in the blood. There was no increased risk of death among children treated with iron. Although it is hypothesized that iron supplementation might harm children who do not have anaemia...
because of the iron overload, we did not find an increased risk for malaria among non anaemic children. When iron was administered with folic acid (a vitamin necessary for DNA synthesis) one large trial suggested there was an increased risk of severe (lethal) malaria. When iron was administered in settings of poor malaria management there was an increased risk for malaria. Iron supplementation increased haemoglobin by about 1 g/dL in areas where malaria is highly prevalent. At the end of follow-up, which varied between two weeks and six months after the end of iron supplementation, the haemoglobin gain was smaller but still present at 0.4 g/dL. Iron did not increase the risk of respiratory infections or other infections. Children given iron visited medical clinics less than children given placebo, but the rate of hospitalization was similar. The children’s weight and height at the end of treatment were similar. Iron did not adversely affect the rates of cure when it was given together with antimalarial treatment in the three trials that examined this issue. Our conclusions are that iron supplementation (without folic acid) does not adversely affect children living in malaria-endemic areas. The evidence shown in our review is limited by the lack of trials examining the relevant outcomes and the limited information available, so that we were unable to fully analyse factors that could affect our results, such as the children’s baseline level of haemoglobin. Based on our review, routine iron supplementation should not be withheld from children living in countries where malaria is prevalent.

Considerations for the Safe and Effective Use of Iron Interventions in Areas of Malaria Burden - Executive Summary

Background: In 2006, the World Health Organization and the United Nations Children's Fund released a joint statement advising that, in regions where the prevalence of malaria and other infectious diseases is high, iron and folic acid supplementation should be limited to those who are identified as iron-deficient. Although precipitated, in large part, by a recent report of adverse events associated with iron supplementation in children, questions about the risk/benefit of iron deficiency and mechanisms underlying potential adverse effects of iron in the context of infection are long-standing. Moreover, the implementation of this revised policy is compromised in most settings by the lack of consensus on the best methods to screen for iron deficiency.

Methods: In response to these concerns a comprehensive review was conducted by a Technical Working Group (TWG), constituted by the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the U.S. National Institutes of Health, in partnership with the Bill and Melinda Gates Foundation. The review included an evaluation of the putative mechanisms associated with adverse effects of iron in the context of malaria; applicability of available biomarkers for assessing iron status in the context of infections; and evaluation of evidence with regard to the safety and effectiveness of available interventions to prevent iron deficiency, particularly in areas of endemic malaria. The aim of this paper is to summarize the technical details of the larger TWG review conclusion that the occurrence and mechanism(s) of adverse effects associated with providing iron supplements (i.e., pills/liquid)
under conditions of malaria and high infection exposure remain a concern, especially in settings where care and treatment are not readily available or accessible.

**Results:** Iron deficiency remains a problem that demands appropriate clinical care. When target groups have already been identified as being iron-deficient, iron supplementation is the intervention of choice for the treatment of anemia and other manifestations of iron deficiency. Of available intervention options to prevent iron deficiency, supplements are probably least desirable, particularly for infants and children.

**Conclusions:** This paper also provides a synopsis of the TWG responses to the recently published Cochrane Review on the safety of iron supplementation for children in the context of malaria, and a research agenda outlined by the TWG that can best address outstanding questions.

- **Guideline: Use of Multiple Micronutrient Powders for Home Fortification of Foods Consumed by Pregnant Women**

This guideline provides global, evidence-informed recommendations on the use of multiple micronutrient powders for home fortification of foods consumed by pregnant women. The guideline will help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Millennium Development Goals, in particular, the eradication of extreme poverty and hunger (MDG 1), reduction of child mortality (MDG 4) and improvement of maternal health (MDG 5). The guideline is intended for a wide audience including policy-makers, their expert advisers, and technical and programme staff at organizations involved in the design, implementation and scaling-up of nutrition actions for public health.

- **Multiple Micronutrient Powders for Home (Point of Use) Fortification of Foods in Pregnant Women: A Systematic Review**

Home (point of use) fortification of foods with multiple micronutrient powders consists of sprinkling a mixture of vitamins and minerals (which are supplied in powdered form in single-serving sachets) over any semi-solid food before consumption. Home fortification with multiple micronutrient powders of food consumed by pregnant women is being implemented in several countries, but its safety and effectiveness in relation to pregnancy outcomes has not been systematically evaluated. This review aimed to assess the effects and safety of antenatal home (point of use) fortification of foods with multiple micronutrient powders with regard to newborn and maternal health outcomes. Several databases, the Cochrane Central
Register of Controlled Trials (The Cochrane Library), MEDLINE, EMBASE, CINAHL EBSCO, POPLINE and LILACS, were searched for studies that fulfilled the inclusion criteria, with no language or publication time restrictions. The International Clinical Trials Registry Platform (ICTRP) was searched for ongoing studies and relevant organizations were also contacted. The inclusion criteria were as follows: (i) randomized (both individual and cluster randomization) and quasi-randomized trials, and prospective non-randomized trials, interrupted time series (with at least three points) and observational studies having a control group; (ii) study participants needed to be apparently healthy pregnant women; and (iii) the study should have aimed to compare home fortification of foods with multiple micronutrient powders (with at least three micronutrients, one of them being iron) with no intervention, iron-only supplements, iron and folic acid supplements, or the same multiple micronutrients in supplement form. Two review authors independently extracted data and assessed the quality of the trials potentially identified as suitable in the searches. However, no study satisfied the inclusion criteria, and the review concluded that despite the widespread implementation of interventions with multiple micronutrient powders, there have been no studies evaluating the effects of this intervention in pregnant women on maternal and newborn health outcomes. There is an urgent need for randomized controlled trials evaluating the effectiveness and safety of the use of multiple micronutrient powders in pregnant women to inform policy-making.

**Iron and Folic Acid Supplements and Reduced Early Neonatal Deaths in Indonesia**

**Objective:** Examine the impact of antenatal supplementation with multiple micronutrients or iron and folic acid compared with folic acid alone on birth weight, duration of gestation, and maternal haemoglobin concentration in the third trimester.

**Design:** Cluster randomised double blind controlled trial. Setting: Two rural counties in northwest China. Participants: 5828 pregnant women and 4697 live births. Interventions: Villages were randomised for all pregnant women to take either daily folic acid (control), iron with folic acid, or multiple micronutrients with a recommended allowance of 15 vitamins and minerals. Main outcome measures: Birth weight, length, and head circumference measured within 72 hours after delivery. Neonatal survival assessed at the six week follow-up visit.

**Results:** Birth weight was 42 g (95% confidence interval 7 to 78 g) higher in the multiple micronutrients group compared with the folic acid group. Duration of gestation was 0.23 weeks (0.10 to 0.36 weeks) longer in the iron-folic acid group and 0.19 weeks (0.06 to 0.32 weeks) longer in the multiple micronutrients group. Iron-folic acid was associated with a significantly reduced risk of early preterm delivery (34 weeks) (relative risk 0.50, 0.27 to 0.94, P=0.031). There was a significant increase in haemoglobin concentration in both iron-folic acid (5.0 g/l, 2.0 to 8.0 g/l, P=0.001) and multiple micronutrients (6.9 g/l, 4.1 to 9.6 g/l, P=0.001) groups compared with folic acid alone. In post hoc analyses there were no significant differences for perinatal mortality, but iron-folic acid was associated with a significantly
reduced early neonatal mortality by 54% (relative risk 0.46, 0.21 to 0.98).

**Conclusion**: In rural populations in China antenatal supplementation with iron-folic acid was associated with longer gestation and a reduction in early neonatal mortality compared with folic acid. Multiple micronutrients were associated with modestly increased birth weight compared with folic acid, but, despite this weight gain, there was no significant reduction in early neonatal mortality. Pregnant women in developing countries need sufficient doses of iron in nutrient supplements to maximize reductions in neonatal mortality.

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**Maternal Iron-Folic Acid Supplementation Programs: Evidence of Impact and Implementation**

**Background**: According to a World Health Organization (WHO) review of nationally representative surveys from 1993 to 2005, 42% of pregnant women have anemia worldwide. Almost 90% of anemic women reside in Africa or Asia. Most countries have policies and programs for prenatal iron-folic acid supplementation, but coverage remains low and little emphasis is placed on this intervention within efforts to strengthen antenatal care services. The evidence of the public health impact of iron-folic acid supplementation and documentation of the potential for scaling up have not been reviewed recently.

**Objective**: The purpose of this review is to examine the evidence regarding the impact on maternal mortality of iron-folic acid supplementation and the evidence for the effectiveness of this intervention in supplementation trials and large-scale programs.

**Methods**: The impact on mortality is reviewed from observational studies that were analyzed for the Global Burden of Disease Analysis in 2004. Reviews of iron-folic acid supplementation trials were analyzed by other researchers and are summarized. Data on anemia reduction from two large-scale national programs are presented, and factors responsible for high coverage with iron-folic acid supplementation are discussed.

**Results**: Iron-deficiency anemia underlies 115,000 maternal deaths per year. In Asia, anemia is the second highest cause of maternal mortality. Even mild and moderate anemia increase the risk of death in pregnant women. Iron-folic acid supplementation of pregnant women increases hemoglobin by 1.17 g/dL in developed countries and 1.13 g/dL in developing countries. The prevalence of maternal anemia can be reduced by one-third to one-half over a decade if action is taken to launch focused, large-scale programs that are based on lessons learned from countries with successful programs, such as Thailand and Nicaragua.

**Conclusions**: Iron-folic acid supplementation is an under-resourced, affordable intervention with substantial potential for contributing to Millennium Development Goal 5 (maternal mortality reduction) in countries where iron intakes among pregnant women are low and anemia prevalence is high. This can be achieved in the near term, as policies are already in place in most countries and iron-folic acid supplements are already in lists of essential drugs. What is needed is to systematically adopt lessons about how to strengthen demand and
**Multiple Micronutrient Supplementation During Pregnancy in Low-Income Countries: A Meta-Analysis of Effects on Stillbirths and on Early and Late Neonatal Mortality**

**Background:** Multiple micronutrient deficiencies are common among women in low-income countries and may adversely affect pregnancy outcomes.

**Objective:** To conduct a meta-analysis of the effects on stillbirths and on early and late neonatal mortality of supplementation during pregnancy with multiple micronutrients compared with iron-folic acid in recent randomized, controlled trials.

**Methods:** Twelve randomized, controlled trials were included in the analysis (Bangladesh; Burkina Faso; China; Guinea-Bissau; Indramayu and Lombok, Indonesia; Mexico; Sarlahi and Janakur, Nepal; Niger; Pakistan; and Zimbabwe), all providing approximately 1 recommended dietary allowance (RDA) of multiple micronutrients or iron-folic acid to presumed HIV-negative women.

**Results:** Supplementation providing approximately 1 RDA of multiple micronutrients did not decrease the risk of stillbirth (OR = 1.01; 95% CI, 0.88 to 1.16), early neonatal mortality (OR = 1.23; 95% CI, 0.95 to 1.59), late neonatal mortality (OR = 0.94; 95% CI, 0.73 to 1.23), or perinatal mortality (OR = 1.11; 95% CI, 0.93 to 1.33).

**Conclusions:** Our meta-analysis provides consistent evidence that supplementation providing approximately 1 RDA of multiple micronutrients during pregnancy does not result in any reduction in stillbirths or in early or late neonatal deaths compared with iron-folic acid alone.

**Treatment Response to Iron and Folic Acid Alone is the Same as with Multivitamins and/or Anthelmintics in Severely Anemic 6- to 24-Month-Old Children**

**Background:** We assessed the effectiveness of iron+folic acid for the treatment of severe anemia [hemoglobin (Hb) <70 g/L] and the efficacy of added multivitamins and/or anthelmintics among children aged 6-24 mo in periurban Karachi, Pakistan.

**Methods:** The study design was a double blind, placebo-controlled, randomized trial of currently recommended daily iron (25 mg) and folic acid (100 ?g) for 90 d with daily
multivitamins [vitamin A (300 ?g, as retinol palmitate), vitamin E (6 mg tocopherol equivalents), vitamin B-12 (0.9 ?g), vitamin C (15 mg), riboflavin (0.5 mg)] and/or anthelminthics (100 mg mebendazole twice daily for 3 d) compared with placebos.

**Results:** Treatment response was defined as reaching a Hb concentration ?100 g/L at the end of 90 d. The prevalence of severe anemia in the 9518 children screened was 5.7% and a total of 462 severely anemic children were enrolled in the study. Adherence to treatment was ?70% for iron+folic acid, ?80% for multivitamins, and almost 100% for mebendazole. Children receiving iron+folic acid alone had a response rate of 38.7% at 90 d. The additional treatment with mebendazole or multivitamins did not significantly improve cure rates or change the Hb concentration over and above iron+folic acid treatment alone. Adherence to iron+folic acid of higher than the median resulted in a better treatment response rate of 50%.

**Conclusions:** High-dose daily iron+folic acid performed as well as iron+folic acid with anthelminthics and multivitamins in the treatment of severe anemia in this setting. Higher adherence may be important in enhancing treatment impact.

* Treatment Response to Standard of Care for Severe Anemia in Pregnant Women and Effect of Multivitamins and Enhanced Anthelmintics

**Background:** Severe anemia (hemoglobin <70 g/L) in pregnancy may increase the risk of maternal and perinatal mortality.

**Objectives:** We assessed response to standard treatment with high-dose iron?folic acid for 90 d and single-dose (500 mg) mebendazole among severely anemic pregnant women in periurban Karachi, Pakistan. In addition, we evaluated the efficacy of 2 enhanced treatment regimens.

**Design:** We screened pregnant women (n = 6288) for severe anemia and provided them all with the standard treatment. To test the efficacy of 2 additional treatments, women were randomly assigned to standard treatment alone (control) or with 100 mg mebendazole twice daily for 3 d or 90 d of daily multivitamins or both using a 2 × 2 factorial design.

**Results:** Prevalence of severe anemia was high (10.5%) during pregnancy. Prevalence of geohelminths and malaria was low. Treatment response was defined as hemoglobin >100 g/L at the 90-d or >25 g/L at the 60-d follow-up visit. The standard-of-care treatment resulted in a response rate of 49% at follow-up, although an adherence of >85% elicited a higher response (67%). The effect of the additional treatments was weak. Although response was higher in the enhanced groups than for the standard treatment at the final assessment, the differences were not statistically significant. However, hemoglobin concentration increased significantly in all groups and was higher in the enhanced mebendazole group compared with the standard
Conclusions: Iron deficiency was high in this population, and the standard-of-care treatment resulted in a treatment response of 50%, although better treatment adherence showed a higher response. Multivitamins and the enhanced mebendazole regimen had a modest benefit over and above the standard treatment.

Impact of Multiple Micronutrient Versus Iron-Folic Acid Supplements on Maternal Anemia and Micronutrient Status in Pregnancy

Background: Multiple micronutrient supplements could increase hemoglobin and improve micronutrient status of pregnant women more than iron supplements alone or iron with folic acid.

Objective: To compare the effects of multiple micronutrients with those of iron supplements alone or iron with folic acid, on hemoglobin and micronutrient status of pregnant women.

Methods: Studies were identified in which pregnant women were randomized to treatment with multiple micronutrients, or with iron with or without folic acid. A pooled analysis was conducted to compare the effects of these supplements on maternal hemoglobin, anemia, and micronutrient status. Effect size was calculated for individual and combined studies, based on mean change from baseline to final measure in the group receiving iron, with or without folic acid, minus the mean change in the group, divided by the pooled standard deviation of the two groups. The effect on the relative risk of anemia or iron deficiency was calculated as the probability of anemia or iron deficiency in the group receiving multiple micronutrients divided by the probability in the group receiving iron, with or without folic acid.

Results: Multiple micronutrient supplements had the same impact on hemoglobin and iron status indicators as iron with or without folic acid. There was no overall effect on serum retinol or zinc. In the only study in which status of other micronutrients was analyzed, a high prevalence of multiple deficiencies persisted in the group receiving multiple micronutrients provided with daily recommended intakes of each nutrient.

Conclusions: Multiple micronutrient supplements increased hemoglobin synthesis to the same extent as supplementation with iron with or without folic acid, although often they contained lower amounts of iron. The amount of supplemental iron and other nutrients that can enable pregnant women with micronutrient deficiencies to achieve adequate status remains to be determined.

Multiple Micronutrients in Pregnancy and Lactation: An
Overview

This overview of multiple micronutrients during pregnancy and lactation emphasizes 2 relatively neglected issues. The first is that maternal micronutrient status in the periconceptional period, and throughout pregnancy and lactation, should be viewed as a continuum; too often these 3 stages are treated and discussed separately from both a scientific and a public health perspective. Iron and vitamin B-12 are included as examples to stress how status at conception affects maternal, fetal, and infant status and health until the child is weaned. The second issue is that while most attention has been focused on a few micronutrients, for example iron and folate as discussed elsewhere in this Supplement, multiple micronutrient deficiencies occur simultaneously when diets are poor. Some of these deserve more attention as causes of poor pregnancy outcome, including other B vitamin deficiencies that result in homocysteinemia, antioxidants, vitamin D, and iodine. In lactation, maternal status or intake of the B vitamins (except folate), vitamin A, selenium and iodine strongly affect the amount of these nutrients secreted in breast milk. This can result in the infant consuming substantially less than the recommended amounts and further depleting stores that were low at birth. While the optimal mode of meeting recommended micronutrient intakes is an adequate diet, in some situations supplementation is also important. Unfortunately, information is lacking on the optimal formulation of micronutrient supplements for pregnant women, and the need to continue these supplements during lactation is not recognized in many situations where maternal and infant health could benefit.

Iron Supplementation: Overcoming Technical and Practical Barriers

Iron supplementation is probably the best available option to effectively address iron deficiency in pregnant women and young children because it can be targeted specifically to these high-risk groups. However, technical and practical barriers exist: limited information on the effectiveness of supplementation interventions, side effects that affect compliance, and supply/distribution constraints. An innovative approach to addressing these constraints is the use of sprinkles of powdered, microencapsulated ferrous fumarate that can be added directly to any semi-liquid food without changing their taste or consistency. This technique has been tested in initial trials in Ghana and found to be as effective as iron drops. Another approach to improve the effectiveness of iron interventions is through information, education and communication (IEC) programs. These interventions can help modify consumer behavior in some cases, but in some countries, geographic location, variations in language and population size can make the cost of IEC programs very high. IEC strategies in Indonesia aimed at increasing demand for iron supplements by systematic dissemination of specific messages, improving the quality and variety of tablets, increasing the availability and access to supplements by engaging the commercial sector, enrolling traditional birth attendants and other community volunteers in selling supplements. Key issues to be addressed include clarifying optimal starting points and duration of supplementation interventions?based on
individual status or population prevalence, defining hemoglobin and ferritin cutoffs at which treatment should be instigated and evaluating the effectiveness of intermittent supplementation with multiple micronutrients.

- **Prevention and Control of Anemia: Thailand Experiences**

Thailand has addressed nutrition in national development policy since the mid-1970s, including efforts to reduce iron deficiency anemia. Nutritional improvement has been implemented as an integral part of primary health care and community development extending beyond government services to include community participation. Utilization of village health volunteers has been a crucial feature of the program. Available data indicate that anemia rates have declined among pregnant women and preschool children, although there has been no formal evaluation of the program effect. Universal iron supplementation has been the major strategy for pregnant women, using village health volunteers to encourage continuation of the antenatal care schedule and encouraging a preventive approach by health service providers. Program obstacles have included lack of access to iron tablets by some populations and lack of understanding of the importance of anemia. Women's compliance was complicated by fear of having a large fetus, forgetfulness and side effects. Weekly iron supplementation of school children was piloted in 2000, and is now being extended. Other strategies utilized to address iron deficiency include food fortification, dietary improvement and complementary public health measures. Program monitoring and evaluation require strengthening to assess the effectiveness of intervention strategies and provide proper data for decision-making.

- **The Role of Vitamins in the Prevention and Control of Anaemia**

**Objective:** While iron deficiency is regarded as the major cause of nutritional anaemia, changes in vitamins A, B12, C and E, folic acid and riboflavin status have also been linked to its development and control. This paper provides a systematic review of vitamin supplementation trials relating to the control of nutritional anaemia.

**Methods:** A MEDLINE search was used to find reports of vitamin supplementation trials that reported changes in anaemia or iron status.

**Results:** Vitamin A can improve haematological indicators and enhance the efficacy of iron supplementation. Both folate and vitamin B12 can cure and prevent megaloblastic anaemia. Riboflavin enhances the haematological response to iron, and its deficiency may account for a significant proportion of anaemia in many populations. Vitamin C enhances the absorption of dietary iron, although population-based data showing its efficacy in reducing anaemia or iron deficiency are lacking. Vitamin E supplementation given to preterm infants has not
reduced the severity of the anaemia of prematurity. Vitamin B6 effectively treats sideroblastic anaemia. Multivitamin supplementation may raise haemoglobin (Hb) concentration, but few studies have isolated the effect of multivitamins from iron on haematological status.

**Conclusions:** In general, the public health impact of vitamin supplementation in controlling anaemia is not clear. Neither are the complex interactions involving multiple vitamins in haematopoiesis sufficiently understood to explain the observed variability in haematological responses to vitamins by age, population, vitamin mixture and dosages. Further research is needed to understand the roles of individual and combined vitamin deficiencies on anaemia to design appropriate micronutrient interventions to prevent anaemia.

*The Potential Impact of Iron Supplementation during Adolescence on Iron Status in Pregnancy*

Iron deficiency anemia (IDA) during pregnancy is associated with significant morbidity for mothers and infants. Over 50% of pregnant women in developing countries suffer from IDA. It is also prevalent among adolescent girls because the growth spurt and onset of menstruation increase iron requirements. Women who conceive during or shortly after adolescence are likely to enter pregnancy with low or absent iron stores or IDA. Iron supplementation during adolescence is one of the new strategies advocated to improve iron balance in pregnancy. However, iron requirements are highest in the second and third trimesters and the model described here indicates that iron balance at this stage depends more on adequate intakes of bioavailable iron than on the size of the iron stores at conception. Furthermore, although supplementation will correct anemia and increase iron stores in girls, the positive effect on iron status will be temporary if their diets do not contain adequate bioavailable iron. Although iron status in early pregnancy may be improved if the period of supplementation continues up to the time of conception, supplementation before pregnancy should be viewed as an additional strategy to supplementation during the second and third trimesters.

*Antenatal Iron Supplementation as a Child Survival Strategy*


*Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia*

While the main focus of these guidelines is on iron supplementation programs and parasite
control, these guidelines acknowledge the beneficial role food fortification and dietary diversification can have in controlling iron deficiency anemia. Further information on these approaches can be found in other INACG documents as well as those of other organizations. It is hoped that these guidelines, which reflect our current state of knowledge, will be useful to those charged with planning and implementing iron supplementation programs. Please feel free to send your comments regarding these guidelines, so that they might be improved at a future date.

- The Effects of Iron Supplementation During Pregnancy, Given by Traditional Birth Attendants, on the Prevalence of Anaemia and Malaria

A randomized, double-blind, placebo-controlled community-based trial of oral iron supplementation (200 mg ferrous sulphate daily) administered to multigravid pregnant women by traditional birth attendants (TBAs) was carried out in a rural area of The Gambia. Iron supplementation led to a significant reduction in the prevalence of anaemia and of iron deficiency. Iron supplementation was not accompanied by increased susceptibility to malaria infection; there was no difference in the prevalence and severity of peripheral blood or placental malaria infection between the 2 groups of women. The birth weight of children born to women who received iron prophylaxis was increased by an average of 56 g. It is concluded that oral iron prophylaxis can be successfully delivered through TBAs integrated into a primary health care programme. This simple intervention can produce significant beneficial effects on the health of the mother without inducing increased susceptibility to malaria and has the potential for reducing perinatal mortality by increasing birth weight.

- MotherCare Indonesia Anemia Control Counseling Cards

- MotherCare Indonesia Iron Pill Reminder

This card is an easy to use reminder for pregnant/ postpartum women. A box is used to record each iron pill dosage, during 90 days of the pregnancy and 40 days postpartum.

- Qualitative Research Instrument on Perceptions of Anemia and Use of Iron Tablets?The Indramayu Project,
Indonesia

The following plan and research instrument was developed for the USAID-funded MotherCare/John Snow, Inc. Project by the Manoff Group. This plan and the research instrument were used in formative research for the Indramayu Project. One component of this project tested ways to improve the existing iron supplementation program for pregnant women. Social scientists from the Manoff Group gave technical assistance to this process by developing these instruments, training non-medical interviewers and analyzing the results. The results were used to develop messages for counseling women and a social marketing campaign, to train health workers and other delivering iron tablets and to identify and develop delivery mechanisms/strategies for the improved iron supplementation program.

Iron-Folic Acid Preventive and Treatment Doses

<table>
<thead>
<tr>
<th>Group</th>
<th>Iron Folic Acid Dose</th>
<th>Duration</th>
<th>Iron Folic Acid Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight infants (&lt;1000 grams)</td>
<td>3.5 mg iron/3 mg folic acid</td>
<td>5 months</td>
<td>7 mg iron/14 mg folic acid</td>
<td>5 months</td>
</tr>
<tr>
<td>6-23 months children</td>
<td>2 mg iron/0.5 mg folic acid</td>
<td>At least one dose in first 3 months</td>
<td>7 mg iron/2 mg folic acid</td>
<td>5 months</td>
</tr>
<tr>
<td>24-53 months children</td>
<td>2 mg iron/0.5 mg folic acid</td>
<td>At least one dose in first 3 months</td>
<td>3 months</td>
<td></td>
</tr>
<tr>
<td>School age children (&lt;15 years)</td>
<td>1,05 mg iron/1 mg folic acid</td>
<td>At least one dose in first 3 months</td>
<td>3 months</td>
<td></td>
</tr>
<tr>
<td>Adolescent/teenage females</td>
<td>3 mg iron/0.5 mg folic acid</td>
<td>At least one dose in first 3 months</td>
<td>3 months</td>
<td></td>
</tr>
</tbody>
</table>

Iron-Folic Acid Preventive and Treatment Doses

Resources:

- Effects of Different Regimens of Iron Prophylaxis on Maternal Iron Status and Pregnancy Outcome: A Randomized Control Trial
**Purpose:** Iron supplementation is associated with side effects and overload risk. We compared different regimens of iron supplementation on maternal hematological status and pregnancy outcome in a cohort of healthy pregnant women.

**Materials and methods:** Eighty non-anemic women with a normal singleton pregnancy were recruited at 11?13 weeks and randomized into controls (C; n?=20) and groups supplemented with ferrous iron 30?mg (FI; n?=20), liposomal iron 14?mg (Sideral® Pharmanutra, Pisa PI, Italy) (LI14; n?=20) and liposomal iron 28?mg/daily (LI28; n?=20) up to 6 weeks post-partum. Longitudinal maternal blood samples for iron markers were collected. Data on birth outcome were recorded. The treatment effect was evaluated using a mixed-effect regression model.

**Results:** Both LI28 and LI14 groups showed significantly higher hemoglobin and ferritin concentrations compared with controls. Birth weight showed a trend to increase with supplementation, resulting in higher birth weight in the LI28 group compared with controls (3499±464.1?g and 3092±469.5?g, respectively, p?less than?0.01).

**Conclusions:** Our data show the effectiveness of 28?mg and 14?mg LI on maternal anemia prevention, as previously reported with FI 40?mg. LI has similar effects of higher doses of ferrous iron on maternal hematological parameters, thus allowing to reduce iron doses and side effects.

**Kenya's Regional Iron Folic Acid Supplementation Calendars (Kiswahili)**

Women report that forgetting to take IFA supplements is one of the main reasons they don?t take IFA. As part of its efforts to improve its IFA supplementation program and help women remember to take all their IFA, Kenya's MOH has developed a calendar for pregnant women to record when they take IFA. These three iron folic acid (IFA) calendars each feature a pregnant woman representative of one of three regions in Kenya and aims to help remind women to take their IFA supplementation daily during their pregnancy. There is a calendar for each month of pregnancy as well as information reinforcing the importance of taking IFA supplements, coming regularly for ANC, sleeping under a mosquito net and eating a variety of nutritious foods throughout pregnancy.

**Coverage of IFA Supplements: USAID Priority Countries**
The Safety of Iron

As discussed in the Prevalence, Causes, and Consequences tab, iron is an important mineral for human health and helps to generate energy in the body and ensure optimal neuro-development. Most minerals, including iron, can be toxic if intake is excessive of the recommended daily intake. Unsupervised children in the United States have over-dosed on their mother’s prenatal iron supplements so messages should be given to women during antenatal care to keep IFA supplements out of the reach of young children (see Program Guidance tab).

Iron is sequestered in the liver as a protective mechanism during infection because, like humans, many micro-organisms also need iron to live and thrive. The amount of freely-circulating iron in the body, not stored iron, puts individuals at-risk of increased infection. However, freely-circulating iron is usually low because iron absorption in the gut is tightly controlled in most individuals. People with the genetic disorder called hereditary hemochromatosis do not have this control mechanism and are at risk of what is often called ‘iron-overload’. Some white males of Northern European descent also absorb too much iron. Enteral (injected) iron also can lead to high levels of freely circulating iron.

Currently, there is uncertainty about the safety of giving iron to young children in malaria endemic areas. This is not a new concern (Oppenheimer, 1986), although this concern was resolved for oral iron in the 1990s. The USAID-funded International Nutritional Anemia Consultative Group (INACG) reviewed the evidence of the safety of giving oral iron to several age groups (infants, preschool children, school-age children, adults, and pregnant women). They reviewed 13 trials and found a weak relationship between increased risk of several outcomes of malaria and giving iron, but significant reductions in anemia.
In 2006, a large study in Pemba, Zanzibar, where malaria transmission is high it was found that preschool children receiving iron and folic acid were at higher risk of hospitalization and mortality compared with infants receiving a placebo (Sazawal et al, 2006). However, in another study in rural Nepal, where malaria transmission is low, iron supplements did not cause increased morbidity or mortality (Tielsch et al, 2006). However, a sub-study in the Pemba study found that children with iron deficiency at the beginning of the study had no adverse outcomes when given iron and in fact benefited from receiving iron. The conclusion was that children who were iron replete (i.e., had adequate iron status) were the ones at risk from adverse outcomes when they received iron.

The study in Pemba and a consultation about the study findings led the World Health Organization (WHO, 2007) to recommend giving iron to iron-deficient children living in malaria-endemic regions. Because tests for iron deficiency and anemia are not available in most developing countries, WHO changed the recommendation and now advises on its website that children be given iron in conjunction with malaria prevention, diagnosis, and treatment programs. However, these recommendations continue to make it difficult to implement iron supplementation programs for young children that would help reduce the high burden of anemia because robust malaria control programs do not always exist. In the Africa region, where malaria and iron deficiency are both significant causes of anemia, anemia prevalence rates are over 70% in children 6-23 months in some countries.

In 2011, a symposium on giving iron to children was held at the annual meeting for the American Society for Nutrition. Click here to view the entire series of papers presented.

For more background information on this issue, read the overview by Harding et al, 2012. In the paper by Stoltzfus, 2012, practical recommendations are presented about giving iron where screening is not available:

- Iron status at birth is dependent on the size of the baby and the iron status of the mother?implement nutrition and health interventions (e.g., corticosteroids, IFA supplements, adequate food intake) to prevent preterm births and low birth weight; ensure total body iron at birth is optimal by through maternal IFA. supplements and delayed cord clamping which transfers iron from the mother to the infant at birth.

- Lower the dose of iron which will reduce the risk of morbidity but ensure children get some iron.

- Use food-based interventions such as giving iron in a micronutrient powder or fortified complementary food which will slow the absorption and reduce the dose of iron.

- Work to improve malaria control and treat malaria in young children.
Since the Pemba study, several analyses and studies have been conducted to add to the knowledge-base on the subject, although the findings do not clarify the situation and in some cases add to the confusion.

- In 2011, an updated Cochrane review of 68 trials found that iron supplementation alone or with anti-malaria treatment did not increase malaria risk or death with regular malaria surveillance and treatment programs in place. Trials that did not have active malaria surveillance showed a higher risk for clinical malaria among children receiving iron (Okebe et al, 2011). For a commentary on the first review see Roth et al, 2010.

- In 2012, in an area of Tanzania with high transmission of malaria, 785 children were enrolled at birth and monitored for parasitemia and illness, including malaria, for three years. Children who were iron-replete had significantly more malaria infection, morbidity, and mortality (Gwamaka et al, 2012).

- In 2013, a study in Pakistan was published (Soofi et al, 2013) that gave micronutrient powders with iron to children 6-18 months and found an increased proportion of days of diarrhea, increased incidence of bloody diarrhea, and increased reported chest-in-drawing. Incidence of febrile episodes, and admission to hospital for diarrhea, respiratory problems, and febrile episodes did not increase.

- The 2013 Lancet on Maternal and Child Nutrition examined studies on the benefit of giving iron to young children and found that in children younger than four years of age, there was evidence that iron deficiency affects motor development, but no consistent effect on mental development. The authors offer caveats their findings, however: the studies were complicated by the fact that there were only small improvements in iron status and may have been too short in duration which may have limited the effect.

**Final Words**

Sorting out the context in which iron can be given to children will need more research. Before those studies are conducted and synthesized, the following considerations should be taken into account:

- Disaggregate areas by high and moderate-low malaria transmission areas which may differ within countries.

- Implement widespread screening of children using clinical signs to identify those with severe anemia and get them treated for malaria or other infections along with receiving iron.

- Strengthen deworming programs for children starting at one year of age.

- Educate mothers on danger signs for malaria and other infections to ensure immediate treatment and to withhold iron on the days the child is sick.
Giving Folic Acid with IPTp-SP

The World Health Organization (WHO) recommends a dose of 60 mg of iron and 0.4 mg of folic acid during pregnancy, ideally in one combined supplement to make it easier for women to take IFA. Taking one pill instead of two improves women’s compliance with iron-folic acid (IFA) supplements. A dose of 0.4 mg of folic acid is sufficient to prevent anemia and meet increased requirements for folic acid during pregnancy. It also is a safe level of folic acid for administration with intermittent preventive treatment in pregnancy (IPTp) using sulfadoxine-pyrimethamine (SP). Because the malaria parasite needs folic acid to survive and thrive, a dose of 5 mg or more of folic acid reduces the effectiveness of SP as an antimalarial. The Roll Back Malaria Partnership Malaria in Pregnancy Working Group issued a Consensus Statement recommending a dose of folic acid of less than 5 mg per day during pregnancy. A new brief, developed by the Maternal and Child Survival Program (MCSP), the Centers for Disease Control, and the President’s Malaria Initiative (PMI), explains the importance of both IPTp-SP and IFA supplementation during pregnancy and why the dose of folic acid can and should be 0.4 mg per day, particularly when given in malaria endemic areas. Next steps for nutritionists:

- Work with malaria control program staff in country to ensure women are receiving the combined dose of iron folic acid with 60 mg of iron and 0.4 mg of folic acid.
- Reduce stores of the 5 mg dose of folic acid.
- Scale-up IPTp-SP and IFA supplementation to ensure that at least 80 percent of pregnant women in sub-Saharan Africa.
- Monitor the coverage and impact of the package of interventions to reduce anemia including IPTp, IFA, and deworming.

For additional reading and resources on this topic, click here.

Resources:

- Controlling Maternal Anemia and Malaria: Ensuring Pregnant Women Receive Effective Interventions to Prevent Malaria and Anemia: What Program Managers and Policymakers Should Know
This brief describes World Health Organization recommendations for IPTp to prevent malaria in pregnancy and iron-folic acid supplementation to prevent iron deficiency anemia in sub-Saharan Africa countries, with an emphasis on giving the correct dose of folic acid to maximize the effectiveness of interventions to prevent malaria. The brief is for program managers of health programs and policymakers to guide them in designing programs and developing policies.

- **Roll Back Malaria Partnership Malaria in Pregnancy Working Group: Consensus Statement on Folic Acid Supplementation during Pregnancy**

The Roll Back Malaria (RBM) Partnership Malaria in Pregnancy Working Group supports the following for all pregnant women living in sub-Saharan Africa:

- In malaria-endemic areas, intermittent preventive treatment using sulfadoxine-pyrimethamine (IPTp-SP) should be provided to pregnant women at each scheduled antenatal care (ANC) visit for protection against malaria. This should start early in the second trimester and continue until the time of delivery, with the doses given at least one month apart.

  - IPTp-SP has been shown to reduce maternal anemia, antenatal maternal parasitemia, low birthweight infants and neonatal deaths.

  - Co-trimoxazole provides some protection through its antimalarial activity; however, IPTp-SP should NOT be given to women who are taking daily co-trimoxazole prophylaxis (i.e. mainly those living with HIV) as this increases the risk of adverse events.

- Daily oral supplementation of 30-60 mg elemental iron and 400 µg (0.4 mg) folic acid should be provided as early as possible in pregnancy to meet iron and folic acid requirements. In cases where a combined folic acid-iron tablet is not available, a daily dose of 400 µg (0.4 mg) folic acid can be used separately.

  - There is evidence that high doses of folic acid (i.e. 5,000 µg or more) may interfere with the efficacy of sulfadoxine-pyrimethamine as an antimalarial. The higher 5,000 µg (5 mg) dose for pregnant women should be restricted for use in very specific clinical cases.

High doses of folic acid are not needed during low-risk pregnancies and may counteract the efficacy of both sulfadoxine-pyrimethamine and co-trimoxazole as antimalarials. The RBM Malaria in Pregnancy Working Group strongly advises that countries currently prioritize the procurement and distribution of the available combined dose of 400 µg (0.4 mg) folic acid plus 30-60 mg elemental iron as part of routine ANC. It also recommends that countries substantially reduce current stores and supplies of folic acid at a dose of 5,000 µg (5 mg) or higher at all facilities, as this dose should only be used for specific medical conditions as outline by the World Health Organization (WHO), and as indicated below in the answer to
Guideline: Daily Iron and Folic Acid Supplementation in Pregnant Women

It is estimated that 41.8% of pregnant women worldwide are anaemic. At least half of this anaemia burden is assumed to be due to iron deficiency. Member States have requested guidance from the World Health Organization (WHO) on the effectiveness and safety of daily iron and folic acid supplementation in pregnant women as a public health measure to improve pregnancy outcomes in support of their efforts to achieve the Millennium Development Goals.

WHO developed the present evidence-informed recommendations using the procedures outlined in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was followed to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

The guideline advisory group for nutrition interventions, the Nutrition Guidance Expert Advisory Group, comprises content experts, methodologists, representatives of potential stakeholders and consumers. These experts participated in several WHO technical consultations concerning this guideline, held in Geneva, Switzerland, and in Amman, Jordan, in 2010 and 2011. Members of the External Experts and Stakeholders Panel were identified through a public call for comments, and this panel was involved throughout the guideline development process. Guideline advisory group members voted on the strength of the recommendation, taking into consideration: (i) desirable and undesirable effects of this intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings. All the members of the guideline advisory group completed a Declaration of Interests Form before each meeting.

Daily oral iron and folic acid supplementation is recommended as part of the antenatal care to reduce the risk of low birth weight, maternal anaemia and iron deficiency (strong recommendation). The overall quality of the evidence for iron supplementation versus no iron was moderate for low birth weight, preterm birth, maternal anaemia at term and maternal iron deficiency at term. The evidence was of low quality for birth weight, neonatal death, congenital anomalies, maternal death, maternal severe anaemia, and infections during pregnancy; whereas it was of very low quality for side-effects.

Intermittent Iron and Folic Acid Supplementation in Non-
Anaemic Pregnant Women

It is estimated that 41.8% of pregnant women worldwide are anaemic. At least half of this anaemia burden is assumed to be due to iron deficiency. Member States have requested guidance from the World Health Organization (WHO) on the effectiveness and safety of different schemes of iron and folic acid supplementation in pregnant women as a public health measure to improve pregnancy outcomes in support of their efforts to achieve the Millennium Development Goals.

WHO developed the present evidence-informed recommendations using the procedures outlined in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

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Intermittent iron and folic acid supplementation is recommended in non-anaemic pregnant women to prevent development of anaemia and to improve gestational outcomes (strong recommendation). The quality of the evidence for low birth weight, birth weight, premature birth, maternal anaemia at term, iron deficiency at term, and side-effects was very low.

Use of Multiple Micronutrient Powders for Home Fortification of Foods Consumed by Infants and Children 6-23 Months of Age

It is estimated that 190 million preschool infants and children are affected by vitamin A
deficiency and 293 million children in the same age group have anaemia. Member States have requested guidance from the World Health Organization (WHO) on the effects and safety of the use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 months of age in support of their efforts to achieve the Millennium Development Goals.

WHO has developed the present evidence-informed recommendations using the procedures outlines in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

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Home fortification of foods with micronutrient powders containing at least iron, vitamin A and zinc is recommended to improve iron status and reduce anaemia among infants and children 6–23 months of age (strong recommendation). The overall quality of the evidence for iron deficiency was found to be high, whereas for anaemia, haemoglobin concentration, iron status and growth it was moderate. Ideally, interventions with multiple micronutrient powders should be implemented as part of a national infant and young child feeding programme.

Use of Multiple Micronutrient Powders for Home Fortification of Foods Consumed by Pregnant Women

It is estimated that 41.8% of pregnant women worldwide are anaemic. Approximately 60% of these cases in non-malarious areas, and 50% in malaria-endemic settings, are assumed to be due to iron deficiency. Vitamin and mineral deficiencies in pregnancy are associated with adverse health outcomes in both the mother and her newborn. Member States have requested guidance from the World Health Organization (WHO) on the effects and safety of multiple micronutrient powders for home fortification of foods consumed by pregnant women.
in support of their efforts to achieve the Millennium Development Goals.

WHO developed the present evidence-informed recommendations using the procedures outlined in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline.

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Currently, there is no evidence available to assess the potential benefits or harms of the use of multiple micronutrient powders for home fortification of foods consumed by pregnant women with regard to maternal and infant health outcomes. Thus the routine use of this intervention is not recommended as an alternative to iron and folic acid supplementation in pregnancy (strong recommendation).

**Interritten Iron and Folic Acid Supplementation in Menstruating Women**

Women of reproductive age are at increased risk of anaemia because of chronic iron depletion during the menstrual cycle. It is estimated that worldwide there are 469 anaemic women of reproductive age. At least half of the cases are attributed to iron-deficiency. Member States have requested guidance from the World Health Organization (WHO) on the effects and safety of intermittent supplementation with iron and folic acid in menstruating women as a public health measure to prevent anaemia in support of their efforts to achieve the Millennium Development Goals.

WHO developed the present evidence-informed recommendations using the procedures outlined in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and
Evaluation (GRADE) methodology was used to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

The guideline development group for nutrition interventions, the Nutrition Guidance Expert Advisory Group (NUGAG), comprises content experts, methodologists, representatives of potential stakeholders and consumers. These experts participated in several WHO technical consultations concerning this guideline, held in Geneva, Switzerland, and in Amman, Jordan, in 2010 and 2011. Members of the External Experts and Stakeholders Panel were identified through a public call for comments, and this panel was involved throughout the guideline development process. NUGAG members voted on the strength of the recommendation, taking into consideration: (i) desirable and undesirable effects of this intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings. All NUGAG members completed a Declaration of Interests Form before each meeting.

Intermittent iron and folic acid supplementation is recommended as a public health intervention in menstruating women living in settings where anaemia is highly prevalent, to improve their haemoglobin concentrations and iron status and reduce the risk of anaemia (strong recommendation). The overall quality of the evidence for anaemia, haemoglobin, iron deficiency and ferritin was found to be low for the comparison between intermittent iron supplementation and no intervention or placebo. When this intervention was compared with daily iron supplementation, the quality of the evidence for anaemia was moderate, low for haemoglobin and ferritin, and very low for iron deficiency.

Helminth Prevention and Control

What are Helminths?

Helminths or parasites, often called "worms", are widespread throughout the world. It is estimated that half of the world's population is infected with at least one helminth (Hall et al, 2008). Helminth prevention and control is an effective intervention to reduce anemia and should be integrated with other anemia control programs including iron-folic acid supplementation and malaria prevention and control.

There are over 340 species of helminths; most are rare in humans but may infect animals that can serve as a reservoir for infection. Click here for more information on common helminths affecting humans and the diseases they cause. The four main species of helminths that infect people are *Ascaris lumbricoides* (roundworm); *Trichuris trichiura* (whipworm); and *Necator americanus* and *Ancylostoma duodenale* (hookworm) (WHO, 2013). These four helminths also are commonly associated with malnutrition, including anemia, and disease in children (Hall et al, 2008). These worms are often called soil-transmitted helminths? which refers to their mode of transmission. Although they are not intestinal helminths, schistosomes (commonly called blood
flukes and bilharzia) also are prevalent and cause anemia in some geographic locations close to bodies of water.

**Helminth Transmission**

Helminths can be contracted by humans in various ways. Ingestion of contaminated feces through soil, water or food is a main mode of transmission. Hookworm is most commonly contracted directly through the soles of the feet, usually around open areas of defecation and latrines, when people do not wear shoes or food coverings. Schistosomiasis is contracted by swimming or wading in contaminated water.

Morbidity from helminth infections, including anemia, is determined by the intensity of the infection (number of worms in the gut) and the duration of the infection (Hall, 2008; Crompton et al, 1993). Moderate to heavy infections with hookworm are strongly associated with anemia (Hall, 2008; Roche et al, 1966).

**The Most Vulnerable Groups**

Preschool-aged children (ages 1-4) and pregnant women are the most affected by the consequences of helminth infections even though prevalence may be higher in other groups such as school-aged and all adults. Consequences of helminth infections include:

- Preschool children are at-risk of nutritional deficiencies caused by helminth infections. Helminths cause vitamin A malabsorption (Mahalanabis, 1976). In fact, deworming improves iron status in children and has improved growth in some studies.

- Pregnant women are at risk of nutritional deficiencies caused by helminth infections. Several large-scale studies have demonstrated that deworming and iron supplementation reduced anemia among pregnant women and have led to positive birth outcomes (Brooker, 2008; Smith, 2010).

School-aged children are mentioned here because school deworming programs have been an initiative globally. This group is particularly at risk of helminth infections because they are active and may be more inclined to play in the dirt and water. If a child is infected with helminths, their growth can be impaired, learning capacities diminished, and they are more susceptible to other infections. Making school-age children a target for deworming programs also may have may benefits for the entire population by reducing transmission in untreated students and other groups. For example, one study in Kenya found that when school-age children were dewormed in one school, untreated children in that school and in neighboring schools also benefited (Miguel et al, 2002).

**Helminth Treatment**
WHO recommends preventive doses of anthelminthic medication, treatment, and mass treatment depending on the prevalence of helminths. Click here for the drug doses for helminth prevention and treatment.

**Complementary Interventions**

Long-term solutions to controlling helminth infections are improving the quality of the water supply, sanitation, and hygiene (WASH). Education to ensure the safe and hygienic handling of human feces and wearing shoes in areas designated for defecation are effective measures in controlling transmission. Sanitation is key to the elimination of helminth infections. Soil transmitted helminths are common among school-aged children, with an estimated 50% of children five to nine years of age infected with helminths in developing countries. Much of this burden is due to poor sanitation and open defecation. Children can be treated for helminths but unless their living environments are clean, they will be reinfected. Improvements to WASH are essential for achieving sustained control of helminths in the medium- and long-terms.

**Resources:**

- **Investigations into the Association Between Soil-Transmitted Helminth Infections, Haemoglobin and Child Development Indices in Manufahi District, Timor-Leste**

**Background:** Timor-Leste has a high prevalence of soil-transmitted helminth (STH) infections. High proportions of the population have been reported as being anaemic, and extremely high proportions of children as stunted or wasted. There have been no published analyses of the contributions of STH to these morbidity outcomes in Timor-Leste.

**Methods:** Using baseline cross-sectional data from 24 communities (18 communities enrolled in a cluster randomised controlled trial, and identically-collected data from six additional communities), analyses of the association between STH infections and community haemoglobin and child development indices were undertaken. Stool samples were assessed for STH using qPCR and participant haemoglobin, heights and weights were measured. Questionnaires were administered to collect demographic and socioeconomic data. Intensity of infection was categorised using correlational analysis between qPCR quantification cycle values and eggs per gram of faeces equivalents, with algorithms generated from seeding experiments. Mixed-effects logistic and multinomial regression were used to assess the association between STH infection intensity classes and anaemia, and child stunting, wasting and underweight.

**Results:** Very high stunting (60%), underweight (60%), and wasting (20%) in children, but
low anaemia prevalence (15%), were found in the study communities. STH were not significantly associated with morbidity outcomes. Male children and those in the poorest socioeconomic quintile were significantly more likely to be moderately and severely stunted. Male children were significantly more likely than female children to be severely underweight. Increasing age was also a risk factor for being underweight. Few risk factors emerged for wasting in these analyses.

Conclusions: According to World Health Organization international reference standards, levels of child morbidity in this population constitute a public health emergency, although the international reference standards need to be critically evaluated for their applicability in Timor-Leste. Strategies to improve child development and morbidity outcomes, for example via nutrition and iron supplementation programmes, are recommended for these communities. Despite the apparent lack of an association from STH in driving anaemia, stunting, wasting and underweight, high endemicity suggests a need for STH control strategies.

Impact of Combined Intermittent Preventive Treatment of Malaria and Helminths on Anaemia, Sustained Attention, and Recall in Northern Ghanaian Schoolchildren

Background: The benefits of integrated control of malaria, schistosomiasis, and soil-transmitted helminth infections have not been fully explored in Ghanaian schoolchildren.

Objective: To assess the impact of co-administered artemether-lumefantrine plus albendazole, and artemether-lumefantrine plus albendazole plus praziquantel compared to albendazole plus praziquantel on anaemia, sustained attention, and recall in schoolchildren.

Design: This three-arm, open-label intervention study was carried out in Ghana among class three schoolchildren. Artemether-lumefantrine and albendazole were co-administered to 131 schoolchildren in Study Arm 1; artemether-lumefantrine, albendazole, and praziquantel to 90 children in Study Arm 2 versus albendazole and praziquantel to 127 children in Control Arm 3. Medicines were administered to all children at least 30 min after a meal. A HemoCue® photometer was used to measure haemoglobin (Hb), while the code transmission test (CTT), adapted from the Test of Everyday Attention for Children (TEA-Ch), was used to measure sustained attention and recall before-and-after interventions in June 2011 and June 2012.

Results: We observed significant malaria parasite prevalence reductions of 62.8 and 59.2% in Study Arm 1 from 24.2 to 9.0%, p <0.01, and 59.2% in Study Arm 2 from 26.7 to 10.9%, p <0.01), respectively, compared to 8.93% in Control Arm 3 (from 34.7 to 31.6%, p <0.05). Meanwhile, anaemia prevalence reduced significantly (p <0.01) in all three study arms after interventions by 38.4% (from 19.8 to 12.2%), 20.7% (from 26.6 to 21.1%), and 36.0% (from 28.3 to 18.1%) in Study Arms 1, 2, and 3, respectively. Although the interventions had no significant effects on Hb levels, anaemia prevalence reduced insignificantly by 38.4 and 20.7% in Study Arms 1 and 2, respectively, compared to 36.0% in Control Arm 3. Among
schoolchildren in Study Arms 1 and 2, mean CTT score improved significantly after interventions by 10.4% (from 3.18 to 3.55, p = 0.01) and 20.5% (from 2.83 to 3.56, p = 0.01) respectively, compared to 5.75% in Control Arm 3 (from 2.95 to 3.13, p = 0.09). Likewise, mean recall test score improvements after interventions were 16.9% (from 2.07 to 2.49, p = 0.01) and 27.9% (from 1.91 to 2.65, p = 0.01) in Study Arms 1 and 2, respectively, compared to 18.3% (from 1.92 to 2.35, p = 0.01) in Control Arm 3.

**Conclusion:** Combined intermittent preventive treatment of malaria and deworming reduced prevalence of anaemia and improved sustained attention and recall in schoolchildren. Best results for sustained attention and recall were seen in Study Arm 2.

- **Parasites - Soil-Transmitted Helminths (STHs)**

Soil-transmitted helminths refer to the intestinal worms infecting humans that are transmitted through contaminated soil (“helminth” means parasitic worm): *Ascaris lumbricoides* (sometimes called just "*Ascaris*"), whipworm (*Trichuris trichiura*), and hookworm (*Anclostoma duodenale* and *Necator americanus*).

- **Deworming Drugs for Soil-Transmitted Intestinal Worms in Children: Effects on Nutritional Indicators, Hemoglobin and School Performance**

The World Health Organization (WHO) recommends treating all school children at regular intervals with deworming drugs in areas where helminth infection is common. The WHO state this will improve nutritional status, haemoglobin, and cognition and thus will improve health, intellect, and school attendance. Consequently, it is claimed that school performance will improve, child mortality will decline, and economic productivity will increase. Given the important health and societal benefits attributed to this intervention, we sought to determine whether they are based on reliable evidence.

- **Deworming to Combat the Health and Nutritional Impact of Soil-Transmitted Helminths**
Soil-transmitted helminths, which include roundworms (Ascaris lumbricoides), whipworms (Trichuris trichiura) and hookworms (Necator americanus and Ancylostoma duodenale), are among the most common causes of infection in people who live in the developing world. WHO estimates that over 270 million preschool children and over 600 million school-age children are living in areas where these parasites are intensively transmitted, and are in need of treatment and preventive interventions.


Soil-transmitted helminthiases (STH) affect more than 2 billion people worldwide. In 2001, the World Health Assembly resolved to attain by 2010 a minimum target of regular administration of chemotherapy to at least 75% and up to 100% of all school-age children at risk of morbidity from the disease.

To achieve the target set by World Health Assembly Resolution WHA54.19, efforts must be intensified to eliminate STH as a public-health problem. In 2010, only about a third of children requiring treatment had access to anthelminthic medicines and two thirds had not been reached.

Eliminating soil-transmitted helminthiasis as a public health problem in children: progress report 2001-2010 and strategic plan 2011-2020 reports the progress made during the first 10 years of implementing control programmes, and identifies new opportunities and challenges for scaling up control activities. A timeline is proposed for achieving the 75% coverage target by 2020. The strategic plan sets out a dynamic approach to achieve the elements of Resolution WHA54.19 based on an evaluation of progress and an analysis of why the target has not been universally achieved. Identification of the problems that impede greater access to anthelminthic medicines is the key to proposing practical solutions that can be implemented within the context of preventive chemotherapy.

Anthelmintic Treatment During Pregnancy is Associated with Increased Risk of Infantile Eczema: Randomised-Controlled Trial Results

Background: Allergy is commoner in developed than in developing countries. Chronic worm infections show inverse associations with allergy, and prenatal exposures may be critical to allergy risk.
Objective: To determine whether anthelminthic treatment during pregnancy increases the risk of allergy in infancy.

Methods: A randomised, double-blind, placebo-controlled trial on treatment in pregnancy with albendazole versus placebo and praziquantel versus placebo was conducted in Uganda, with a 2 × 2 factorial design; 2507 women were enrolled; infants' allergy events were recorded prospectively. The main outcome was doctor-diagnosed infantile eczema.

Results: Worms were detected in 68% of women before treatment. Doctor-diagnosed infantile eczema incidence was 10.4/100 infant years. Maternal albendazole treatment was associated with a significantly increased risk of eczema [Cox HR (95% CI), p: 1.82 (1.26-2.64), 0.002]; this effect was slightly stronger among infants whose mothers had no albendazole-susceptible worms than among infants whose mothers had such worms, although this difference was not statistically significant. Praziquantel showed no effect overall but was associated with increased risk among infants of mothers with Schistosoma mansoni [2.65 (1.16-6.08), interaction p = 0.02]. In a sample of infants, skin prick test reactivity and allergen-specific IgE were both associated with doctor-diagnosed eczema, indicating atopic aetiology. Albendazole was also strongly associated with reported recurrent wheeze [1.58 (1.13-2.22), 0.008]; praziquantel showed no effect.

Conclusions: The detrimental effects of treatment suggest that exposure to maternal worm infections in utero may protect against eczema and wheeze in infancy. The results for albendazole are also consistent with a direct drug effect. Further studies are required to investigate mechanisms of these effects, possible benefits of worms or worm products in primary prevention of allergy, and the possibility that routine deworming during pregnancy may promote allergic disease in the offspring.

Impact of Hookworm Infection and Deworming on Anaemia in Non-Pregnant Populations: A Systematic Review

Objectives: To summarise age- and intensity-stratified associations between human hookworm infection and anaemia and to quantify the impact of treatment with the benzimidazoles, albendazole and mebendazole, on haemoglobin and anaemia in non-pregnant populations.

Methods: Electronic databases (MEDLINE, EMBASE, PubMed) were searched for relevant studies published between 1980 and 2009, regardless of language, and researchers contacted about potential data. Haemoglobin concentration (Hb) was compared between uninfected individuals and individuals harbouring hookworm infections of different intensities, expressed as standardised mean differences (SMD) and 95% confidence intervals (CI). Meta-analysis of randomised control trials (RCTs) investigated the impact of treatment on Hb and
anaemia.

Results: Twenty-three cross-sectional studies, six pre- and post-intervention studies and 14 trials were included. Among cross-sectional studies, moderate- and heavy-intensity hookworm infections were associated with lower Hb in school-aged children, while all levels of infection intensity were associated with lower Hb in adults. Among RCTs using albendazole, impact of treatment corresponded to a 1.89 g?l increase (95%CI: 0.13?3.63) in mean Hb while mebendazole had no impact. There was a positive impact of 2.37 g?l (95%CI: 1.33?3.50) on mean Hb when albendazole was co-administered with praziquantel, but no apparent additional benefit of treatment with benzimidazoles combined with iron supplementation. The mean impact of treatment with benzimidazoles alone on moderate anaemia was small (relative risk (RR) 0.87) with a larger effect when combined with praziquantel (RR 0.61).

- Monitoring Drug Coverage for Preventive Chemotherapy

In a drive to promote the control and reduction of morbidity attributable to lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiasis, the World Health Organization, through its Department of Control of Neglected Tropical Diseases, has developed a rapid-impact strategy known as preventive chemotherapy. This public health intervention depends on the integration and delivery of a tried and tested drug package. It may also form a component of the approach for the control and reduction of morbidity caused by trachoma known as SAFE (Surgery, Antibiotics, Facial cleanliness and Environmental improvement). How to plan and use preventive chemotherapy is explained in the manual Preventive chemotherapy in human helminthiasis, published by the Organization in 2006. Health professionals should note that preventive chemotherapy is one of the elements needed to overcome neglected tropical diseases; case management, health education, improved sanitation and clean water supplies are equally important.

- Treatment Response to Iron and Folic Acid Alone is the Same as with Multivitamins and/or Anthelmintics in Severely Anemic 6- to 24-Month-Old Children

Background: We assessed the effectiveness of iron+folic acid for the treatment of severe anemia [hemoglobin (Hb) <70 g/L] and the efficacy of added multivitamins and/or anthelmintics among children aged 6-24 mo in periurban Karachi, Pakistan.

Methods: The study design was a double blind, placebo-controlled, randomized trial of currently recommended daily iron (25 mg) and folic acid (100 ?g) for 90 d with daily multivitamins [vitamin A (300 ?g, as retinol palmitate), vitamin E (6 mg tocopherol equivalents), vitamin B-12 (0.9 ?g), vitamin C (15 mg), riboflavin (0.5 mg)] and/or
anthelmintics (100 mg mebendazole twice daily for 3 d) compared with placebos.

**Results:** Treatment response was defined as reaching a Hb concentration ≥100 g/L at the end of 90 d. The prevalence of severe anemia in the 9518 children screened was 5.7% and a total of 462 severely anemic children were enrolled in the study. Adherence to treatment was ≥70% for iron+folic acid, ≥80% for multivitamins, and almost 100% for mebendazole. Children receiving iron+folic acid alone had a response rate of 38.7% at 90 d. The additional treatment with mebendazole or multivitamins did not significantly improve cure rates or change the Hb concentration over and above iron+folic acid treatment alone. Adherence to iron+folic acid of higher than the median resulted in a better treatment response rate of 50%.

**Conclusions:** High-dose daily iron+folic acid performed as well as iron+folic acid with anthelmintics and multivitamins in the treatment of severe anemia in this setting. Higher adherence may be important in enhancing treatment impact.

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**Treatment Response to Standard of Care for Severe Anemia in Pregnant Women and Effect of Multivitamins and Enhanced Anthelmintics**

**Background:** Severe anemia (hemoglobin <70 g/L) in pregnancy may increase the risk of maternal and perinatal mortality.

**Objectives:** We assessed response to standard treatment with high-dose iron?folic acid for 90 d and single-dose (500 mg) mebendazole among severely anemic pregnant women in periurban Karachi, Pakistan. In addition, we evaluated the efficacy of 2 enhanced treatment regimens.

**Design:** We screened pregnant women (n = 6288) for severe anemia and provided them all with the standard treatment. To test the efficacy of 2 additional treatments, women were randomly assigned to standard treatment alone (control) or with 100 mg mebendazole twice daily for 3 d or 90 d of daily multivitamins or both using a 2 × 2 factorial design.

**Results:** Prevalence of severe anemia was high (10.5%) during pregnancy. Prevalence of geohelmiths and malaria was low. Treatment response was defined as hemoglobin >100 g/L at the 90-d or ≥25 g/L at the 60-d follow-up visit. The standard-of-care treatment resulted in a response rate of 49% at follow-up, although an adherence of ≥85% elicited a higher response (67%). The effect of the additional treatments was weak. Although response was higher in the enhanced groups than for the standard treatment at the final assessment, the differences were not statistically significant. However, hemoglobin concentration increased significantly in all groups and was higher in the enhanced mebendazole group compared with the standard group (P < 0.05).
Conclusions: Iron deficiency was high in this population, and the standard-of-care treatment resulted in a treatment response of 50%, although better treatment adherence showed a higher response. Multivitamins and the enhanced mebendazole regimen had a modest benefit over and above the standard treatment.

Polyparasite Helminth Infections and Their Association to Anaemia and Undernutrition in Northern Rwanda

Background: Intestinal schistosomiasis and soil-transmitted helminth (STH) infections constitute major public health problems in many parts of sub-Saharan Africa. In this study we examined the functional significance of such polyparasitic infections in anemia and undernutrition in Rwandan individuals.

Methods: Three polyparasitic infection profiles were defined, in addition to a reference profile that consisted of either no infections or low-intensity infection with only one of the focal parasite species. Logistic regression models were applied to data of 1,605 individuals from 6 schools in 2 districts of the Northern Province before chemotherapeutic treatment in order to correctly identify individuals who were at higher odds of being anaemic and/or undernourished.

Findings: Stunted relative to nonstunted, and males compared to females, were found to be at higher odds of being anaemic independently of polyparasite infection profile. The odds of being wasted were 2-fold greater for children with concurrent infection of at least 2 parasites at M+ intensity compared to those children with the reference profile. Males compared to females and anaemic compared to nonanaemic children were significantly more likely to be stunted. None of the three polyparasitic infection profiles were found to have significant effects on stunting.

Conclusion: The present data suggest that the levels of polyparasitism, and infection intensities in the Rwandan individuals examined here may be lower as compared to other recent similar epidemiological studies in different regions across sub-Saharan Africa. Neither the odds of anaemia nor the odds of stunting were found to be significantly different in the three-polyparasite infection profiles. However, the odds of wasting were higher in those children with at least two parasites at M+ intensity compared to those children with the reference profile. Nevertheless, despite the low morbidity levels indicated in the population under study here, we recommend sustainable efforts for the deworming of affected populations to be continued in order to support the economic development of the country.

Controlling Schistosomiasis: Significant Decrease of Anaemia Prevalence One Year after a Single Dose of
Praziquantel in Nigerien Schoolchildren

**Background:** In the framework of the monitoring and evaluation of the Nigerien schistosomiasis and soil-transmitted helminth control programme, a follow-up of children took place in eight sentinel sites. The objective of the study was to assess the evolution of Schistosoma haematobium infection and anaemia in schoolchildren after a single administration of praziquantel (PZQ) and albendazole.

**Methods/Principal Findings:** Pre-treatment examination and follow-up at one year post-treatment of schoolchildren aged 7, 8, and 11 years, including interview, urine examination, ultrasound examination of the urinary tract, and measurement of haemoglobin. Before treatment, the overall prevalence of S. haematobium infection was 75.4% of the 1,642 enrolled children, and 21.8% of children excreted more than 50 eggs/10 ml urine. Prevalence increased with age. The overall prevalence of anaemia (haemoglobin <11.5 g/dl) was 61.6%, decreasing significantly with increasing age. The mean haemoglobinemia was 11 g/dl. In bivariate analysis, anaemia was significantly more frequent in children infected with S. haematobium, although it was not correlated to the intensity of infection. Anaemia was also associated with micro-haematuria and to kidney distensions. In a sub-sample of 636 children tested for P. falciparum infection, anaemia was significantly more frequent in malaria-infected children. In multivariate analysis, significant predictors of anaemia were P. falciparum infection, kidney distension, and the village. One year after a single-dose praziquantel treatment (administered using the WHO PZQ dose pole) co-administered with albendazole (400 mg single dose) for de-worming, the prevalence of S. haematobium infection was 38%, while the prevalence of anaemia fell to 50.4%. The mean haemoglobinemia showed a statistically significant increase of 0.39 g/dl to reach 11.4 g/dl. Anaemia was no longer associated with S. haematobium or to P. falciparum infections, or to haematuria or ultrasound abnormalities of the urinary tract.

**Conclusions:** The high prevalence of anaemia in Nigerian children is clearly a result of many factors and not of schistosomiasis alone. Nevertheless, treatment of schistosomiasis and de-worming were followed by a partial, but significant, reduction of anaemia in schoolchildren, not explainable by any other obvious intervention.

**A Review and Meta-Analysis of the Impact of Intestinal Worms on Child Growth and Nutrition**

More than a half of the world's population are infected with one or more species of intestinal worms of which the nematodes *Ascaris lumbricoides*, *Trichuris trichiura* and the hookworms are the most common and important in terms of child health. This paper: (1) introduces the main species of intestinal worms with particular attention to intestinal nematodes; (2) examines how such worms may affect child growth and nutrition; (3) reviews the biological and epidemiological factors that influence the effects that worms can have on the growth and
nutrition of children; (4) considers the many factors that can affect the impact of treatment with anthelmintic drugs; (5) presents the results of a meta-analysis of studies of the effect of treating worm infections on child growth and nutrition; (6) discusses the results in terms of what is reasonable to expect that deworming alone can achieve; (7) describes some important characteristics of an ideal study of the effects of deworming; and (8) comments on the implications for programmes of recommendations concerning mass deworming.

Hookworm-Related Anaemia among Pregnant Women: A Systematic Review

**Background:** Hookworm infection is among the major causes of anaemia in poor communities, but its importance in causing maternal anaemia is poorly understood, and this has hampered effective lobbying for the inclusion of anthelmintic treatment in maternal health packages. We sought to review existing evidence on the role of hookworm as a risk factor for anaemia among pregnant women. We also estimate the number of hookworm infections in pregnant women in sub-Saharan Africa (SSA).

**Methods:** Structured searches using MEDLINE and EMBASE as well as manual searched of reference lists were conducted, and unpublished data were obtained by contacting authors. Papers were independently reviewed by two authors, and relevant data were extracted. We compared haemoglobin concentration (Hb) according to intensity of hookworm infection and calculated standardised mean differences and 95% confidence intervals. To estimate the number of pregnant women, we used population surfaces and a spatial model of hookworm prevalence.

**Findings:** One hundred and five reports were screened and 19 were eligible for inclusion: 13 cross-sectional studies, 2 randomised controlled trials, 2 non-randomised treatment trials and 2 observational studies. Comparing uninfected women and women lightly (1?1,999 eggs/gram [egp]) infected with hookworm, the standardised mean difference (SMD) was 20.24 (95% CI: 20.36 to 20.13). The SMD between women heavily (4000+ epg) infected and those lightly infected was 20.57 (95% CI: 20.87 to 20.26). All identified intervention studies showed a benefit of deworming for maternal or child health, but since a variety of outcomes measures were employed, quantitative evaluation was not possible. We estimate that 37.7 million women of reproductive age in SSA are infected with hookworm in 2005 and that approximately 6.9 million pregnant women are infected.

**Conclusions:** Evidence indicates that increasing hookworm infection intensity is associated with lower haemoglobin levels in pregnant women in poor countries. There are insufficient data to quantify the benefits of deworming, and further studies are warranted. Given that between a quarter and a third of pregnant women in SSA are infected with hookworm and at risk of preventable hookworm-related anaemia, efforts should be made to increase the coverage of anthelmintic treatment among pregnant women.
Associations between Mild-to-Moderate Anemia in Pregnancy and Helminth, Malaria and HIV Infection in Entebbe, Uganda

**Background:** It is suggested that helminths, particularly hookworm and schistosomiasis, may be important causes of anaemia in pregnancy.

**Methods:** We assessed the associations between mild-to-moderate anaemia (haemoglobin >8.0 g/dl and <11.2 g/dl) and helminths, malaria and HIV among 2507 otherwise healthy pregnant women at enrolment to a trial of deworming in pregnancy in Entebbe, Uganda.

**Results:** The prevalence of anaemia was 39.7%. The prevalence of hookworm was 44.5%, Mansonella perstans 21.3%, Schistosoma mansoni 18.3%, Strongyloides 12.3%, Trichuris 9.1%, Ascaris 2.3%, asymptomatic Plasmodium falciparum parasitaemia 10.9% and HIV 11.9%. Anaemia showed little association with the presence of any helminth, but showed a strong association with malaria (adjusted odds ratio (AOR) 3.22, 95% CI 2.43?4.26) and HIV (AOR 2.46, 95% CI 1.90?3.19). There was a weak association between anaemia and increasing hookworm infection intensity.

**Conclusions:** Thus, although highly prevalent, helminths showed little association with mild-to-moderate anaemia in this population, but HIV and malaria both showed a strong association. This result may relate to relatively good nutrition and low helminth infection intensity. These findings are pertinent to estimating the disease burden of helminths and other infections in pregnancy.

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**Effect of Administration of Intestinal Anthelmintic Drugs on Haemoglobin: Systematic Review of Randomised Controlled Trials**

**Objective:** To evaluate the effect of routine administration of intestinal anthelmintic drugs on haemoglobin.

**Design:** Systematic review of randomised controlled trials.

**Data Sources:** Electronic databases and hand search of reviews, bibliographies of books, and abstracts and proceedings of international conferences.

**Study Selection:** Included studies were randomised or quasi-randomised controlled trials using an intestinal anthelmintic agent in the intervention group, in which haemoglobin was evaluated as an outcome measure. Trials in which treatment for schistosoma (praziquantel)
was given exclusively to the intervention group were excluded.

**Results:** The search identified 14 eligible randomised controlled trials. Data were available for 7829 subjects, of whom 4107 received an anthelmintic drug and 3722 received placebo. The pooled weighted mean difference (random effect model) of the change in haemoglobin was 1.71 (95% confidence interval 0.70 to 2.73) g/l (P<0.001; test for heterogeneity: Cochran Q=51.17, P<0.001; I²=61% (37% to 76%)). With the World Health Organization's recommended haemoglobin cut-offs of 120 g/l in adults and 11 g/l in children, the average estimated reduction in prevalence of anaemia ranged from 1.1% to 12.4% in adults and from 4.4% to 21.0% in children. The estimated reductions in the prevalence of anaemia increased with lower haemoglobin cut-offs used to define anaemia.

**Conclusions:** Routine administration of intestinal anthelmintic agents results in a marginal increase in haemoglobin (1.71 g/l), which could translate on a public health scale into a small (5% to 10%) reduction in the prevalence of anaemia in populations with a relatively high prevalence of intestinal helminthiasis.

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**Lack of Risk of Adverse Birth Outcomes after Deworming in Pregnant Women**

**Background:** Pregnant women who live in hookworm-endemic areas may benefit from deworming during their pregnancy. The benefit derives from reducing anemia, primarily iron-deficiency anemia caused by hookworm infection-attributable blood loss. Where the prevalence of hookworm is more than 20% to 30%, the World Health Organization recommends that pregnant women receive anthelminthic treatment (mebendazole, albendazole, levamisole or pyrantel) after their first trimester. The objective of this study is to report, describe and compare the occurrence of adverse birth outcomes in a large randomized, controlled trial of antenatal mebendazole (500 mg single dose) plus iron supplements versus placebo plus iron supplements conducted between April 2003 and June 2004 in the Amazon region of Peru.

**Methods:** Physician-recorded data on adverse birth outcomes occurring during the trial (N = 1042) were obtained. Proportions were compared using chi analysis.

**Results:** No statistically significant difference (P = 0.664) was found between the mebendazole group and the placebo group in terms of numbers of miscarriages, malformations, stillbirths, early neonatal deaths and premature babies (28 versus 31, respectively).

**Conclusions:** The evidence provided by this large randomized, controlled trial of mebendazole administered during pregnancy indicates that deworming with mebendazole can be safely included in antenatal care programs in hookworm-endemic areas.
Antenatal Anthelmintic Treatment, Birthweight, and Infant Survival in Rural Nepal

Anthelmintic treatment, which is recommended during pregnancy in areas where there is a high rate of anaemia, needs further investigation. We examined prospectively the association between anthelmintic treatment and maternal anaemia, birthweight, and infant mortality in a study of prenatal supplements, in which women received albendazole twice during pregnancy. Women given albendazole in the second trimester of pregnancy had a lower rate of severe anaemia during the third trimester. Birthweight of infants of women who had received two doses of albendazole rose by 59 g (95% CI 19-98), and infant mortality at 6 months fell by 41% (RR 0.59; 95% CI 0.43-0.82). Antenatal anthelmintics could be effective in reducing maternal anaemia and improving birthweight and infant survival in hookworm-endemic regions.

How to Add Deworming to Vitamin A Distribution

This manual is written for health planners and aims to promote the deworming of preschool children where vitamin A distribution campaigns are conducted. In this manual, preschool children are defined as all children older than 1 year who are not yet attending school.

Attention is focused on this group because while school-age children (classified from the age of around 6 years onwards) are normally dewormed through school health programmes, preschool children are often not reached by deworming interventions.

In recognition of the constant demands made on health planners to prioritize health interventions, often with limited financial and human resources, this manual describes some of the advantages of combining two programmes which are often delivered separately: vitamin A distribution and deworming.

The manual is divided into three main sections that describe:

- The benefits of deworming preschool children;
- Practical information about deworming drugs;
- Experiences from three countries where deworming has been added to existing vitamin A distribution programmes.

Albendazole Therapy and Reduced Decline in Haemoglobin Concentration during Pregnancy (Sierra Leone)
**Background:** WHO recommends that anthelmintic treatment be included in strategies to improve maternal nutrition in areas where hookworms are endemic and anaemia is prevalent. At present, few countries have adopted this recommendation, partly owing to the lack of data to support the adverse effects of hookworms on maternal health.

**Methods:** A longitudinal study was conducted on 125 women in Sierra Leone (in 1995/96) to measure the impact of single-dose albendazole (400 mg) and daily iron-folate supplements (36 mg iron and 5 mg folate) on haemoglobin and serum ferritin concentration during pregnancy.

**Results:** Women who received both albendazole and iron-folate supplements experienced no significant change (P > 0.05) in the prevalence of anaemia and iron-deficiency anaemia between the first and third trimesters. These prevalence levels significantly increased (P < 0.05) in women who received either albendazole or iron-folate supplements or neither. After controlling for baseline haemoglobin concentration and season, the mean decline in haemoglobin concentration between the first and third trimester in women who received albendazole was 6.6 g/L less than in women who received the control (P = 0.0034). The corresponding value for iron-folate supplements was 13.7 g/L haemoglobin (P < 0.001).

**Conclusions:** The effects of albendazole and iron-folate supplements were additive. These findings lend support to WHO's recommendation for anthelmintic treatment during pregnancy.

- **Anthelmintic Treatment and Haemoglobin Concentrations During Pregnancy**

  A longitudinal study was conducted in Sierra Leone to measure the impact of a single dose anthelminthic (400 mg albendazole) and daily iron-folate supplements (36 g iron and 5 mg folate) on haemoglobin (HG) concentration during pregnancy. After controlling for baseline Hb concentration and season, the mean benefit of anthelmintic treatment, relative to the control, on the change in haemoglobin concentration between baseline and the third trimester was 6.6 g/L Hb (p=0.0034). The corresponding value for iron-folate supplements was 13.7 g/L Hb (p<0.0001). These findings indicate that anthelminthic treatment should be included in strategies to control maternal anaemia in Sierra Leone.

- **Hookworm Control as a Strategy to Prevent Iron Deficiency**

  The hookworms *Necator americanus* and *Ancylostoma duodenale* infect approximately 1 billion people worldwide. The prevalence of hookworm infection increases with age in children, typically reaching a plateau in late adolescence, whereas the intensity of infection
may continue to increase throughout adulthood. Hookworms cause intestinal blood loss in amounts proportional to the number of adult worms in the gut. The relationship between hookworm infection intensity and hemoglobin concentration is evident in epidemiologic studies, but may be apparent only above a threshold worm burden that is related to the iron stores of the population. Current hookworm control efforts are focused on reducing infection load and transmission potential through periodic anthelmintic chemotherapy. Several controlled trials have demonstrated a positive impact of anthelmintic treatment on hemoglobin levels, with best results obtained in settings where iron intakes were also increased. Evidence suggests that anthelmintic programs will have modest impacts on iron deficiency anemia in the short term, with greater impacts on more severe anemia. Hookworms are an important cause of anemia in women, who are often overlooked by current helminth control programs. Current WHO recommendations for use anthelmintics in schoolchildren and women are reviewed. There is a need to clarify whether hookworms are an important etiology of iron deficiency anemia in preschool children.

**Evaluation of Effectiveness of Iron-Folate Supplementation and Anthelmintic Therapy against Anemia in Pregnancy: A Study in the Plantation Sector of Sri Lanka**

**Background:** Intervention measures against anemia available to plantation workers during pregnancy include fortified food supplements (thriposha) and iron-folate supplements containing 60 mg elemental Fe.

**Methods:** The effectiveness of these intervention measures was studied in 195 subjects whose iron and nutritional status were assessed at < 24 and > 32 wk of gestation. Taking thriposha conferred no significant benefit on maternal nutritional status, probably because sufficient amounts were not consumed.

**Results:** An increase in the duration of iron-folate supplementation to > 17 wk caused a significant positive change (P < 0.01) in hemoglobin, whereas an increase in the dose frequency had no significant benefit. Anthelminthic therapy in addition to iron-folate supplements caused a significant positive change in hemoglobin (P < 0.001) and serum ferritin (P < 0.005) compared with no supplementation.

**Conclusions:** Thus, anthelminthic therapy significantly increased the beneficial effects of iron supplementation on hemoglobin concentration and iron status.

**Hookworm Infections and Human Iron Metabolism**
Ancylostoma duodenale and Necator americanus are extremely common species of soil-transmitted helminth which flourish where poverty and malnutrition prevail. Hookworms contribute significantly to iron-deficiency anaemia, which remains one of the world's major nutritional problems, through the feeding activities of intestinal stages leading to chronic blood loss into the gut. In this article, a mathematical model is proposed to explain how human iron metabolism may respond to hookworm infection of varying intensity. The model draws attention to the importance of the regulation of stored iron levels in the process. The results from the model are presented for the effects of hookworm infection on the iron metabolism of a healthy adult male. Calculations are also presented in which the effects of hookworms on the iron metabolism of a non-pregnant woman are compared with those of a pregnant woman. Use of the model may help develop a better understanding of the pathology of hookworm disease.

Nature and Causes of Hookworm Anemia

A number of studies have shown the prevalence of anemia in tropical areas--in great majority of the iron deficiency type--to be staggering; and it is probable that lack of iron is even more wide spread than figures for circulating hemoglobin would indicate, if the rate of intestinal absorption for this substance can be taken as an early indication of its want. Yet the reasons for the wide distribution of iron deficiency are not clearly known: in affected areas, often iron ingestion is relatively high, hookworm infections may be of low intensity, and there are no other obvious avenues of iron loss. More information of a quantitative nature on the subject of iron metabolism in the tropics and its relation with anemia and hookworm was clearly needed, and, in 1955, we began measuring, in Venezuelan rural populations, chiefly by means of radioactive isotopes, various factors which influence the utilization and loss of iron. The present work is an attempt to bring together the studies done thus far. We have centered the review around hookworm because, at least in the Venezuelan context, it has emerged by far as the most important single cause of iron loss, and we suspect that this may be so in many other tropical areas of the world. The conclusions reached on such a geographic disease as hookworm infection are naturally colored by the authors' personal experience with the particular conditions of nutrition, climate and customs prevailing in the particular areas under study. We have attempted however, to correlate our experience with that of other workers in the field, by reviewing critically what we judged to be the pertinent literature. Without anticipating too much of the substance of the monograph, two factors may be said to lie at the heart of the problem: a chronic drain of blood produced by the hookworm--whose order of magnitude we now know--and the relative unavailability for absorption of what would often seem an adequate supply of food iron?hunger in the midst of plenty. That in some cases the robbing of the host's blood by the worm may be compensated for by food iron is no reason for belittling the role of the parasite, as some are wont to do. This point of view is not unlike that of a bank president who, rather than firing a dis honest teller who every day pockets some of the organization's money, chooses to replace the daily loss from a special fund. The present data, which might help shape up practical policy from a public health standpoint, give us, in addition, certain vistas of an interesting aspect of the disease:
host-parasite relationship, or the manner in which the parasite influences its host (of which we now know a good deal, because of our naturally anthropocentric interest), or the host its parasite (of which we know but little). It lies not within the scope of this work to speak of solutions, but the liberty afforded by the style of a preface permits some lines for a pressing appeal. Some of the remedies--vermifuges, the wearing of shoes--have been known for many years, and yet hookworm remains rampant, producing, we believe, enormous misery and suffering. If Norman Stoll's estimate is still valid, more than 600 million people on earth are infected by hookworm. Proper education and housing, and a general rise in the standard of living would help. But to this end are needed social changes, which do not depend directly upon those who, like ourselves, describe in detail some of the ills. If the work discussed here can provide even a small bit of the leaven required for such changes, we shall rest happy.

Common Helminths in Humans

<table>
<thead>
<tr>
<th>Types of disease caused by some helminths and the most common helminths affecting humans</th>
</tr>
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<tbody>
<tr>
<td><strong>Intestinal Types</strong></td>
</tr>
<tr>
<td>Ceasodes (tapeworms)</td>
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<tr>
<td></td>
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<td></td>
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</tbody>
</table>

Most common species of worms affecting humans:

- Ascaris lumbricoides (roundworm)
- Trichinella spiralis (roundworm)
- Necator americanus (hookworm)
- Ancylostoma duodenale (hookworm)

Estimating Doses of Praziquantel

Use of a Tablet Pole for Determining the Correct Dose of Praziquantel

Praziquantel (also known as Biltricide) is the drug given to children for treatment of schistosomiasis. The dose of praziquantel for each child depends on their weight? 40mg of praziquantel per kg of body weight. Since weight and height are related, height can be used instead of weight to find the correct dose of praziquantel for each child.

Height poles (tablet poles), developed by Partnership for Child and Development, are constructed of straight lengths of hardwood to measure the height of each child. The poles are marked to show the correct number of praziquantel tablets, to the nearest half tablet, that should be given to each child, depending on their height.
Height pole consisting of five height intervals and the dosage of praziquantel (in tablets) assigned to each height interval.

<table>
<thead>
<tr>
<th>Height Interval</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>279 cm</td>
</tr>
<tr>
<td>5</td>
<td>250 cm</td>
</tr>
<tr>
<td>1½</td>
<td>225 cm</td>
</tr>
<tr>
<td>2</td>
<td>200 cm</td>
</tr>
<tr>
<td>1½</td>
<td>175 cm</td>
</tr>
</tbody>
</table>

Using the Tablet Pole

1. The pole should be held upright on a flat surface. If necessary, flatten the ground and then hold the pole on a large flat piece of wood. One way to make sure that the pole is held upright is to hold it near to a piece of string that has a weight attached to one end, and the other end tied to a roof beam or tree branch, making a plumb line. This can be used to judge whether the Tablet Pole is upright.

2. For each child to be treated, ask them to stand so that their spine is against the face of the pole on which the number of tablets is written. Put the child’s feet together so that they touch the base of the pole. The child should stand upright, looking straight ahead.

3. Place a ruler on the child’s head and press down the hair so that the ruler is flat against the skull. Make sure that the ruler is level and makes an angle of 90 degrees with the height pole. Read the number of tablets that the child needs from the pole. If the ruler exactly touches the line between two doses of tablets (e.g., on the line between 1½ and 2), then give the higher dose of tablets. If children are taller than the markings on the pole for the highest dose of tablets, they should be referred to a clinic, for determining the correct dose of praziquantel.

Prevention and Treatment for All Groups

<table>
<thead>
<tr>
<th>Helminth Prevention and Treatment Doses for Pregnant Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment routine: oral praziquantel (400 mg) daily for three consecutive days. The following table shows the treatment doses for pregnant women in the third trimester of pregnancy.</td>
</tr>
<tr>
<td>Dose</td>
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<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Albendazole</td>
</tr>
<tr>
<td>Mebendazole</td>
</tr>
<tr>
<td>Ivermectin</td>
</tr>
<tr>
<td>Praziquantel</td>
</tr>
</tbody>
</table>

Malaria Prevention and Control

What is Malaria?

Malaria is transmitted to humans by infected mosquitoes that carry a parasite called *Plasmodium*. Malaria parasites infect the liver and red blood cells, leading to their dysfunction and destruction. Malaria reduces the number of red blood cells in the body, which results in anemia.

*Plasmodium falciparum* is the most life-threatening type of malaria, with greatest prevalence in Sub-Saharan Africa. *Plasmodium vivax* is another type of malaria which is less dangerous than *Plasmodium falciparum*, although it is more widespread across regions. The symptoms of malaria are fever and headache. Severe cases put individuals at high risk of dying.

Where is Malaria Found, and How Many People are Affected?

Malaria is a widespread problem in tropical and subtropical regions generally around the equator. In 2010, there were an estimated 219 million cases of malaria, with 80% of these cases occurring in just 17 countries. Three countries, the Democratic Republic of Congo, Nigeria, and India, account for 40% of all estimated malaria cases (WHO World Malaria Report, 2012).
What are the Consequences of Malaria?

Malaria causes over 600,000 deaths annually, with 90% of the malaria deaths occurring in Africa. In 2010, there were an estimated 660,000 deaths due to malaria, and 80% of these deaths were from just 14 countries. Globally, both the Democratic Republic of the Congo and Nigeria account for over 40% of these estimated deaths (WHO World Malaria Report, 2012). Malaria also contributes to anemia in both pregnant women and children and is associated with prematurity and low birth weight in newborns.

Who is Most Affected by Malaria?

In malaria-endemic areas, most people are exposed as children to malaria. If they survive childhood malaria and other infections and malnutrition, they acquire immunity to malaria, which provides protection from severe morbidity from malaria throughout life. Children younger than two years of age who have not acquired immunity are at high risk of dying from malaria. Repeated episodes of malaria result in severe anemia, from which untreated children may eventually die. Pregnant women, particularly those in their first and second pregnancies, lose some of their immunity to malaria, which puts them at risk of anemia and poor delivery and birth outcomes. In malaria-endemic areas, it is estimated that around 19% of infant low birth weights (LBWs) are due to malaria and 6% of infant deaths are due to LBW caused by malaria (Guyatt et al, 2004). These deaths are mediated by LBW, which is caused because the malaria parasite residing in the placenta and umbilical cord blocks nutrients to the fetus. Preventing malaria in pregnancy could reduce LBW in infants by 20% (WHO, 2011).

The anemia caused by malaria in children and in pregnancy is accompanied by iron deficiency, which is prevalent in both these groups. There are concerns about giving and withholding iron in areas where malaria transmission is high. Ensuring that malaria prevention and control and nutrition programs work together to integrate and monitor these two interventions is imperative to maximize the outcomes for both. Click here for information on IFA supplementation and the safety of giving iron.

Malaria Prevention and Control Interventions

Malaria is a preventable and treatable disease. Interventions to prevent malaria include:

- Vector control: sleeping under insecticide-treated nets (ITNs), indoor residual spraying (IRS), and, in some specific settings, larval control
• Intermittent preventive treatment for pregnant women and infants and seasonal chemoprophylaxis for children 1-5 years of age
• Diagnosis and treatment of malaria

Specific Prevention and Treatment Measures for Pregnant Women and Children

All the interventions above should be part of the integrated package. We provide more information interventions for pregnant and lactating women and young children.

Prevention of Malaria using ITNs
Pregnant women and children younger than two years of age should sleep under ITNs to prevent infection by malaria. The coverage of ITNs in these groups has increased dramatically in some African countries. Eighty-nine countries have a policy to provide ITNs free of charge (UNICEF). In 2012, 41% of children younger than five slept under a bednet in Africa. More information on the coverage of ITNs and other anemia-related programs is coming soon here.

Malaria Prevention in Pregnancy (MiP)
In areas of moderate-to-high malaria transmission in sub-Saharan Africa, intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is recommended for all pregnant women at each scheduled antenatal care visit. The first dose should be given as early in the second trimester as possible and at each antenatal care visit thereafter, with spacing of doses one month apart. It is safe to give the last dose after the 36th month of pregnancy. Because large doses of folic acid (5 mg or greater) interfere with IPTp-SP, the World Health Organization recommends that women receive less than a 5 mg dose of folic acid during pregnancy. Click here for more information on Malaria Prevention and Treatment Regimens.

Currently, coverage is still low for MiP. Click here for a compilation of anemia prevalence and anemia control-related indicators including IPTp from Demographic and Health Surveys.

The most recent policy brief from WHO can be viewed by clicking here.

Malaria Prevention in Infants
Where malaria prevalence is moderate to high, intermittent preventive treatment in infants (IPTi) using sulfadoxine-pyrimethamine (SP-IPTi) also is recommended for infants (WHO, 2010). IPTi should be administered with the second and third diphtheria-pertussis-tetanus (DPT) and measles vaccinations of infants (usually at 10 weeks, 14 weeks and 9 months of age) through Expanded Programme on Immunization (EPI). Click here for more information click on immunization schedules.

The use of SP as the drug of choice is dependent on parasite resistance and each country should monitor drug resistance SP-IPTi should not be given to infants receiving a sulfa-based medication including co-trimoxazole which is widely used as prophylaxis against opportunistic infections in HIV-infected infants.
Seasonal malaria chemoprevention (SMC) with amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) for children aged 3?59 months is recommended in areas of highly seasonal malaria transmission across the Sahel sub-region in Africa.

For more information on Malaria Prevention and Treatment Regimens, click here.

The most recent recommendations from WHO can be viewed by clicking here.

Malaria Treatment and Case Management in Women and Children
Regimens for treatment differ by country. For pregnant women, regimens differ by first and second-third trimesters and the first and second line treatments. Many countries use quinine plus clindamycin in the first trimester when the risk of severe anemia and hypoglycemia are lower and concerns are higher about using artemisinin-based therapies (ACT). Click here for more information on the types of treatment regimens (but not the actual doses) for pregnant and lactating women and children.

Click here for the complete WHO guidelines on Malaria Treatment.

Resources:

- Malaria Control Interventions Contributed to Declines in Malaria Parasitemia, Severe Anemia, and All-Cause Mortality in Children Less Than 5 Years of Age in Malawi, 200-2010

Malaria control intervention coverage increased nationwide in Malawi during 2000-2010. Trends in intervention coverage were assessed against trends in malaria parasite prevalence, severe anemia (hemoglobin less than 8 g/dL), and all-cause mortality in children under 5 years of age (ACCM) using nationally representative household surveys. Associations between insecticide-treated net (ITN) ownership, malaria morbidity, and ACCM were also assessed. Household ITN ownership increased from 27.4% (95% confidence interval [CI] = 25.9-29.0) in 2004 to 56.8% (95% CI = 55.6-58.1) in 2010. Similarly intermittent preventive treatment during pregnancy coverage increased from 28.2% (95% CI = 26.7-29.8) in 2000 to 55.0% (95% CI = 53.4-56.6) in 2010. Malaria parasite prevalence decreased significantly from 60.5% (95% CI = 53.0-68.0) in 2001 to 20.4% (95% CI = 15.7-25.1) in 2009 in children aged 6-35 months. Severe anemia prevalence decreased from 20.4% (95% CI: 17.3-24.0) in 2004 to 13.1% (95% CI = 11.0-15.4) in 2010 in children aged 6-23 months. ACCM decreased 41%, from 188.6 deaths per 1,000 live births (95% CI = 179.1-198.0) during 1996-2000, to 112.1 deaths per 1,000 live births (95% CI = 105.8-118.5) during 2006-2010. When controlling for other covariates in random effects logistic regression models, household ITN ownership was protective against malaria parasitemia in children (odds ratio [OR] = 0.81, 95% CI = 0.72-0.92) and severe anemia (OR = 0.82, 95% CI = 0.72-0.94). After considering the magnitude of changes in malaria intervention coverage and nonmalaria
factors, and given the contribution of malaria to all-cause mortality in malaria-endemic countries, the substantial increase in malaria control interventions likely improved child survival in Malawi during 2000-2010.

**Anemia Offers Stronger Protection Than Sickle Cell Trait Against the Erythrocytic Stage of Falciparum Malaria and This Protection Is Reversed by Iron Supplementation**

**Background:** Iron deficiency causes long-term adverse consequences for children and is the most common nutritional deficiency worldwide. Observational studies suggest that iron deficiency anemia protects against *Plasmodium falciparum* malaria and several intervention trials have indicated that iron supplementation increases malaria risk through unknown mechanism(s). This poses a major challenge for health policy. We investigated how anemia inhibits blood stage malaria infection and how iron supplementation abrogates this protection.

**Methods:** This observational cohort study occurred in a malaria-endemic region where sickle-cell trait is also common. We studied fresh RBCs from anemic children (135 children; age 6-24 months; hemoglobin<11 g/dl) participating in an iron supplementation trial (ISRCTN registry, number ISRCTN07210906) in which they received iron (12 mg/day) as part of a micronutrient powder for 84 days. Children donated RBCs at baseline, Day 49, and Day 84 for use in flow cytometry-based *in vitro* growth and invasion assays with *P. falciparum* laboratory and field strains. *In vitro* parasite growth in subject RBCs was the primary endpoint.

**Findings:** Anemia substantially reduced the invasion and growth of both laboratory and field strains of *P. falciparum in vitro* (~10% growth reduction per standard deviation shift in hemoglobin). The population level impact against erythrocytic stage malaria was 15.9% from anemia compared to 3.5% for sickle-cell trait. Parasite growth was 2.4-fold higher after 49 days of iron supplementation relative to baseline (*p*<0.001), paralleling increases in erythropoiesis.

**Interpretation:** These results confirm and quantify a plausible mechanism by which anemia protects African children against *falciparum* malaria, an effect that is substantially greater than the protection offered by sickle-cell trait. Iron supplementation completely reversed the observed protection and hence should be accompanied by malaria prophylaxis. Lower hemoglobin levels typically seen in populations of African descent may reflect past genetic selection by malaria.

**Impact of Combined Intermittent Preventive Treatment of Malaria and Helminths on Anaemia, Sustained Attention, and Recall in Northern Ghanaian Schoolchildren**
Background: The benefits of integrated control of malaria, schistosomiasis, and soil-transmitted helminth infections have not been fully explored in Ghanaian schoolchildren.

Objective: To assess the impact of co-administered artemether-lumefantrine plus albendazole, and artemether-lumefantrine plus albendazole plus praziquantel compared to albendazole plus praziquantel on anaemia, sustained attention, and recall in schoolchildren.

Design: This three-arm, open-label intervention study was carried out in Ghana among class three schoolchildren. Artemether-lumefantrine and albendazole were co-administered to 131 schoolchildren in Study Arm 1; artemether-lumefantrine, albendazole, and praziquantel to 90 children in Study Arm 2 versus albendazole and praziquantel to 127 children in Control Arm 3. Medicines were administered to all children at least 30 min after a meal. A HemoCue® photometer was used to measure haemoglobin (Hb), while the code transmission test (CTT), adapted from the Test of Everyday Attention for Children (TEA-Ch), was used to measure sustained attention and recall before-and-after interventions in June 2011 and June 2012.

Results: We observed significant malaria parasite prevalence reductions of 62.8 and 59.2% in Study Arm 1 from 24.2 to 9.0%, p <0.01, and 59.2% in Study Arm 2 from 26.7 to 10.9%, p <0.01, respectively, compared to 8.93% in Control Arm 3 (from 34.7 to 31.6%, p <0.05). Meanwhile, anaemia prevalence reduced significantly (p <0.01) in all three study arms after interventions by 38.4% (from 19.8 to 12.2%), 20.7% (from 26.6 to 21.1%), and 36.0% (from 28.3 to 18.1%) in Study Arms 1, 2, and 3, respectively. Although the interventions had no significant effects on Hb levels, anaemia prevalence reduced insignificantly by 38.4 and 20.7% in Study Arms 1 and 2, respectively, compared to 36.0% in Control Arm 3. Among schoolchildren in Study Arms 1 and 2, mean CTT score improved significantly after interventions by 10.4% (from 3.18 to 3.55, p = 0.01) and 20.5% (from 2.83 to 3.56, p = 0.01) respectively, compared to 5.75% in Control Arm 3 (from 2.95 to 3.13, p = 0.09). Likewise, mean recall test score improvements after interventions were 16.9% (from 2.07 to 2.49, p = 0.01) and 27.9% (from 1.91 to 2.65, p = 0.01) in Study Arms 1 and 2, respectively, compared to 18.3% (from 1.92 to 2.35, p = 0.01) in Control Arm 3.

Conclusion: Combined intermittent preventive treatment of malaria and deworming reduced prevalence of anaemia and improved sustained attention and recall in schoolchildren. Best results for sustained attention and recall were seen in Study Arm 2.

Does Iron Supplementation Benefit Development in Children Younger than Two Years?

On September 15, 2013 at the International Congress of Nutrition in Granada, Spain, MCHIP’s Nutrition Team convened a Symposium Panel on, "Giving Iron to Children: Implications for Public Health Programs in Developing Countries." Co-moderated by Dr. Francesco Branca, Director of Nutrition at the World Health Organization, and Ms. Rae Galloway, Nutrition Team Lead at the USAID-funded Maternal and Child Health Integrated
Program (MCHIP), five panelists discussed the "hot topic" of the risks and benefits of giving iron to young children in developing countries. Presentations were given by Drs. Robert Black, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Zulfiqar Bhutta, Aga Khan University, Karachi, Pakistan; Clara Menendez, University of Barcelona, Barcelona, Spain; Susan Walker, University of the West Indies, Mona Campus, Jamaica; and Michael Georgieff, University of Minnesota, Minneapolis, MN, USA.

**Giving Iron Supplementation to Malaria Exposed Children: What is the Way Forward?**

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**The Risks of Giving Young Children Iron on Growth and Infectious Diseases and Possible Mechanisms**

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**The Specific Role of Iron in Early Brain Development**
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- **Malaria Control in Schools in Mali: Results from a Cluster Randomized Control Trial in Sikasso Region, Mali**

  The goal of the national Malaria control programme in Mali is to reduce malaria related morbidity and mortality by 80% by 2015 from 2005 rates, by ensuring: universal coverage of Long Lasting Insecticide Treated Nets (LLINs) and prompt diagnosis and treatment of malaria; and by developing community-based interventions to bring prevention, diagnosis and treatment closer to the household. The Ministry of Education?s recently approved national school health policy aims to create a health system in schools which promotes school children?s health. Although both policies include opportunities for integrating malaria control in schools and a focus on school age children, until today, there has been insufficient evidence to inform specific strategies and interventions for schools in Mali.

  This paper presents research funded through Save the Children?s Child Sponsorship resources with additional support from the Wellcome Trust. It contributes to the evidence base needed to advance malaria control in schools in Mali.

  Some key messages include:

  - School age children is the population group most likely to be infected with malaria
  - 80% of school age children in Sikasso are infected with malaria
  - Most cases are asymptomatic and therefore never get treated
  - Malaria causes anemia which reduces children?s capacity to concentrate and learn

- **WHO Malaria Report 2012**
The World Malaria Report 2012 summarizes information received from 104 malaria-endemic countries and other sources, and updates the analyses presented in the 2011 report. It highlights the progress made towards the global malaria targets set for 2015, and describes current challenges for global malaria control and elimination.

**Implications of Malaria on Iron Deficiency Control Strategies**

The populations in greatest need of iron supplementation are also those at greatest risk of malaria: pregnant women and young children. Iron supplementation has been shown to increase malaria risk in these groups in numerous studies, although this effect is likely diminished by factors such as host immunity, host iron status, and effective malaria surveillance and control. Conversely, the risk of anemia is increased by malaria infections and preventive measures against malaria decrease anemia prevalence in susceptible populations without iron supplementation. Studies have shown that subjects with malaria experience diminished absorption of orally administered iron, so that as a consequence, iron supplementation may have generally reduced efficacy in malarious populations. A possible mechanistic link between malaria, poor absorption of iron, and anemia is provided by recent research on hepcidin, the human iron control hormone. Our improved understanding of iron metabolism may contribute to the control of malaria and the treatment of anemia. Malaria surveillance and control are necessary components of programs to control iron deficiency and may enhance the efficacy of iron supplementation.

**The Effects of Malaria and Intermittent Preventive Treatment During Pregnancy on Fetal Anemia in Malawi**

**Background:** Fetal anemia is common in malarious areas and is a risk factor for infant morbidity and mortality. Malaria during pregnancy may cause decreased cord hemoglobin (Hb) and fetal anemia among newborns. Intermittent preventive treatment during pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is protective against malaria but may also affect hematopoiesis and contribute to fetal anemia.

**Methods:** Peripheral, placental, and cord blood were examined for malaria parasitemia and Hb concentration in a cross-section of 3848 mothers and infants delivered at Queen Elizabeth Central Hospital in Blantyre, Malawi between 1997 and 2006. Unconditional linear and logistic regressions were performed with multiple imputation for missing covariates to assess the associations between malaria, IPTp with SP, and fetal anemia.

**Results:** The overall prevalence of fetal anemia was 7.9% (n = 304). Malaria parasitemia at
delivery was associated with an adjusted decrease in cord Hb of -0.24 g/dL (95% confidence interval [CI], -.42 to -.05). The adjusted prevalence odds ratio for the effect of malaria on fetal anemia was 1.41 (95% CI, 1.05-1.90). Primigravidae who did not take IPTp had infants at highest risk for fetal anemia, and density of parasitemia was correlated with the decrease in cord Hb. There was no significant association between SP use and cord Hb or fetal anemia.

**Conclusions:** Malaria during pregnancy, but not IPTp, decreases cord Hb and is a risk factor for fetal anemia in Malawi. Intermittent preventive treatment during pregnancy with SP may continue to be safe and effective in preventing malaria during pregnancy and fetal anemia despite development of SP resistance.

**Maternal Anemia at First Antenatal Visit: Prevalence and Risk Factors in a Malaria-Endemic Area of Benin**

The risk factors for maternal anemia (hemoglobin level less than 110 g/L) were studied in human immunodeficiency virus-negative pregnant women in Benin at the time of the first antenatal visit and prior to any prevention. Data for the first 1,005 pregnant women included in a multicentre randomized controlled trial were analyzed. Anemia was common (68.3%), and malaria and helminth infestations were prevalence in 15.2% and 11.1% of the women. A total of 33.3%, 31.3% and 3.6% of the women were iron, folic acid and vitamin B12 deficient, respectively. These parasitic infections and nutrient deficiencies were associated with a high risk of anemia. Twenty-one percent, 15%, 12%, 11% and 7% of anemia were attributable to malnutrition, malaria, iron, folic acid deficiencies, and helminth infestations, respectively. Most anemia was caused by factors that could be prevented by available tools, stressing the need to reinforce their implementation and to evaluate their effectiveness throughout the course of the pregnancy.

**Conclusions and Recommendations of the WHO Consultation on Prevention and Control of Iron Deficiency in Infants and Young Children in Malaria-Endemic Areas**

The Consultation reached consensus on several important issues related to providing additional iron to infants and young children in malaria-endemic areas. The conclusions in this report apply specifically to regions where malaria is endemic.

In this report, ?iron supplements? refers to medicinal iron supplements given orally to population groups for the prevention and control of iron deficiency. ?Iron therapy? refers to medicinal iron supplements given orally or parenterally for treatment of iron deficiency of individual patients. ?Iron preparations for home fortification? refers to iron mixed with foods at
home. Such iron preparations may be in the form of a powder, crushable tablet, or fat-based spread. Processed foods fortified with iron? refers to food fortified with iron during food processing.

Effects of Routine Prophylactic Supplementation with Iron and Folic Acid on Admission to Hospital and Mortality in Preschool Children in a High Malaria Transmission Setting: Community-Based, Randomised, Placebo-Controlled Trial

Background: Anaemia caused by iron deficiency is common in children younger than age 5 years in eastern Africa. However, there is concern that universal supplementation of children with iron and folic acid in areas of high malaria transmission might be harmful.

Methods: We did a randomised, placebo-controlled trial, or children aged 1?35 months and living in Pemba, Zanzibar. We assigned children to daily oral supplementation with: iron (12.5 mg) and folic acid (50 µg; n=7950), iron, folic acid, and zinc (n=8120), or placebo (n=8006); children aged 1?11 months received half the dose. Our primary endpoints were all-cause mortality and admission to hospital. Analyses were by intention to treat. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN59549825.

Findings: The iron and folic acid-containing groups of the trial were stopped early on August 19, 2003, on the recommendation of the data and safety monitoring board. To this date, 24,076 children contributed a follow-up of 25,524 child-years. Those who received iron and folic acid with or without zinc were 12% (95% CI 2-23, p=0.02) more likely to die or need treatment in hospital for an adverse event and 11% (1-23%, p=0.03) more likely to be admitted to hospital; there were also 15% (?7 to 41, p=0.19) more deaths in these groups.

Interpretation: Routine supplementation with iron and folic acid in preschool children in a population with high rates of malaria can result in an increased risk of severe illness and death. In the presence of an active programme to detect and treat malaria and other infections, iron-deficient and anaemic children can benefit from supplementation. However, supplementation of those who are not iron deficient might be harmful. As such, current guidelines for universal supplementation with iron and folic acid should be revised.

Impact of Malaria during Pregnancy on Low Birth Weight in Sub-Saharan Africa
It is estimated that each year over 30 million women become pregnant in malarious areas of Africa, with most living in areas of stable malaria transmission. Although the cast majority of women with malaria infections during pregnancy remain asymptomatic, infection increases the risk of maternal anemia and delivering a low-birth-weight (LBW) baby. LBW (2,500 g) is an important risk factor for infant mortality, and this review focuses on the impact of malaria during pregnancy on LBW and subsequent infant mortality in sub-Saharan Africa. There have been many papers describing the impact of malaria during pregnancy and, more recently, attempts to quantify this burden. However, there remains a poor understanding of the effects under different levels of transmission and in different gravidity groups. It is frequently reported that primigravidae and secundigravidae are the most at risk, and much of the literature on the burden of malaria during pregnancy has focused on women of these gravidities. However, there is an increasing recognition that women of higher gravidities may also be at risk, particularly in areas of high transmission levels. The aim of this review was to investigate the impact of malaria during pregnancy on low birth weight (LBW) across all gravidities by collating data from areas in sub-Saharan Africa with various levels of malaria transmission. The present review benefits from a wealth of recently published data on malaria and LBW for all pregnant women in these areas and undertakes a novel analysis of the associations between LBW and rate of malaria transmission. A similar analysis of maternal anemia has been conducted previously.

The Burden of Malaria in Pregnancy in Malaria-Endemic Areas

Pregnant women in malarious areas may experience a variety of adverse consequences from malaria infection including maternal anemia, placental accumulation of parasites, low birth weight (LBW) from prematurity and intrauterine growth retardation (IUGR), fetal parasite exposure and congenital infection, and infant mortality (IM) linked to preterm-LBW and IUGR-LBW. We reviewed studies between 1985 and 2000 and summarized the malaria population attributable risk (PAR) that accounts for both the prevalence of the risk factors in the population and the magnitude of the associated risk for anemia, LBW, and IM. Consequences from anemia and human immunodeficiency virus infection in these studies were also considered. Population attributable risks were substantial: malaria was associated with anemia (PAR range 3-15%), LBW (8-14%), preterm-LBW (8-36%), IUGR-LBW (13-70%), and IM (3-8%). Human immunodeficiency virus was associated with anemia (PAR range 12-14%), LBW (11-38%), and direct transmission in 20-40% of newborns, with direct mortality consequences. Maternal anemia was associated with LBW (PAR range 7-18%), and fetal anemia was associated with increased IM (PAR not available). We estimate that each year 75,000 to 200,000 infant deaths are associated with malaria infection in pregnancy. The failure to apply known effective antimalarial interventions through antenatal programs continues to contribute substantially to infant deaths globally.
Intermittent Sulfadoxine-Pyrimethamine in Pregnancy: Effectiveness Against Malaria Morbidity in Blantyre, Malawi, in 1997-99

Plasmodium falciparum malaria in pregnancy predisposes to maternal and foetal morbidity. In 1993 Malawi adopted intermittent presumptive therapy with sulfadoxine-pyrimethamine (SP) as malaria prophylaxis for all pregnant women. To assess operational effectiveness of SP, we examined (in 1997-99) the relationship between number of doses of SP prescribed in antenatal clinic and indicators of malaria infection and morbidity at delivery, including peripheral and placental parasitaemia, maternal and neonatal anaemia, and birthweight. Among Malawian women delivering in a large urban hospital, SP prescription was associated with a decrease in placental malaria prevalence (from 31.9% with no SP prescription to 22.8% with > or = 2 doses SP) and density, decreased prevalence of low birthweight (from 23% in women not receiving SP to 10.3% in women given > or = 2 doses), and higher maternal haemoglobin concentrations. These effects were most marked in first and second pregnancies, in which malaria prevalence was highest. Maternal and cord blood malaria prevalence and mean cord blood haemoglobin concentrations did not differ with SP usage. Implementation of the SP administration policy was incomplete: 24% of women were not prescribed any SP, and only 30% were prescribed at least 2 doses as recommended. Intermittent presumptive treatment with SP is having a positive impact on some, but not all indicators of malaria infection and morbidity in Malawi. Improved implementation and continued surveillance are essential.

Malaria is an Important Cause of Anaemia in Primigravidae: Evidence from a District Hospital in Coastal Kenya

A study was undertaken in order to determine the prevalence and aetiology of anaemia in pregnancy in coastal Kenya, so as to establish locally important causes and enable the development of appropriate intervention strategies. 275 women attending the antenatal clinic at Kilifi district hospital, Kenya, were recruited in November 1993. The prevalence of anaemia (haemoglobin 11 g/dL) was 75.6%, and the prevalence of severe anaemia (7g/dL) was 9.8% among all parities; 15.3% of 73 primigravidae were severely anaemic, compared with 7.9% of 202 multigravidae (P = 0.07). In primigravidae, malaria infection (Plasmodium falciparum) was strongly associated with moderate and severe anaemia (chi 2 test for trend, P = 0.003). Severe anaemia was more than twice as common in women with peripheral parasitaemia as in those who were aparasitaemic, and parasitaemia was associated with a 2.2g/dL decrease in mean haemoglobin level (0.001). In multigravidae, iron deficiency and hookworm infection were the dominant risk factors for anaemia. Folate deficiency and human immunodeficiency
virus infection were not strongly associated with anaemia. It is suggested that an intervention that can effectively reduce malaria infection in primigravidae could have a major impact on the health of these women and their infants.

## Malaria Prevention and Treatment Regimen

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard of Care</td>
<td>Treatment is given daily throughout the course of the regimen: oral dihydrochalcone (DHHC) or oral artemether (ART)</td>
<td>Treatment of fever is given at baseline (March 2013) to define exposure and outcome, respectively.</td>
</tr>
<tr>
<td>High-risk factors</td>
<td>Higher iron stores, defined by serum ferritin (SF) concentration, may increase malaria risk.</td>
<td>Objective: We evaluated the association between SF assessed during low malaria season and the risk of malaria during high malaria season, controlling for inflammation.</td>
</tr>
<tr>
<td>Low-risk factors</td>
<td>Background: Higher iron stores, defined by serum ferritin (SF) concentration, may increase malaria risk.</td>
<td>Methods: Data for this prospective study were collected from children aged 4-8 y (n = 745) participating in a biofortified maize efficacy trial in rural Zambia. All malaria cases were treated at baseline (September 2012). We used baseline SF and malaria status indicated by positive microscopy at endline (March 2013) to define exposure and outcome, respectively.</td>
</tr>
</tbody>
</table>

### Resources:

- **High Iron Stores in the Low Malaria Season Increase Malaria Risk in the High Transmission Season in a Prospective Cohort of Rural Zambian Children**

  **Background:** Higher iron stores, defined by serum ferritin (SF) concentration, may increase malaria risk. **Objective:** We evaluated the association between SF assessed during low malaria season and the risk of malaria during high malaria season, controlling for inflammation.

  **Methods:** Data for this prospective study were collected from children aged 4-8 y (n = 745) participating in a biofortified maize efficacy trial in rural Zambia. All malaria cases were treated at baseline (September 2012). We used baseline SF and malaria status indicated by positive microscopy at endline (March 2013) to define exposure and outcome, respectively.
Iron status was defined as deficient (corrected or uncorrected SF

**Results:** We observed an age-dependent, positive dose-response association between ferritin in the low malaria season and malaria incidence during the high malaria season in younger children. In children aged

**Conclusions:** Iron adequacy in 4- to 8-y-old children in rural Zambia was associated with increased malaria risk. Our findings underscore the need to integrate iron interventions with malaria control programs.

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## Giving Folic Acid with IPTp-SP

The Global Call to Action to Increase National Coverage of Intermittent Preventive Treatment of Malaria in Pregnancy for Immediate Impact recommends a low dose of folic acid to ensure the effectiveness of sulfadoxine-pyrimethamine (SP) as an anti-malarial. To support this guidance, the Roll Back Malaria Partnership Malaria in Pregnancy Working Group issued a Consensus Statement recommending giving less than 5 mg of folic acid per day during pregnancy. A new brief, developed by the Maternal and Child Survival Program (MCSP), and the President?s Malaria Initiative (PMI), explains the importance of both IPTp-SP and IFA supplementation during pregnancy, and why the dose of folic acid can and should be 0.4 mg per day, particularly when given in malaria endemic areas.

Next steps for malaria control programs:

- Work with nutritionists in country to ensure women are receiving the combined dose of IFA with 60 mg of iron and 0.4 mg of folic acid.
- Reduce stores of the 5 mg dose of folic acid.
- Scale-up IPTp-SP and IFA supplementation to ensure that at least 80 percent of pregnant women in sub-Saharan Africa receive these life-saving interventions.
- Monitor the coverage and impact of the package of interventions to reduce anemia including IPTp, IFA, and deworming.

For additional reading and resources on malaria and folic acid, click [here](#).

**Resources:**

- Controlling Maternal Anemia and Malaria: Ensuring Pregnant Women Receive Effective Interventions to
Prevent Malaria and Anemia: What Program Managers and Policymakers Should Know

This brief describes World Health Organization recommendations for IPTp to prevent malaria in pregnancy and iron-folic acid supplementation to prevent iron deficiency anemia in sub-Saharan Africa countries, with an emphasis on giving the correct dose of folic acid to maximize the effectiveness of interventions to prevent malaria. The brief is for program managers of health programs and policymakers to guide them in designing programs and developing policies.

Roll Back Malaria Partnership Malaria in Pregnancy Working Group: Consensus Statement on Folic Acid Supplementation during Pregnancy

The Roll Back Malaria (RBM) Partnership Malaria in Pregnancy Working Group supports the following for all pregnant women living in sub-Saharan Africa:

- In malaria-endemic areas, intermittent preventive treatment using sulfadoxine-pyrimethamine (IPTp-SP) should be provided to pregnant women at each scheduled antenatal care (ANC) visit for protection against malaria. This should start early in the second trimester and continue until the time of delivery, with the doses given at least one month apart.

  - IPTp-SP has been shown to reduce maternal anemia, antenatal maternal parasitemia, low birthweight infants and neonatal deaths.

  - Co-trimoxazole provides some protection through its antimalarial activity; however, IPTp-SP should NOT be given to women who are taking daily co-trimoxazole prophylaxis (i.e. mainly those living with HIV) as this increases the risk of adverse events.

- Daily oral supplementation of 30-60 mg elemental iron and 400 µg (0.4 mg) folic acid should be provided as early as possible in pregnancy to meet iron and folic acid requirements. In cases where a combined folic acid-iron tablet is not available, a daily dose of 400 µg (0.4 mg) folic acid can be used separately.

  - There is evidence that high doses of folic acid (i.e. 5,000 µg or more) may interfere with the efficacy of sulfadoxine-pyrimethamine as an antimalarial. The higher 5,000 µg (5 mg) dose for pregnant women should be restricted for use in very specific clinical cases.

High doses of folic acid are not needed during low-risk pregnancies and may counteract the efficacy of both sulfadoxine-pyrimethamine and co-trimoxazole as antimalarials. The RBM Malaria in Pregnancy Working Group strongly advises that countries currently prioritize the procurement and distribution of the available combined dose of 400 µg (0.4 mg) folic acid.
plus 30-60 mg elemental iron as part of routine ANC. It also recommends that countries substantially reduce current stores and supplies of folic acid at a dose of 5,000 µg (5 mg) or higher at all facilities, as this dose should only be used for specific medical conditions as outline by the World Health Organization (WHO), and as indicated below in the answer to Question 2.

• The Global Call to Action to Increase National Coverage of Intermittent Preventive Treatment of Malaria in Pregnancy for Immediate Impact

The intermittent preventive treatment against malaria in pregnancy (IPTp) is a highly cost-effective intervention with the potential to save many maternal and neonatal lives. However, IPTp coverage remains low in sub-Saharan Africa (SSA) where immediate action is needed for dramatic scale up. While some obstacles to IPTp uptake relate to large health-systems issues, many barriers are common across countries and could be overcome with relative ease and speed. This is a pivotal moment for the scale up of IPTp. To maximize its public health impact, we must prioritize IPTp by acting to:

1. Incorporate the World Health Organization’s (WHO) 2012 policy update for IPTp into national guidelines and practices;
2. Rally efforts that will narrow achievement gaps in Millennium Development Goals No. 4 and No. 5 before the end of 2015;
3. Prepare for Sustainable Development Goal No. 6 as it becomes the focal point of health sector action.

From the Roll Back Malaria (RBM) Partnership and its malaria in pregnancy (MIP) Working Group, we urge you to take immediate action as outlined below to protect pregnant women and their babies from malaria, drawing on your institutional mandates and comparative advantages. The RBM Partnership, through its core partners that work in malaria-endemic countries, will support governments of SSA to implement this Call to Action and will disseminate best practices and lessons learned to accelerate IPTp scale up.

• WHO Policy Brief for the Implementation of Intermittent Preventive Treatment of Malaria in Pregnancy Using Sulfadoxine-Pyrimethamine (IPTp-SP)

Malaria infection during pregnancy is a major public health problem, with substantial risks for the mother, her fetus and the newborn. In areas with moderate to high transmission of *Plasmodium falciparum*, the World Health Organization (WHO) recommends a package of interventions for controlling malaria and its effects during pregnancy, which includes the
promotion and use of insecticide-treated nets (ITNs), the administration during pregnancy of intermittent preventive treatment with sulfadoxin-pyrimethamine (IPTp-SP), and appropriate case management through prompt and effective treatment of malaria in pregnant women.

During the last few years, WHO has observed a slowing of efforts to scale-up IPTp-SP in a number of countries in Africa. Although there may be several reasons for this, an important factor is confusion among health workers about sulfadoxine-pyrimethamine administration for intermittent preventive treatment in pregnancy.

At a recent WHO evidence review, a meta-analysis of seven trials evaluating IPTp-SP was undertaken. It showed that three or more doses of IPTp-SP were associated with higher mean birth weight and fewer low birth weight (LBW) births than two doses of IPTp-SP. The estimated relative risk reduction for LBW was 20% (95% CI 6-31). This effect was consistent across a wide range of SP resistance levels. The 3+ dose group also was found to have less placental malaria. There were no differences in serious adverse events between the two groups.

Based on this evidence review, in October 2012, WHO updated the recommendations on IPTp-SP as outlined below, and urges national health authorities to disseminate this update widely and ensure its correct application. IPTp-SP is an integral part of WHO's three-pronged approach to the prevention and treatment of malaria in pregnancy, which also includes the use of insecticide-treated nets and prompt and effective case management.

- **Impact of Folate Supplementation on the Efficacy of Sulfadoxine/Pyrimethamine in Preventing Malaria in Pregnancy: The Potential of 5-methyl-tetrahydrofolate**

Malaria remains the leading cause of mortality and morbidity in children under the age of 5 years and pregnant women. To counterbalance the malaria burden in pregnancy, an intermittent preventive treatment strategy has been developed. This is based on the use of the antifolate sulfadoxine/pyrimethamine, taken at specified intervals during pregnancy, and reports show that this approach reduces the malaria burden in pregnancy. Pregnancy is also associated with the risk of neural tube defects (NTDs), especially in women with low folate status, and folic acid supplementation is recommended in pregnancy to lower the risk of NTDs. Thus, in malaria-endemic areas, pregnant women have to take both antifolate medication to prevent malaria and folic acid to lower the risk of NTDs. However, the concomitant use of folate and antifolate is associated with a decrease in antifolate efficacy, exposing pregnant women to malaria. Thus, there is genuine concern that this strategy may not be appropriate. We have reviewed work carried out on malaria folate metabolism and antifolate efficacy in the context of folate supplementation. This review shows that: (i) the folate supplementation effect on antifolate efficacy is dose-dependent, and folic acid doses required to protect pregnant women from NTDs will not decrease antifolate activity; and (ii) 5-methyl-tetrahydrofolate, the predominant form of folate in the blood circulation, could be
administered (even at high dose) concomitantly with antifolate without affecting antifolate efficacy. Thus, strategies exist to protect pregnant women from malaria while maintaining adequate folate levels in the body to reduce the occurrence of NTDs.

A Randomized Controlled Trial of Folate Supplementation when Treating Malaria in Pregnancy with Sulfadoxine-Pyrimethamine

**Objectives:** Sulfadoxine-pyrimethamine (SP) is an antimalarial drug that acts on the folate metabolism of the malaria parasite. We investigated whether folate (FA) supplementation in a high or low dose affects the efficacy of SP for the treatment of uncomplicated malaria in pregnant women.

**Design:** This was a randomized, placebo-controlled, double-blind trial.

**Setting:** The trial was carried out at three hospitals in western Kenya.

**Participants:** The participants were 488 pregnant women presenting at their first antenatal visit with uncomplicated malaria parasitaemia (density of ≤ 500 parasites/µl), a haemoglobin level higher than 7 g/dl, a gestational age between 17 and 34 weeks, and no history of antimalarial or FA use, or sulfa allergy. A total of 415 women completed the study.

**Interventions:** All participants received SP and iron supplementation. They were randomized to the following arms: FA 5 mg, FA 0.4 mg, or FA placebo. After 14 days, all participants continued with FA 5 mg daily as per national guidelines. Participants were followed at days 2, 3, 7, 14, 21, and 28 or until treatment failure.

**Outcome Measures:** The outcomes were SP failure rate and change in haemoglobin at day 14.

**Results:** The proportion of treatment failure at day 14 was 13.9% (19/137) in the placebo group, 14.5% (20/138) in the FA 0.4 mg arm (adjusted hazard ratio [AHR], 1.07; 98.7% confidence interval [CI], 0.48 to 2.37; \( p = 0.8 \)), and 27.1% (38/140) in the FA 5 mg arm (AHR, 2.19; 98.7% CI, 1.09 to 4.40; \( p = 0.005 \)). The haemoglobin levels at day 14 were not different relative to placebo (mean difference for FA 5 mg, 0.17 g/dl; 98.7% CI, -0.19 to 0.52; and for FA 0.4 mg, 0.14 g/dl; 98.7% CI, -0.21 to 0.49).

**Conclusions:** Concomitant use of 5 mg FA supplementation comprises the efficacy of SP for the treatment of uncomplicated malaria in pregnant women. Countries that use SP for treatment or prevention of malaria in pregnancy need to evaluate their antenatal policy on timing or dose of FA supplementation.
Lack of Inhibition of the Anti-Malaria Action of Sulfadoxine-Pyrimethamine by Folic Acid Supplementation when Used for Intermittent Preventative Treatment in Gambian Primigravidae

Folic acid is frequently given to pregnant women at the same time as intermittent preventive treatment (IPTp) with sulfadoxine/pyrimethamine (SP), but it is not known if it interferes with the anti-malarial activity of SP. To investigate this concern, 1,035 Gambian primigravidae were randomized to receive either folic acid (500?1,500 ?g/day) together with oral iron (522) or oral iron alone (513) for 14 days at the same time as they received IPTp with SP. On presentation, 261 women (25%) had Plasmodium falciparum asexual parasitemia. Prevalences of parasitemia on day 14 after treatment were similar in both groups: 5.7% (26 of 458) in the iron plus folic acid group and 4.9% (22 of 446) in the iron alone group (risk difference = 0.74%, 95% confidence interval [CI] = ?2.2% to 3.7%). Parasitologic cure was observed in 116 (91%) of 128 of women who were parasitemic on presentation and who received iron and folic acid and in 122 (92%) of 133 women who received iron alone (difference = 1.1%, 95% CI = ?5.6% to 8.0%). Women who received folic acid and iron had a slightly higher mean hemoglobin concentration at day 14 than women who had received iron alone (difference = 0.14 g/dL, 95% CI = 0.01?0.27 g/dL). The results of this study suggest that in an area of low SP resistance, administration of folic acid to pregnant women in a dose of 500?1,500 ?g/day will not interfere with the protective effect of SP when used for IPTp.

Reduction of the Efficacy of Antifolate Antimalarial Therapy by Folic Acid Supplementation

Malaria and anemia are common conditions in patients presenting to outpatient clinics in Kenya. Anemia is usually due to malaria infection with underlying micronutrient deficiency. Iron therapy has been shown to enhance recovery from anemia in children with malaria, without affecting malaria treatment. Iron and folic acid are often prescribed together for anemic individuals. Until recently in Kenya, the drug of first choice for non-severe malaria was sulfadoxine-pyrimethamine (SP), an antifolate antimalarial drug. In this study, 303 patients of all ages with anemia and uncomplicated Plasmodium falciparum malaria attending an outpatient clinic in an area of seasonal malaria were treated with SP and iron, and were randomized to receive folic acid. Parasite clearance rates were measured using a survival analysis plot for both parasitologic and clinical failure. There was a significant reduction in the efficacy of SP in patients taking standard therapeutic doses of folic acid using the survival curve for parasitologic failure ($P < 0.0001$), but no difference for clinical failure ($P = 0.7008$). Folic acid supplementation did not enhance recovery from anemia.
Iron, but not Folic Acid, Combined with Effective Antimalarial Therapy Promotes Haematological Recovery in African Children after Acute Falciparum Malaria

Whether children with malarial anaemia should receive supplementation with iron or folic acid is uncertain. Therefore, the effects of supplementary treatment with iron or folic acid, given together with chloroquine or pyrimethamine-sulfadoxine (Fansidar®), has been assessed in 600 Gambian children with uncomplicated falciparum malaria. After one month, haematological recovery was significantly better in the group treated with Fansidar® than in the chloroquine-treated group (difference in mean haemoglobin level = 0.54 g/dL, \(P = 0.01\)). Children who received iron had a significantly better response than those given placebo (differences in mean haemoglobin level after one month and at dry season follow-up = 0.70 g/dL, \(P = 0.006\), and 0.81 g/dL, \(P = 0.001\), respectively). Iron supplementation was not associated with increased prevalence of malaria. Supplementation with folic acid did not improve the haematological response but, among children who received Fansidar®, the treatment failure rate was significantly higher among those given folic acid than among those given placebo. Thus, supplementation with iron, but not folic acid, improves haematological recovery without increasing susceptibility to malaria.

Program Guidance

While this Toolkit recommends an integrated package to control anemia, in most countries the components of the integrated package already exist as a policy of the Ministry of Health, although coverage of malaria control, deworming, and iron-folic acid supplements still may be low. Global programs have emphasized an integrated package, in particular the Integrated Management of Childhood Illnesses (IMCI) which includes addressing anemia in children. Family planning has been combined with various health themes with some evidence of improved health outcomes.

Food-based approaches to control anemia are most promising through increased production of iron-rich foods, food fortification and biofortification. Increasing the production of meat and fruit to improve iron status of poor families is not often part of an integrated package implemented by the agriculture sector. The Ministry of Education also can play a role by providing useful nutrition
information in school curriculums. Since older siblings care for their younger siblings, school children should be learning practical skills in feeding young children. The Ministry of Education can deworm school children and give them iron supplements, as resources permit. Where school feeding programs exist, school lunch programs should include iron-rich or fortified foods.

This Program Guidance tab focuses on helpful actions in planning an integrated approach to anemia control, within the health sector and across relevant public sectors and the private sector that can contribute to reducing the problem. The Toolkit also provides information and tools on how to improve existing programs. Many of our examples (e.g., behavior change communications) are related to iron-folic acid supplementation. We would like to add examples of trainings, messages and materials, and monitoring and evaluation related to all components of the integrated package (e.g., nutrition, malaria, helminths, agriculture). Please send any resources you think would be helpful to sstraubinger@path.org or agottwalt@path.org.

While the Toolkit starts with a sub-tab on developing a strategy, improving existing programs can and should take place at any time during the strategy development process. Many of the problems with existing programs (lack of supplies, demand, and monitoring and evaluation) are probably already known, and the Toolkit provides some tools and resources to address these barriers. This Toolkit does not give information on the benefits of integrating these services within health or among sectors as this information has not been extensively collected for anemia prevention and control or for other health problems. Click here for information on developing an anemia prevention and control strategy.

Partners should be invited to the table within health and nutrition divisions, among sectors (Ministries of Agriculture, Education and Finance), and representatives from the private sector. Conducting a situational analysis on the state of existing programs will be useful in planning the way forward. Click here for an instrument for a situational analysis on anemia control programs which can be easily adapted to collect information on the entire integrated package.

Most surveys do not collect data on causes of anemia, so surveys can be limited in helping decide on effective strategies to address anemia. This is why country-level information on the prevalence of factors which contribute to the development of anemia, which include iron deficiency and also parasitic and infectious diseases, are useful to guide a country-level strategy on anemia. For migrant communities or specific segments of a population, check with partners working in specific geographic areas to see if any surveys have been conducted that may include useful data on these groups.
MCHIP has developed a visual decision tree for delivering IFA and other components of the integrated package which countries can use in identifying which channels are the most effective in reaching the target group. Activities and interventions for anemia control should cover both demand and supply issues needed to make delivery of the integrated package possible. Coverage of antenatal care is an important factor in determining the channels for IFA distribution. If coverage of women coming is low or they come in for ANC late, then community-based distribution may be the most effective channel in providing IFA. Ministries of Health do not want IFA distributed in the community because they think it will discourage use of ANC which is needed by women for many other interventions; however, where community-based distribution has been used, it has increased ANC utilization. Click here for the MCHIP brief on Community-Based Distribution of IFA.

Strategy development should determine the cost of anemia prevention and control, secure funding, and define timing (usually 3-5 years). Development of the strategy might be spearheaded by a small task force involving interested and relevant stakeholders which uses a collaborative process to develop the strategy. Development of a monitoring and evaluation plan should be designed during strategy development and before implementation of programs.

Click on the following sub-tabs for more information and tools on cross-cutting program components important to BCC Strategy Development, Developing BCC Messages and Materials, Logistics and Supplies, and Monitoring and Evaluation.

Resources:

- **Compendium of Actions for Nutrition**

  The Compendium of Actions for Nutrition (CAN) is a practical resource which comprehensively compiles, in one place, a concise description of possible nutrition actions. The CAN was developed by the UN Network for SUN/REACH Secretariat in consultation with FAO, IFAD, UNICEF, WFP and WHO as well as academic experts. The CAN helps to understand the broad spectrum of diverse but relevant actions, from breastfeeding, to fortification, to handwashing, to latrine construction, to insect production that can contribute to make a difference for people’s nutrition. This compendium is a resource for the SUN Movement to support SUN country teams as they set priorities and take informed decisions for concrete, impact-oriented action on nutrition.
Gap Analysis: Information Needed for Consensus on Policies and Programs to Improve Iron Nutrition

Despite over 50 years of research, nutritional iron deficiency remains the most prevalent micronutrient deficiency disorder worldwide. As stated in a recent UNICEF/UNU/WHO publication (2001): “Iron deficiency affects a significant part, and often a majority, of the population in nearly every country in the world. Programs for the prevention of iron deficiency, particularly iron supplementation for pregnant women, are under way in 90 of 112 countries as reported to WHO in 1992 (WHO, 1992). Most of these programs, however, are neither systematically implemented nor well monitored or evaluated.” Nevertheless, significant advances in addressing iron deficiency anemia have been made in the last 10-15 years, by applying established scientific observations to the design, implementation, and evaluation of interventions. At the same time, the increased emphasis on outcome analysis has uncovered new problems that require more rigorous scientific evaluation, the most urgent being the possible risks of delivering iron in regions where malaria is endemic. There is also a pressing need to find safe and effective mechanisms for providing iron to infants and young children. This paper seeks to identify the key gaps in information that must be filled to move towards consensus on policies and programs to improve iron nutrition.

- **Anemia Prevention and Control: What Works. Program Guidance, Parts I and II**

  This document provides program and project managers background information on the causes and consequences of anemia and guidance on formulating and monitoring anemia prevention and control programs.

- **Major Issues in the Control of Iron Deficiency**

  This book has been compiled by the Micronutrient Initiative and the United Nations Children's Fund (UNICEF) with the objective of synthesizing the various anemia-control strategy components that clearly need to fit together. We hope that it will be useful to policymakers and program managers alike in planning and implementing programs that make significant inroads to alleviate anemia by the end of this decade.

- **Qualitative Research Instrument on Perceptions of Anemia and Use of Iron Tablets?The Indramayu Project,**
Indonesia

The following plan and research instrument was developed for the USAID-funded MotherCare/John Snow, Inc. Project by the Manoff Group. This plan and the research instrument were used in formative research for the Indramayu Project. One component of this project tested ways to improve the existing iron supplementation program for pregnant women. Social scientists from the Manoff Group gave technical assistance to this process by developing these instruments, training non-medical interviewers and analyzing the results. The results were used to develop messages for counseling women and a social marketing campaign, to train health workers and other delivering iron tablets and to identify and develop delivery mechanisms/strategies for the improved iron supplementation program.

• Anemia Control Programs Questionnaire

Adapted from The Anemia Prevention and Control Guide: What Works.

Developing a Strategy for Anemia Prevention and Control

This portion of the Toolkit draws heavily from a seminal document, which outlines the below steps for strategy development, which can be found here.

1. Know the problem

  ○ Determine the prevalence of anemia and identify priority target groups (those with the highest anemia and who suffer most from the consequences of anemia); collect available information on the causes of anemia; and programs to prevent and control it.

  ○ Determine what people know about anemia and their experience with anemia prevention and control.

The Demographic and Health Surveys provide information on anemia prevalence in children 6-59 months and all reproductive age women 15-49 years of age which is disaggregated to pregnant women, breastfeeding women, and women who are not pregnant or breastfeeding. Surveys also may collect information on the coverage of IFA supplementation, deworming, IPTp, ITNs/LLINs, food intake, and other anemia-related programs. Click here to visit the DHS website. Click here to view the relevant information by country and indicator from DHS which was collated for this
Toolkit. These tables will be updated periodically with new information as it becomes available.

2. **Raise awareness and develop partnerships**

- **Raise awareness about the costs to individuals and countries of not addressing anemia** and the integrated package to prevent and control anemia within health teams and across sectors: advocate and educate.

- **Build partnerships in health, agriculture, food, and pharmaceutical sectors among government ministries and agencies, nongovernmental organizations (NGO), donors, industry, and commerce.**

Advocacy about the importance of addressing anemia could start with partners within health, particularly to talk about defining the integrated packaging and making its delivery a priority. Within health, people working on malaria, helminths, and nutrition need to be involved and family planning staff. Within nutrition, micronutrient specialists need to work with infant and young child feeding specialists to ensure that optimal feeding practices are integrated into anemia control programming for young children. It also will be important to reach out to the funders of programs including the Ministry of Finance and donors to discuss the costs to individuals and national development and the cost of programs to address anemia. Click here for a brief that can be used or adapted on what policy makers can do advocate for the importance of addressing anemia.

Click here for information on a useful tool, PROFILES, which has been used in many countries to assist in determining the costs of malnutrition, including anemia, to national development and in starting a national discussion about malnutrition.

Click here for information about the costs of nutrition programs.

**Delivering an integrated package, in most countries, requires a multi-sectoral response** by preventing and controlling anemia in certain groups through advocacy and partnership with the Public Health Service/Ministry of Health. Within the Public Health Services/Ministry of Health departments such as nutrition, maternal health, reproductive health, and infectious diseases will be important partners in defining and delivering the integrated package. Other ministries that can address anemia in the populations they serve include:

- **The Ministry of Education**, which can include practical nutrition information in school curriculums, implement school health and nutrition programs, including giving iron, treating malaria and hookworm infections, and promoting the consumption of iron-rich foods to children in pre-school programs and children in primary and secondary school

- **The Ministry of Agriculture**, which can assist with increasing the production and availability of iron-rich foods including introducing new micronutrient-rich varieties, and train extension workers to give nutrition messages;

- **The Ministry of Industry**, which can support food fortification programs in the private food industry and make long-lasting, insecticide-treated nets (LLINs) available to private vendors
and health sector workers; *The Ministry of Finance*, which can put anemia control into the budget of several ministries;

- *The Ministry of Women’s Affairs*, which can advocate for addressing anemia through its network of community workers;

- *The Ministry of Water and Sanitation*, which can improve hygiene and decrease transmission of helminth infections that cause anemia; and

- *The Ministry of Local Government*, which can assist with coordinating anemia prevention and control programs at lower levels of administration.

3. **Develop interventions and implementation plans**

- Identify priorities, responsibilities, and timeframes.

- Identify specific objectives.

- Identify potential collaborating groups (universities, government agencies, NGOs, civic groups, commercial entities).

- Review existing programs and determine and develop anemia prevention and control activities.

- Determine and secure staffing, funding, and other resources for implementing activities.

- Develop a monitoring and evaluation plan.

Formative research may be needed in the beginning to identify barriers to current programs and which behaviors of stakeholders need to change to move forward in improving anemia prevention and control programs. This research also could help define priorities and responsibilities of stakeholders. Strategies should be ?strategic? and prioritize objectives and phase in others over time. Objectives should be time-bound and measurable to allow for monitoring and evaluation.

**Resources:**


These documents provide a platform for National and County response to addressing Iron and Folic Acid deficiencies through, among other interventions, supplementation programmes. The Kenya National Health Policy (2012-2030) and the Kenya Health Sector Strategic Plan 2012-2017 provide clear policy objectives and strategies that are supportive of nutrition. The Constitution of Kenya guarantees that every person has the right to health, which includes healthcare services. The Government of Kenya developed the Vision 2030 as its new long-term development plan for the country. To improve the overall livelihoods of Kenyans, the country aims to provide an efficient integrated and high quality affordable health care system. Under the nutrition sector, the Health Strategy aims to strengthen collaboration in order to ensure adequate nutrition for the whole population, through avoiding and managing over or under nutrition and micronutrient deficiencies. Iron and Folic Acid Supplementation was made a flagship project under the MTP 11 under Vision 2030.

According to World Health Organization it is estimated that 41.8% of pregnant women worldwide are anaemic. In Kenya the most recent micronutrient survey in the country indicated the prevalence of anaemia among pregnant women to be 55.1% and 46.4% among non-pregnant women. Anaemia is the leading indirect cause of high maternal and neonatal deaths. Iron and Folic Acid Supplementation (IFAS) for pregnant women is one of the interventions that has been recommended by WHO and implemented by the Ministry of Health to reduce anaemia levels. IFAS has been implemented through Focused Antenatal Care (FANC) and although this is the case, there have been challenges which have resulted in sub-optimal IFAS coverage rates and very low adherence rates.

This strategy provides a road map that is aimed at improving ANC attendance and IFAS coverage and utilization rates among pregnant women in Kenya in alignment with National IFAS plan targets. We call upon all partners and stakeholders to collaborate and ensure good coordination in the implementation of IFAS interventions to improve the chances of maternal and child survival.


Kenya's National Nutrition Action Plan (NAP), is derived principally from the Food and Nutrition Security Policy and Food and Nutrition Security Strategy. The Strategy provides a mechanism through which the Government will facilitate the implementation of strategic actions to improve and ensure food and nutrition security for the Kenyan population.

- **Nepal: National Anemia Control Strategy for Women and Children**

The government of Nepal, Ministry of Health and Population, has taken anemia as a most serious problem of Nepal and recognized the task of reducing its rate as a challenge. For
this, common efforts should be made from all sectors. It is necessary to include the task of reducing the rate of anemia in pregnant women in priority and prepare and enforce a strategy of identifying anemia in small age children and make proper arrangements for its prevention. This booklet presents an outline of the strategy prepared to control anemia in Nepal.

DHS Anemia Prevalence and Anemia Control Programs, January 2013

Decision Tree for Delivering Components of the Integrated Package

BCC Strategy Development
A comprehensive Behavior Change Communication (BCC) Strategy is essential to program implementation and the introduction of any new interventions that comprise an integrated package to prevent and control all causes of anemia (i.e., including helminth and malaria infections). This Strategy should identify all the people whose behaviors need to change to deliver an integrated anemia prevention and control package. While changing the behaviors of consumer and clients is important (and will be discussed under the sub-tab BCC Messages and Materials), behaviors of other people may need to be addressed for programs to work effectively. For example, the Minister of Finance may need to be convinced to fully fund the anemia prevention and control program. If the program (and its integrated package) is delivered through several sectors, a budget line item in several sectors will be needed for effective implementation.

The BCC Strategy should have defined objectives and a set of activities that support meeting these objectives. It should not be a "wish list" of everything that needs to be done. Instead, the Strategy should identify priority groups (e.g., children younger than two and pregnant women) and interventions for the integrated package. If there are multiple causes of anemia, identify champions and other partners and stakeholders who can support the delivery of the integrated package, determine roles and responsibilities of specific people who can implement the interventions, and fully cost the delivery of the package. A defined time period and a monitoring and evaluation plan to measure success also need to be included in the Strategy.

On page 29 of Anemia Prevention and Control: What Works, there is a "good practices checklist" for developing a BCC Strategy for anemia prevention and control.

Resources:

- Using of Health Belief Model to Promote Preventive Behaviors Against Iron-Deficiency Anemia among Pregnant Women

Iron-deficiency anemia is one of the most common nutritional problems during pregnancy.
The aim of this study was to evaluate the effect of education based on the Health Belief Model to promote preventive behaviors against iron-deficiency anemia among pregnant women. The study was performed on 80 pregnant women that were randomized equally into the experimental and control groups. A self-administered questionnaire based on Health Belief Model constructs was applied to gather data. The experimental group received two educational sessions. The mean age of women was 27.96±5.6 years and mean gestational age was 16.6±1 weeks. Before the intervention, no significant differences in terms of demographic characteristics and Health Belief Model constructs were found between the groups, while after the intervention, the scores of the Health Belief Model were different significantly between the control and experimental groups. Since the results of the study indicated the applicability of the Health Belief Model to promote nutritional behavior in regard to anemia in pregnancy, implementing Health Belief Model-based educational sessions in health centers is suggested to reduce complications of this problem.

• **Kenya's National Iron Folic Acid Policy Guideline**

This is a poster size version of Kenya's National Policy Guideline on Combined Iron and Folic Acid (IFA) Supplementation for Pregnant Women in Kenya. This version of the policy is meant for display in a health care facility and serve as easy reference for health care providers. It includes information about the purpose of IFA supplementation, composition, dosage, duration, target group, administration, possible side effects and the recommended action to take if they occur.

The National Iron and Folic Acid Supplementation programme is guided by different Policy and National action frameworks. These policy documents include the Kenya Food and Nutrition Security Policy (2011) and the Kenya National Nutrition Action Plan (2011-2017). These documents provide a platform for National and County response to addressing Iron and Folic Acid deficiencies through, among other interventions, supplementation programmes. The Kenya National Health Policy (2012-2030) and the Kenya Health Sector Strategic Plan 2012-2017 provide clear policy objectives and strategies that are supportive of nutrition. The Constitution of Kenya guarantees that every person has the right to health, which includes healthcare services. The Government of Kenya developed the Vision 2030 as its new long-term development plan for the country. To improve the overall livelihoods of Kenyans, the country aims to provide an efficient integrated and high quality affordable health care system. Under the nutrition sector, the Health Strategy aims to strengthen collaboration in order to ensure adequate nutrition for the whole population, through avoiding and managing over or under nutrition and micronutrient deficiencies. Iron and Folic Acid Supplementation was made a flagship project under the MTP 11 under Vision 2030.

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**Iron Supplementation: Overcoming Technical and Practical Barriers**

Iron supplementation is probably the best available option to effectively address iron deficiency in pregnant women and young children because it can be targeted specifically to these high-risk groups. However, technical and practical barriers exist: limited information on the effectiveness of supplementation interventions, side effects that affect compliance, and supply/distribution constraints. An innovative approach to addressing these constraints is the use of sprinkles of powdered, microencapsulated ferrous fumarate that can be added directly to any semi-liquid food without changing their taste or consistency. This technique has been tested in initial trials in Ghana and found to be as effective as iron drops. Another approach to
improve the effectiveness of iron interventions is through information, education and communication (IEC) programs. These interventions can help modify consumer behavior in some cases, but in some countries, geographic location, variations in language and population size can make the cost of IEC programs very high. IEC strategies in Indonesia aimed at increasing demand for iron supplements by systematic dissemination of specific messages, improving the quality and variety of tablets, increasing the availability and access to supplements by engaging the commercial sector, enrolling traditional birth attendants and other community volunteers in selling supplements. Key issues to be addressed include clarifying optimal starting points and duration of supplementation interventions?based on individual status or population prevalence, defining hemoglobin and ferritin cutoffs at which treatment should be instigated and evaluating the effectiveness of intermittent supplementation with multiple micronutrients.

- **MotherCare Indonesia Iron Pill Taking Directions for Drug Sellers**

These materials are intended to provide local pharmacy workers with clear and concise indications to guide users of iron supplementation pills on dosage and proper use.

**BCC Messages and Materials**

This tab focuses on materials and messages for iron-folic acid supplementation and suggest integration of other interventions to control anemia but the formative research leading to the identification of these messages and development of the materials can be expanded to include helmith and malaria control, improving dietary intake, and other areas. Click here for an excellent presentation on demand-side issues for IFA supplementation.

In most countries, when women are given iron folic-acid (IFA) tablets, the only message they receive is ?take one per day.? There are no additional messages that reinforce why women should be taking IFA, how long they should take them for, or that side effects, such as
black stools, constipation, or indigestion, may occur and how to manage them. Women within and among countries may have varying opinions and views about anemia, its symptoms and importance, and how to prevent and treat it. Mothers may also have different opinions about how anemia and taking IFA supplements affects the health and size of their babies when they are born (Galloway et al, 2004).

Unfortunately, this kind of information is rarely collected but, when it is collected, it can be used to craft evidence-based behavior change communication (BCC) messages and materials, such as counseling cards, to ensure women and mothers practice health behaviors on a daily basis. For the anemia prevention and control integrated package, daily practices should include women, mothers, and children taking or giving iron, sleeping under long-lasting, insecticide-treated nets (LLTNs), and consuming the appropriate foods that will facilitate absorption of available iron. Other healthy practices that are part of the integrated package include women obtaining intermittent presumptive treatment in pregnancy (IPTp) and children being treated for malaria where malaria is endemic. In addition, pregnant women and children one year of age and older should receive twice-yearly deworming medication where the prevalence of hookworm and urinary schistosomiasis is high (20-30% or greater).

Formative research should be conducted with consumers and people who support or influence consumers to use a product. This research is essential in developing evidence-based messages to ensure full-uptake of any regimen. For IFA, women prefer a small, coated (easier to take) and red pill because they associate it with the color of blood. An example of a formative research instrument to determine women’s perceptions of anemia and taking IFA can be found here.

Messages to give with IFA supplementation. Based on research by the USAID-funded, John Snow, Inc.-implemented MotherCare project, messages and materials for maternal anemia prevention and control programs have been developed and can be found in the resources section here.

Messages and materials also can be developed to use during social mobilization of the community for deworming campaigns or promotion of LLINs use. Existing research on women’s perceptions of anemia and taking IFA supplements has found that they recognize the signs and symptoms of anemia. The multiple causes of anemia, including malaria and helminth infections, should link women’s perceptions of anemia and its negative effects to promote healthy behaviors related to controlling these two infections. Formative research to promote micronutrient supplements for children also has been conducted in developing countries.

MCHIP is soliciting examples of other formative research instruments and studies, messages, and materials that have been developed related to the prevention and control of anemia in women, young children, school-age children, and others using an integrated package or individual components of the package. Our interest is in examples related to improving the dietary intake of iron, the use of IFA supplements, malaria, and helminth control programs. Any age group is of interest. Please share what resources you can on this site by contacting us at sstraubinger@path.org or agottwalt@path.org.

Resources:
Using of Information-Motivation-Behavioral Skills Model on Nutritional Behaviors in Controlling Anemia Among Girl Students

High prevalence of iron deficiency anemia is the most common nutritional problem worldwide, which also is reported among Iranian adolescent girls. This problem results from the inadequate intake of dietary iron or low iron intake in diet. Regarding the application of health education models, the aim of this study was to determine the effect of educational program based on Information?Motivation?Behavioral skills (IMB) model in relation to preventive nutritional behaviors against iron deficiency anemia. In this study, 120 participants were selected among Iranian high school girls. The participants were equally allocated to experimental and control groups. The educational intervention was performed as a four-hour workshop designed based on the IMB model constructs for the experimental group. The data were collected using a standard questionnaire based on the IMB constructs, measuring body mass index, and determining average heme iron consumption. The data were gathered before and 3 months after the intervention. The experimental group after the intervention showed a significant increase compared to the control group in the mean scores of IMB with regard to nutritional iron deficiency anemia. In the experimental group, the average daily intake of dietary heme iron increased by 52.0±10.0 mg. Regarding the positive effect of education in promoting iron-rich diets in high school girls, workshops based on the IMB model are suggested to be held in schools aiming at preventing iron deficiency anemia.

Kenya Poster 2: Promoting Iron Folic Acid Supplementation (Female Health Worker)

This poster was created to help motivate health workers and for display in health facilities. The message is to "Be a champion; Give Pregnant Women the Chance to have a Healthy Pregnancy". It encourages the health worker to counsel and support pregnant women on the use of iron folic acid supplements (IFAS) and highlights the benefits of women taking them: 1) prevent anaemia 2) prevent risk of low birth weight 3) prevent unsafe pregnancy and complications during delivery.

Kenya Poster 3 (Regional): Promoting Iron Folic Acid Supplementation Targeting Pregnant Women (Kiswahili)

These three posters are targeted to pregnant women and intended to help raise awareness of the importance of pregnant women taking iron folic acid supplements (IFAS) during
pregnancy. Each poster features a pregnant woman representative of one of three regions in Kenya (national, coastal and north east) and encourage pregnant women to take IFAS. Also attached is a word document with the English translation of these posters; all three posters include the same information.

- **Kenya's Regional Iron Folic Acid Supplementation Calendars (Kiswahili)**

Women report that forgetting to take IFA supplements is one of the main reasons they don't take IFA. As part of its efforts to improve its IFA supplementation program and help women remember to take all their IFA, Kenya's MOH has developed a calendar for pregnant women to record when they take IFA. These three iron folic acid (IFA) calendars each feature a pregnant woman representative of one of three regions in Kenya and aims to help remind women to take their IFA supplementation daily during their pregnancy. There is a calendar for each month of pregnancy as well as information reinforcing the importance of taking IFA supplements, coming regularly for ANC, sleeping under a mosquito net and eating a variety of nutritious foods throughout pregnancy.

- **Kenya's Regional Pregnant Woman's Iron Folic Acid Information Leaflets (Kiswahili)**

This informational booklet for pregnant women is offered in three versions representative of women from different regions of Kenya and is intended to guide pregnant women on iron folic acid supplementation (IFAS) during pregnancy. The leaflets are available in three versions: for national use, use in the coastal region of Kenya and in the north-eastern region of Kenya.

- **Kenya Poster 4: Promoting Iron Folic Acid Supplementation to Potential Mother (Kiswahili)**

This poster is targeted to women of child-bearing age and features a young Kenyan woman. The message encourages women of child-bearing age to take folic acid before they become pregnant. A word document is attached for translation of these messages from Kiswahili into English.

- **Kenya Poster 5: Promoting Iron Folic Acid Supplementation for Healthy Families (Kiswahili)**
This poster is primarily targeted to fathers or potential fathers as well as mothers and potential mothers. It features a healthy looking family of three and encourages pregnant women to take iron folic acid supplements (IFAS) during their pregnancy. Attached is a word document of the Kiswahili to English translation.

• **Kenya's Iron Folic Acid Supplementation Trainer's Guide for Healthcare Providers**

IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focussed Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates. This training has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017. IFAS is one of the performance indicators for the Cabinet Secretary, Ministry of Health, with coverage targets set from a baseline of 8% to 25% improvement by June 2014. Therefore, this course is designed to be integrated into or be delivered as part of focused antenatal care training. It is designed for in service and refresher training, in continuing medical education sessions, on-job training and continuous professional development.

• **Kenya's Iron Folic Acid Supplementation Participant's Manual for Healthcare Providers**

**About this Manual and Training Guide:** IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focused Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates.

This manual is meant to go along with the IFAS Trainer's Guide and has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017.
**Course Participants:** This training is targeted to frontline ANC service providers, including health managers, nurses, nutritionists, and community strategy coordinators. The training module is competency-based and can be used to train health workers at a wide range of education levels such as diploma holders, certificate levels, degree holders, etc.

**Training Approaches:** This training approach is based on adult learning principles, that is, the belief that adults learn best in interactive sessions that include practice between the trainers and the trainees. Structured learning activities will be used including presentations, group discussions, demonstrations, role plays, and practical exercises.

The method of training recommended for use is Teach-back. This methodology is successful because it is based on adult learning principles, adults want training that is participatory, and they want to gain knowledge and skills applied to their jobs, they would like to share knowledge and experiences. The participants receive positive reinforcement and feedback about areas of weakness and practice teach-back training using the course content in a safe and supportive environment.

**Instructions on Use:** The IFAS course includes a Trainer's Guide and Participant Manual. The course follows a modular approach. It is divided into five independent modules that can stand alone or be combined into a 2 1/2 day package of instructional material, as needed. Each module is divided into sessions, which are further divided into topics. The learning objectives of each session are followed by materials needed, advance preparation, and training directions, including cues for brainstorming and group work.

• **Improving the Chances that Nutrient Supplements Will Make a Difference**

Presentation: Global Meeting, Implementing Effective Programs to Prevent Pre-Eclampsia/Eclampsia and Anemia to Improve Maternal and Newborn Outcomes

• **Kenya's Regional Community Health Worker Iron Folic Acid Supplementation Counseling Guides**

This counseling guide is targeted to community health workers providing anemia prevention counseling to pregnant women and family members at the household level. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout their pregnancy. An English version is not available here, but you can refer to the English versions of "Kenya's IFA Supplementation Participant's Manual for Health Care Providers;" "Kenya's IFA Supplementation Trainer's Guide for Health Care Providers;" and "Kenya's Regional
Kenya's Regional Health Care Provider Iron Folic Acid Supplementation Counseling Guides

This dialogue guide or counseling guide is targeted to health care providers providing anemia prevention counseling to pregnant women and family members within a health facility. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout pregnancy. It is available here in three different versions representative of the three regions of Kenya (national, north eastern and the coast). For similar resources, see also "Kenya’s IFA supplementation participants manual for health care providers" (in English); "Kenya’s IFA supplementation trainer’s guide for health care providers" (in English) and "Kenya’s IFA supplementation counseling guide for community health workers" (in Kiswahili).

Kenya Poster 1: Promoting Iron Folic Acid Supplementation (Male Health Worker)

This poster was created for display in health facilities to help motivate health workers to "Give Complete and Accurate Information on Iron Folic Acid Supplements". This particular poster highlights four points a health worker should ensure they provide pregnant women regarding iron folic acid supplementation (IFAS): 1) Ensure that you counsel mothers on benefits of IFAS 2) Ensure you provide IFAS to all pregnant women regardless of their hb (hemoglobin) status 3) Ensure you provide complete dosage to be taken daily from conception to delivery and 4) Ensure you counsel pregnant mothers on managing side effects of IFAS.

Anaemia Prevention Badge Project

Background: FANTA and the Regional Center for Quality of Health Care (RCQHC), in partnership with the African Regional Office of the World Association of Girl Guides and Girl Scouts (WAGGGS), designed the Girl Guides Anemia Prevention Badge Project, a program to reach adolescent girls in East and Southern Africa with information and activities on anemia prevention and control.

Methods: Under the program, Girl Guides (ages 7-18) can earn a badge in anemia prevention through educational programs and community involvement in anemia control. FANTA and RCQHC developed an Anemia Prevention Badge Handbook and Workbook for
the Girl Guides as well as a training manual for Girl Guide leaders.

Results: Anemia and iron deficiency remain at epidemic levels among women and children in many nations. Iron deficiency anemia (IDA) is associated with 22% of maternal deaths and 24% of perinatal deaths, according to a recent meta-analysis.

Conclusions: Correcting anemia of any severity reduces the risk of death, the analysis also showed. These estimates of the maternal and perinatal deaths associated with IDA underscore the importance of implementing a package of interventions, such as the Girl Guides badge project, to address the multiple causes of anemia.

Both the English and French versions are available for download via the link below. Due to file size, the English version of the Guiders’ Training Manual is also available for download by section.

Women's Perceptions of Iron Deficiency and Anemia Prevention and Control in Eight Developing Countries
The World Health Organization estimates that 58% of pregnant women in developing countries are anemic. In spite of the fact that most ministries of health in developing countries have policies to provide pregnant women with iron in a supplement form, maternal anemia prevalence has not declined significantly where large-scale programs have been evaluated. During the period 1991-98, the MotherCare Project and its partners conducted qualitative research to determine the major barriers and facilitators of iron supplementation programs for pregnant women in eight developing countries. Research results were used to develop pilot program strategies and interventions to reduce maternal anemia. Across-region results were examined and some differences were found but the similarity in the way women view anemia and react to taking iron tablets was more striking than differences encountered by region, country or ethnic group. While women frequently recognize symptoms of anemia, they do not know the clinical term for anemia. Half of women in all countries consider these symptoms to be a priority health concern that requires action and half do not. Those women who visit prenatal health services are often familiar with iron supplements, but commonly do not know why they are prescribed. Contrary to the belief that women stop taking iron tablets mainly due to negative side effects, only about one-third of women reported that they experienced negative side effects in these studies. During iron supplementation trials in five of the countries, only about one-tenth of the women stopped taking the tablets due to side effects. The major barrier to effective supplementation programs is inadequate supply. Additional barriers include inadequate counseling and distribution of iron tablets, difficult access and poor utilization of prenatal health care services, beliefs against consuming medications during pregnancy, and in most countries, fears that taking too much iron may cause too much blood or a big baby, making delivery more difficult. Facilitators include women's recognition of improved physical well being with the alleviation of symptoms of anemia, particularly fatigue, a better appetite, increased appreciation of benefits for the fetus, and subsequent increased demand for prevention and treatment of iron deficiency and anemia.

- **MotherCare Indonesia Anemia Control Counseling Cards**

- **MotherCare Indonesia Iron Pill Reminder**

  This card is an easy to use reminder for pregnant/ postpartum women. A box is used to record each iron pill dosage, during 90 days of the pregnancy and 40 days postpartum.

- **MotherCare Indonesia Religious Leader Poster**
In the West-Java subdistrict of Tanjunsari, Indonesia, MotherCare worked through the University of Padjadjaran to address issues of referral and emergency obstetric care. Birthing homes with radios were established in ten of the 27 villages in the district, where trained nurse/midwives provided maternity care on a regular basis. While reduction in maternal mortality after such a short implementation period is difficult to demonstrate, all projects showed improvements in referral and in reduction in perinatal mortality.

**Counseling Messages for IFA Supplementation**

**Dose:** Take one per day and take at least 180 tablets during your pregnancy (and as early as possible in your pregnancy). Come back next month to receive your next package or sachet of 30 tablets and other services at ANC. You should also take one IFA tablet per day for 40 days after you deliver.

**Why:** IFA is good for you and your baby and will make you and your baby healthy and strong.

**How to Take:** Take in between meals or before going to bed with a little fruit juice. Do not take with tea or coffee, as these drinks decrease the effect of IFA.

**Side Effects:** You may experience some discomfort (stomach ache, diarrhea, constipation) or black stools when taking IFA. These side effects are not serious or harmful, and in most women they subside in a few days. If IFA continues to cause discomfort, try taking it with meals.

**Safety:** IFA is safe for mothers and their unborn babies. IFA will not hurt you or your baby. It will not make your baby bigger, cause high blood pressure, or give you too much blood. IFA tablets are designed and prescribed for your use only; do not share them with other family members. Keep IFA supplements out of the reach of children.

**Resources:**

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pregnancy. An English version is not available here, but you can refer to the English versions of "Kenya’s IFA Supplementation Participant's Manual for Health Care Providers;" "Kenya’s IFA Supplementation Trainer's Guide for Health Care Providers;" and "Kenya's Regional Health Care Provider IFA Supplementation Counseling Guides" to get an idea of the messages that are provided in this guide.

• Kenya Poster 1: Promoting Iron Folic Acid Supplementation (Male Health Worker)

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• Kenya Poster 3 (Regional): Promoting Iron Folic Acid Supplementation Targeting Pregnant Women (Kiswahili)

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This informational booklet for pregnant women is offered in three versions representative of women from different regions of Kenya and is intended to guide pregnant women on iron folic acid supplementation (IFAS) during pregnancy. The leaflets are available in three versions: for national use, use in the coastal region of Kenya and in the north-eastern region of Kenya.

- **Kenya Poster 4: Promoting Iron Folic Acid Supplementation to Potential Mother (Kiswahili)**

This poster is targeted to women of child-bearing age and features a young Kenyan woman. The message encourages women of child-bearing age to take folic acid before they become pregnant. A word document is attached for translation of these messages from Kiswahili into English.

- **Kenya Poster 5: Promoting Iron Folic Acid Supplementation for Healthy Families (Kiswahili)**

This poster is primarily targeted to fathers or potential fathers as well as mothers and potential mothers. It features a healthy looking family of three and encourages pregnant women to take iron folic acid supplements (IFAS) during their pregnancy. Attached is a word document of the Kiswahili to English translation.


**About this Manual and Training Guide:** IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focused Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates.

This manual is meant to go along with the IFAS Trainer's Guide and has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS
among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017.

**Course Participants:** This training is targeted to frontline ANC service providers, including health managers, nurses, nutritionists, and community strategy coordinators. The training module is competency-based and can be used to train health workers at a wide range of education levels such as diploma holders, certificate levels, degree holders, etc.

**Training Approaches:** This training approach is based on adult learning principles, that is, the belief that adults learn best in interactive sessions that include practice between the trainers and the trainees. Structured learning activities will be used including presentations, group discussions, demonstrations, role plays, and practical exercises.

The method of training recommended for use is Teach-back. This methodology is successful because it is based on adult learning principles, adults want training that is participatory, and they want to gain knowledge and skills applied to their jobs, they would like to share knowledge and experiences. The participants receive positive reinforcement and feedback about areas of weakness and practice teach-back training using the course content in a safe and supportive environment.

**Instructions on Use:** The IFAS course includes a *Trainer’s Guide* and *Participant Manual*. The course follows a modular approach. It is divided into five independent modules that can stand alone or be combined into a 2 1/2 day package of instructional material, as needed. Each module is divided into sessions, which are further divided into topics. The learning objectives of each session are followed by materials needed, advance preparation, and training directions, including cues for brainstorming and group work.

## Logistics and Supplies

Supplies are still the major limiting factor in delivering the integrated package. From Demographic and Health Surveys, coverage of IFA supplementation, IPTp, and deworming are unacceptably low in most countries. Supply chains have improved for some commodities, particularly long-lasting insecticide-treated bednets and ARVs. But for most anemia control commodities, coverage remains low. Lessons can be learned, however, from logistics supply strengthening programs. Click here and here for presentations on improving supplies.

- A first step to improving supplies and logistics is to accurately estimate the commodities for the integrated package. Forecasting is often based on use rather than need. That is, supplies are ordered based on the number of women coming in for antenatal care rather than the estimated number of pregnant women in the catchment area. Where use of ANC is high, forecasting by use works but where it is not high, forecasting underestimates the need. In addition, supplies may be determined by Central Supplies (usually the main storage site for drugs and IFA in most countries), based on no estimates of pregnant women, and pushed
out? to health centers rather than health centers doing the forecasting themselves and ?pulling? supplies from Central Health Supplies. However, if ANC use is limited, supplies need to be available in the community (delivered by community workers or drug sellers) in order to ensure they are used. A simple method for calculating IFA supplements for routine use in a catchment area where ANC use is low or late:

Total population x fertility rate (or 4% of the total population if the fertility rate is not known) x 180 IFA tablets (required amount for supplementation) = Total number of tablets

In Thailand, each fiscal year, the central division of the Ministry of Public Health (MOPH) sets funds aside to purchase IFA tablets (Winichagoon, 2002) but the IFA is estimated at the provincial level not the national level. The estimates are based on the number of pregnant women in the provinces or attending ANC which works well because ANC use is high. Estimates need to include additional commodities?sulphadoxine-pyrimethamine (SP) for treatment of malaria and severe anemia. Knowledge about the prevalence of anemia and malaria will be needed to estimate the additional SP and IFA needed for treatment. These estimates should be done yearly. Data on prevalence of anemia can come from Demographic Health Surveys, other survey estimates, or from the WHO database on anemia.

- Bottlenecks for logistics and supply systems for anemia control commodities must be identified and cleared. It is probably most effective to do this in coordination with efforts to improve the logistics situation for all drugs. In India, the IFA supply system was decentralized to the state and district levels and a special unit to monitor supplies was created (Galloway, 2003).

- Providing a buffer stock or other back-up sources for anemia control commodities is good ensure to prevent lengthy stock-outs. To ensure a continuity of supplies, an additional buffer stock of 20% of the estimated need should be provided. In Thailand, multiple mechanisms exist to ensure no gaps in supplies occur. Health clinics maintain funds to use when stocks run low which they can use to purchase IFA at emergency depot centers without central level approvals.

- Provide anemia control commodities through community-based and private/retail outlets. Distribution of long-lasting, insecticide-treated bed nets (LLINs) already exists. These nets may not get to pregnant women and children without intervention by the public health sector. Vouchers can be provided to women at ANC to purchase LLINs which works to attract women to ANC and provide a partial or complete subsidy directly to women to obtain their own LLIN. Small shops also can be used to sell IFA which may be convenient for women for resupply. Shop owners should be given messages about taking IFA (why, when, how often, how to manage side effects). In Indonesia, the Ministries of Health and Industry teamed up to create packaging for private sector sales of IFA. The packaging was similar to the IFA sachets obtained through the public health sector so women could easily identify the right product.

Resources:
Supply Chain Considerations

Objectives of the Presentation:

1. To highlight the supply chain barriers to successful IFA supplementation.

2. To present experiences from our programs about supply chain considerations we prioritise and focus on to ensure uninterrupted, timely, adequate and quality stocks of IFA.

Pharmaceutical Management for Micronutrients and Anemia-Reduction Medicines

Supply side considerations

Monitoring Drug Coverage for Preventive Chemotherapy

In a drive to promote the control and reduction of morbidity attributable to lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiasis, the World Health Organization, through its Department of Control of Neglected Tropical Diseases, has developed a rapid-impact strategy known as preventive chemotherapy. This public health intervention depends on the integration and delivery of a tried and tested drug package. It may also form a component of the approach for the control and reduction of morbidity caused by trachoma known as SAFE (Surgery, Antibiotics, Facial cleanliness and Environmental improvement). How to plan and use preventive chemotherapy is explained in the manual Preventive chemotherapy in human helminthiasis, published by the Organization in 2006. Health professionals should note that preventive chemotherapy is one of the elements needed to overcome neglected tropical diseases; case management, health education, improved sanitation and clean water supplies are equally important.

Screening, Monitoring and Evaluating
Screening for Anemia

All women should receive routine doses of IFA, IPTp, and deworming during pregnancy, and this should not be dependent on screening. Ideally, women and children should receive a test for anemia and, if they are anemic, they should be given treatment doses of IFA and tested for malaria and helminths. If the test is positive for these infections, they should be treated for malaria and helminths. Although screening for anemia is the protocol for most Ministries of Health, screening is often not done because the supplies for screening are not available. Where screening is not consistently available, clinical screening by checking for pallor of the palms or conjunctiva for women and palms for young children is fairly sensitive in identifying severe anemia (Dusch et al, 1999; Stoltzfus et al, 1999). Individuals with pallor should be treated for iron deficiency anemia and malaria (if endemic) and possibly dewormed, if worm loads are known to be high. If pallor is not corrected, women or children should be referred to a health center or hospital where accurate tests for anemia are available. New testing devices are under development that would not require that blood is taken. Click here to learn more about these non-invasive anemia tests.

Monitoring and evaluation activities should be designed and incorporated into anemia control programs from the beginning.

Monitoring collects information about programs on a continual basis. Process indicators provide insight as to how the program is working and allow for mid-course changes and adjustments. Components of a process evaluation can assess if the program is working as originally planned, and allows programmers to learn about which components are /are not working and make necessary corrections. Outcomes that can be measured by process evaluation are listed below (taken from: Stotlzful et al, 2001).

Self-monitoring can be effective. A woman who receives a reminder card, like the one above
from India and another one from Indonesia listed in the resources below, can record when she takes her IFA and then share it with her health care provider when she returns for a resupply. This could be the basis for compliance monitoring by health workers. This contact also can be used to discuss compliance with the mother and reinforce the importance of taking IFA every day.

**Measurable Outcomes in Process Evaluation**

- A budget dedicated and spent
- Supplements and other supplies procured
- Quality of supplements and commodities
- Provision of adequate storage
- Distribution system in place
- Availability of supplements and commodities at distribution points
- Training activities planned and conducted for health care workers and others as needed
- Knowledge, attitudes, and practices of health care workers and other agents
- Community education programs in place
- Knowledge, attitudes, and practices of community leaders, family decision makers, and mothers
- Number of supplements and commodities distributed to women/infants
- Number of supplements and commodities reported received by mothers/mothers of infants
- Number of supplements and commodities appropriately used by mothers/infants
- Program coverage (percentage of intended recipients who actually received supplements/commodities)
- Number of supplements/commodities consumed by women/infants

Measuring changes in iron deficiency anemia in target groups can be ascertained through impact evaluations. Nationally-representative surveys are one method of providing information on coverage and compliance of iron supplementation and other anemia control commodities. Using sentinel sites, where anemia testing is conducted with a selected population in a geographic area, is another method of monitoring impact over time. Nationally-representative surveys should take place every 3-5 years, such as through Demographic Health Surveys.
Anemia prevalence should be disaggregated by severe, moderate, mild, and all anemia prevalence. As countries make progress in reducing moderate and severe anemia, mild anemia prevalence may increase and overall anemia prevalence may stay the same. This decrease in the proportion suffering from moderate and severe anemia and increase suffering from mild anemia should be interpreted as a success story.

The Demographic and Health Surveys (DHS) have collected information on use of IFA supplements (primarily in pregnant women, although some surveys have asked if children receive iron) before 2000 and anemia prevalence since the early 2000s. DHS also collects information on iron-rich foods consumed by children. However, the collection of these indicators is not consistent across countries. It should be noted that DHS mother’s questionnaire asks questions of women with a child younger than five. The question for IFA supplementation asks women 15-49 months with a child born in the past five years how many days they received or took iron or iron syrup in their last pregnancy, but does not ask how many IFA supplements women who are currently pregnant have consumed. Asking pregnant women what they have taken would not be representative of the potential number of IFA supplements they could take throughout the course of pregnancy, since they have not finished their pregnancy.

In some surveys, this question is reported as the IFA supplements women received or taken. If presented as the number of IFA supplements women took, this is often misinterpreted as a measure of compliance. Since supplies are a limiting factor for IFA supplementation programs, coverage rates are dependent on supplies. To get more information about compliance with IFA supplementation, one would need to ask women how many IFA supplements they received in their last pregnancy (either given at the clinic or purchased) and, of those IFA supplements, how many supplements women took.

For anemia testing, women 15-49 years of age are tested. DHS also disaggregates anemia prevalence by maternity status (pregnant, breastfeeding, and neither pregnant or breastfeeding).

Resources:

- **Diagnosis of Iron Deficiency Anemia Using Density-Based Fractionation of Red Blood Cells**

Iron deficiency anemia (IDA) is a nutritional disorder that impacts over one billion people worldwide; it may cause permanent cognitive impairment in children, fatigue in adults, and
suboptimal outcomes in pregnancy. IDA can be diagnosed by detection of red blood cells (RBCs) that are characteristically small (microcytic) and deficient in hemoglobin (hypochromic), typically by examining the results of a complete blood count performed by a hematology analyzer. These instruments are expensive, not portable, and require trained personnel; they are, therefore, unavailable in many low-resource settings. This paper describes a low-cost and rapid method to diagnose IDA using aqueous multiphase systems (AMPS)?thermodynamically stable mixtures of biocompatible polymers and salt that spontaneously form discrete layers having sharp steps in density. AMPS are preloaded into a microhematocrit tube and used with a drop of blood from a fingerstick. After only two minutes in a low-cost centrifuge, the tests \((n = 152)\) were read by eye with a sensitivity of 84\% (72?93\%) and a specificity of 78\% (68?86\%), corresponding to an area under the curve (AUC) of 0.89. The AMPS test outperforms diagnosis by hemoglobin alone (AUC = 0.73) and is comparable to methods used in clinics like reticulocyte hemoglobin concentration (AUC = 0.91). Standard machine learning tools were used to analyze images of the resulting tests captured by a standard desktop scanner to 1) slightly improve diagnosis of IDA? sensitivity of 90\% (83?96\%) and a specificity of 77\% (64?87\%), and 2) predict several important red blood cell parameters, such as mean corpuscular hemoglobin concentration. These results suggest that the use of AMPS combined with machine learning provides an approach to developing point-of-care hematology.

- **Kenya's Algorithm or Flow Chart for Counseling Women on Iron Folic Acid Supplementation**

Algorithm or Flow Chart for Iron and Folic Acid Supplementation (IFAS) for pregnant and non-pregnant women

- **Prevention and Control of Iron Deficiency: Policy and Strategy Issues**

Substantial efforts have been made in the past several decades to implement programs to reduce iron deficiency. Yet, compared with other micronutrients such as vitamin A and iodine, overall progress in reducing iron deficiency has been limited. Such limited progress is not attributed to a lack of scientific knowledge about the prevalence, causes or consequences of iron deficiency, but to limited implementation of effective interventions and ineffective communication tools. The challenge is to coordinate and balance research efforts more constructively with the implementation of practical and effective intervention programs. More attention must be paid to evaluating the operational feasibility of various intervention strategies to demonstrate their effectiveness under normal field conditions. Moreover, intervention efforts must be supported by substantially increased attention to communications to achieve effective advocacy for policy support and resource mobilization, foster.
partnerships and alliances, clarify priority target groups, including infants and young children, and support behavioral change. Through collaboration, researchers, program implementers and communicators can achieve substantial progress in reducing iron deficiency.

- **Measuring Performance: A Strategy to Improve Programs**

This article stresses the importance of evaluation as a tool for improving the design and implementation of effective programs to reduce iron deficiency anemia and to advocate for their continued and increased support. Current concepts in program evaluation are applied to the specific issues relevant to iron programs. Evaluations should be designed to meet the needs of specific audiences (e.g., community members, program implementers, policymakers, donors and researchers) and to answer specific questions. Evaluations might answer questions about provision, coverage or impact. The choice of indicators for evaluating impact of iron programs is discussed and illustrated with recent examples. Evaluation design can be broadly categorized as monitoring, plausibility evaluations and probability evaluations. These designs differ in cost and also in the strength of evidence that they provide; however, each has appropriate uses. It is important to document program costs in the evaluation process as policymakers and donors weight impact against costs. To be useful, evaluation findings must be disseminated, usually to multiple audiences. This requires allocation of time and resources and attention to the needs of various stakeholders.

- **Defining Iron-Deficiency Anemia in Public Health Terms: A Time for Reflection**

This paper provides a historical context for this meeting, which aimed to examine critically the way we have defined iron-deficiency anemia as a public health problem. The terms and concepts used to define the problem are reviewed first, followed by estimates of the global prevalence of the problem from 1985 to 2000. It is argued that recent estimates are not credible and that we must redefine the problem in terms that are important, measurable and addressable. This meeting was designed to take first steps toward that goal, namely, to identify the causal factors (e.g., iron deficiency vs. iron-deficiency anemia vs. severe anemia from any cause) that link iron-deficiency anemia to important health outcomes and to estimate the magnitude of their effects in public health terms.

- **Rethinking Anaemia Surveillance**

Iron deficiency and iron-deficiency anemia are common in young children, and there is substantial evidence that iron deficiency has adverse effects on child health and development. Therefore, provision of additional iron to infants and young children who are
iron deficient should be a public health priority.

- **MotherCare Indonesia Iron Pill Reminder**

  This card is an easy to use reminder for pregnant/ postpartum women. A box is used to record each iron pill dosage, during 90 days of the pregnancy and 40 days postpartum.

**Country and Field Experience**

*The Anemia Prevention and Control Toolkit* is collecting country and field experiences on anemia control programs, implemented as either single components (e.g., malaria control) or an integrated package that addresses several causes of anemia. There are countries that have made progress in improving anemia control programs and reducing anemia, either using an integrated approach or making progress through one intervention. Sub-tabs to the right give information on Nepal, Nicaragua, Indonesia, and Thailand, and most recently, information on work in Kenya to improve anemia prevention and control. Kenya resources, policies, plans, and strategies, along with various behavior change communication (BCC) materials targeted to pregnant women as well as health workers, can be found under the Kenya sub-tab. In addition, six short videos of an interview with Madame Terrie Wefwafwa, Head of the Ministry of Health’s Division of Nutrition, conducted in August 2013 highlight how Kenya has improved their iron-folic acid supplementation program and how other sectors are involved in anemia control.

**Resources:**

- **Are We Making Progress on Reducing Anemia in Women? Cross-country Comparison of Anemia**
Prevalence, Reach, and Use of Antenatal Care and Anemia Reduction Interventions

**Purpose:** The purpose of this report is to assess the progress being made on reducing the burden of anemia in women. It also aims to stimulate global and national action to improve the reach and delivery of proven anemia reduction interventions targeting pregnant women.

**Methods:** Data from DHS surveys conducted from 2004 to 2008 were used for cross-country and over-time comparisons of anemia prevalence in pregnant and non-pregnant women. These data were also used to make cross-country comparisons of the major service delivery platform for maternal anemia interventions, including antenatal care visits, and the coverage and/or reach of evidence-based anemia reduction interventions—iron tablet consumption, use of intermittent presumptive treatment for malaria, use of insecticide-treated mosquito nets, and the use of de-worming medicines.

**Findings:**

- The burden of anemia in pregnant women remains serious and unacceptably high.
- Reducing the anemia burden in pregnant women has progressed little, especially in African countries.
- The burden of anemia in non-pregnant women, while somewhat lower than that for pregnant women, puts women at risk of anemia when they become pregnant.
- A high proportion of pregnant women participate in at least one antenatal care (ANC) visit, but the correlation between ANC use and iron tablet consumption is weak.
- In places where access to and participation in ANC care clinics is adequate, other factors need to be examined such as inadequate supply of iron tablets, which can be affected by cost and weak logistic systems; poor quality of counseling by health workers about the need for iron supplementation and its potential benefits and side-effects; lack of knowledge and concern about maternal anemia by both pregnant women and health care providers; and low motivation and some resistance among pregnant women to consume the iron supplement because of undesirable characteristics of the iron tablets or side effects experienced by women.
- Access to and participation in ANC services is not high in all countries.
- Strong evidence of inequitable access to and participation in ANC exist for poorer, less educated, and/or rural women in countries such as Bangladesh, Chad, Egypt, Ethiopia, Nepal, Niger, Nigeria, and Pakistan.
- Improved coverage of intermittent preventive treatment for pregnant women (IPTp) in areas with high malaria endemicity is needed.
- There is a need to increase use of insecticide-treated bednets (ITN) among all household members in malaria-endemic areas.
- There is a need to increase presumptive treatment of hookworms in areas where hookworms are known to be endemic.
Kenya

Kenya’s Anemia Prevention and Control Experience:

Data from Kenya’s 1999 National Micronutrient Survey indicate that 55% of pregnant women are anemic and 2010 data from the Malaria Indicator Survey indicate that 27% of Kenyan children 6 months to 14 years are anemic, with 5% of children 6-59 months severely anemic and 41% moderately anemic. More will be known about the current prevalence of anemia when new data from Kenya’s 2011 National Micronutrient Survey is made available. In recent years, Madame Terrie Wefwafwa, the Head of the Division of Nutrition (DON) within Kenya’s Ministry of Health, has played an instrumental role in moving Kenya’s anemia prevention and control agenda forward and improving program implementation in order to address the country’s high anemia rates.

In an effort to capture and share the challenges Kenya has faced, achievements made and resources developed, members of the MCHIP nutrition team interviewed Madame Wefwafwa in August 2013. The result is six, five-minute videos that encapsulate Kenya’s recent efforts and plans to prevent and treat anemia among women and children. You can find links to all six videos below. Also, at the bottom of this page you will find Kenya’s anemia-related resources including policies, plans and strategies along with behavior change communication (BCC) materials targeted directly to pregnant women as well as health workers.

Video 1: The State of Anemia in Kenya

This video discusses the anemia prevalence in pregnant women and young children in Kenya. It also covers outcomes from the MCHIP-supported, multi-stakeholders’ meetings and the creation of a five-year action plan to reduce iron-deficiency anemia among pregnant women.
**Video 2: Kenya's Iron-Folic Acid (IFA) Supplementation Program for Pregnant Women**

Learn about Kenya's IFA program for pregnant women - challenges they face with ensuring adequate supplies and generating demand as well as their plan moving forward. "We hope to move from our current 2.5% (coverage of women receiving 90+ tablets) of IFA supplements to our target by the end of this plan period to have reached about 80% coverage."

**Video 3: An Integrated Approach to Anemia Prevention and Control**

In this video, Madame Wefwafwa addresses the question, "is Kenya utilizing other programs and approaches, besides iron-folic acid (IFA) supplementation, to help address anemia?"

**Video 4: Generating Demand for IFA Supplementation during Pregnancy among Health Workers**

Watch this video to see Madame Wefwafwa describe Kenya's national policy guideline on the use of IFA supplementation for pregnant women that are meant for display in all health facilities along with motivational posters for health workers about being a champion and helping to ensure all pregnant women are counseled about IFA.

**Video 5: Behavior Change Communication (BCC) Tools Targeting Pregnant Women**

Madame Wefwafwa shows Kenya's new BCC package of tools for IFA supplementation by geographic region and includes motivational posters, flip charts, and brochures for facility-based and community health workers as well as pregnant women themselves.

**Video 6: The Way Forward: Speaking to Stakeholders and Donors**

Here, Madame Wefwafwa speaks directly to donors and other stakeholders about the need for support to scale-up IFA supplementation and "disseminate the message as well as the spirit to the county levels."

**Resources:**

- Kenya Poster 3 (Regional): Promoting Iron Folic Acid Supplementation Targeting Pregnant Women (Kiswahili)
These three posters are targeted to pregnant women and intended to help raise awareness of the importance of pregnant women taking iron folic acid supplements (IFAS) during pregnancy. Each poster features a pregnant woman representative of one of three regions in Kenya (national, coastal and north east) and encourage pregnant women to take IFAS. Also attached is a word document with the English translation of these posters; all three posters include the same information.


The National Iron and Folic Acid Supplementation programme is guided by different Policy and National action frameworks. These policy documents include the Kenya Food and Nutrition Security Policy (2011) and the Kenya National Nutrition Action Plan (2011-2017). These documents provide a platform for National and County response to addressing Iron and Folic Acid deficiencies through, among other interventions, supplementation programmes. The Kenya National Health Policy (2012-2030) and the Kenya Health Sector Strategic Plan 2012-2017 provide clear policy objectives and strategies that are supportive of nutrition. The Constitution of Kenya guarantees that every person has the right to health, which includes healthcare services. The Government of Kenya developed the Vision 2030 as its new long-term development plan for the country. To improve the overall livelihoods of Kenyans, the country aims to provide an efficient integrated and high quality affordable health care system. Under the nutrition sector, the Health Strategy aims to strengthen collaboration in order to ensure adequate nutrition for the whole population, through avoiding and managing over or under nutrition and micronutrient deficiencies. Iron and Folic Acid Supplementation was made a flagship project under the MTP 11 under Vision 2030.

According to World Health Organization it is estimated that 41.8% of pregnant women worldwide are anaemic. In Kenya the most recent micronutrient survey in the country indicated the prevalence of anaemia among pregnant women to be 55.1% and 46.4% among non-pregnant women. Anaemia is the leading indirect cause of high maternal and neonatal deaths. Iron and Folic Acid Supplementation (IFAS) for pregnant women is one of the interventions that has been recommended by WHO and implemented by the Ministry of Health to reduce anaemia levels. IFAS has been implemented through Focused Antenatal Care (FANC) and although this is the case, there have been challenges which have resulted in sub-optimal IFAS coverage rates and very low adherence rates.

This strategy provides a road map that is aimed at improving ANC attendance and IFAS coverage and utilization rates among pregnant women in Kenya in alignment with National IFAS plan targets. We call upon all partners and stakeholders to collaborate and ensure good coordination in the implementation of IFAS interventions to improve the chances of maternal and child survival.
Kenya's Regional Iron Folic Acid Supplementation Calendars (Kiswahili)

Women report that forgetting to take IFA supplements is one of the main reasons they don't take IFA. As part of its efforts to improve its IFA supplementation program and help women remember to take all their IFA, Kenya's MOH has developed a calendar for pregnant women to record when they take IFA. These three iron folic acid (IFA) calendars each feature a pregnant woman representative of one of three regions in Kenya and aims to help remind women to take their IFA supplementation daily during their pregnancy. There is a calendar for each month of pregnancy as well as information reinforcing the importance of taking IFA supplements, coming regularly for ANC, sleeping under a mosquito net and eating a variety of nutritious foods throughout pregnancy.

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Kenya's Regional Pregnant Woman’s Iron Folic Acid Information Leaflets (Kiswahili)

This informational booklet for pregnant women is offered in three versions representative of women from different regions of Kenya and is intended to guide pregnant women on iron folic acid supplementation (IFAS) during pregnancy. The leaflets are available in three versions: for national use, use in the coastal region of Kenya and in the north-eastern region of Kenya.

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Kenya's Applied Basic Agri-Nutrition Resource Toolkit for Trainers

This toolkit along with the training manual were developed to provide the trainer with further knowledge on applied nutrition in order to educate and inform the general public on the importance of nutrition in their day to day lives.

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This training-of-trainers (TOT) manual along with the toolkit were developed to provide the trainer with further knowledge on applied nutrition in order to educate and inform members of the general public on the importance of nutrition in their day-to-day lives.

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Kenya Poster 4: Promoting Iron Folic Acid Supplementation to Potential Mother (Kiswahili)

This poster is targeted to women of child-bearing age and features a young Kenyan woman. The message encourages women of child-bearing age to take folic acid before they become pregnant. A word document is attached for translation of these messages from Kiswahili into English.

Kenya Poster 5: Promoting Iron Folic Acid Supplementation for Healthy Families (Kiswahili)

This poster is primarily targeted to fathers or potential fathers as well as mothers and potential mothers. It features a healthy looking family of three and encourages pregnant women to take iron folic acid supplements (IFAS) during their pregnancy. Attached is a word document of the Kiswahili to English translation.


IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focussed Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates. This training has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017. IFAS is one of the performance indicators for the Cabinet Secretary, Ministry of Health, with coverage targets set from a baseline of 8% to 25% improvement by June 2014. Therefore, this course is designed to be integrated into or be delivered as part of focused antenatal care training. It is designed for in service and refresher training, in continuing medical education sessions, on-job training and continuous professional development.

**About this Manual and Training Guide:** IFA supplementation for pregnant women is one of the key interventions recommended by WHO to help reduce anaemia levels. IFA supplementation has been implemented as a key MOH program, through Focused Antenatal Care (FANC) however, there have been challenges which have resulted in sub-optimal coverage rates and very low adherence rates.

This manual is meant to go along with the IFAS Trainer’s Guide and has been designed to address some of the challenges that contribute to low coverage and utilization rates of IFAS among pregnant women. It is one of the strategies that will help in achieving the National IFAS targets of 80% coverage and 30% utilization of 90 plus of supplements by 2017.

**Course Participants:** This training is targeted to frontline ANC service providers, including health managers, nurses, nutritionists, and community strategy coordinators. The training module is competency-based and can be used to train health workers at a wide range of education levels such as diploma holders, certificate levels, degree holders, etc.

**Training Approaches:** This training approach is based on adult learning principles, that is, the belief that adults learn best in interactive sessions that include practice between the trainers and the trainees. Structured learning activities will be used including presentations, group discussions, demonstrations, role plays, and practical exercises.

The method of training recommended for use is Teach-back. This methodology is successful because it is based on adult learning principles, adults want training that is participatory, and they want to gain knowledge and skills applied to their jobs, they would like to share knowledge and experiences. The participants receive positive reinforcement and feedback about areas of weakness and practice teach-back training using the course content in a safe and supportive environment.

**Instructions on Use:** The IFAS course includes a Trainer’s Guide and Participant Manual. The course follows a modular approach. It is divided into five independent modules that can stand alone or be combined into a 2 1/2 day package of instructional material, as needed. Each module is divided into sessions, which are further divided into topics. The learning objectives of each session are followed by materials needed, advance preparation, and training directions, including cues for brainstorming and group work.

- **Kenya's National Iron Folic Acid Policy Guideline**

This is a poster size version of Kenya’s National Policy Guideline on Combined Iron and Folic Acid (IFA) Supplementation for Pregnant Women in Kenya. This version of the policy is meant for display in a health care facility and serve as easy reference for health care providers. It includes information about the purpose of IFA supplementation, composition, dosage, duration, target group, administration, possible side effects and the recommended action to take if they occur.
The purpose of the 2012-2017 National Nutrition Action Plan (NNAP) is to provide a framework for coordinated implementation of nutrition intervention activities by the government and nutrition stakeholders. The Plan has been developed at a time when the government of Kenya is stepping up efforts to realize Millennium Development Goals through implementation of High impact Nutrition initiatives (HiNi). The HiNi include: exclusive breastfeeding, timely complementary feeding, iron folate, vitamin A and zinc supplementation, hand washing, deworming, food fortification and management of moderate and severe acute malnutrition. The NNAP was a collaborated effort of a task force through the supplementation sub-committee, compromised of members from the Division of Nutrition, Division of Child and Adolescent Health, Division of Reproductive Health, in the Ministry of Health (MoH) as well as multiple partners.

Kenya's Regional Community Health Worker Iron Folic Acid Supplementation Counseling Guides

This counseling guide is targeted to community health workers providing anemia prevention counseling to pregnant women and family members at the household level. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout their pregnancy. An English version is not available here, but you can refer to the English versions of "Kenya's IFA Supplementation Participant's Manual for Health Care Providers;" "Kenya's IFA Supplementation Trainer's Guide for Health Care Providers;" and "Kenya's Regional Health Care Provider IFA Supplementation Counseling Guides" to get an idea of the messages that are provided in this guide.

Kenya's Algorithm or Flow Chart for Counseling Women on Iron Folic Acid Supplementation

Algorithm or Flow Chart for Iron and Folic Acid Supplementation (IFAS) for pregnant and non-pregnant women

Kenya's Regional Health Care Provider Iron Folic Acid
Supplementation Counseling Guides

This dialogue guide or counseling guide is targeted to health care providers providing anemia prevention counseling to pregnant women and family members within a health facility. It covers the importance of regular ANC visits, sleeping under a mosquito net, deworming, eating a variety of nutritious foods, and the importance of taking an IFA supplement daily throughout pregnancy. It is available here in three different versions representative of the three regions of Kenya (national, north eastern and the coast). For similar resources, see also "Kenya’s IFA supplementation participants manual for health care providers" (in English); "Kenya’s IFA supplementation trainer’s guide for health care providers" (in English) and Kenya's IFA supplementation counseling guide for community health workers" (in Kiswahili).

• Kenya Poster 1: Promoting Iron Folic Acid Supplementation (Male Health Worker)

This poster was created for display in health facilities to help motivate health workers to "Give Complete and Accurate Information on Iron Folic Acid Supplements". This particular poster highlights four points a health worker should ensure they provide pregnant women regarding iron folic acid supplementation (IFAS): 1) Ensure that you counsel mothers on benefits of IFAS 2) Ensure you provide IFAS to all pregnant women regardless of their hb (hemoglobin) status 3) Ensure you provide complete dosage to be taken daily from conception to delivery and 4) Ensure you counsel pregnant mothers on managing side effects of IFAS.

• Kenya Poster 2: Promoting Iron Folic Acid Supplementation (Female Health Worker)

This poster was created to help motivate health workers and for display in health facilities. The message is to "Be a champion; Give Pregnant Women the Chance to have a Healthy Pregnancy". It encourages the health worker to counsel and support pregnant women on the use of iron folic acid supplements (IFAS) and highlights the benefits of women taking them: 1) prevent anaemia 2) prevent risk of low birth weight 3) prevent unsafe pregnancy and complications during delivery.

• Kenya’s National Nutrition Action Plan 2012-2017

Kenya's National Nutrition Action Plan (NAP), is derived principally from the Food and Nutrition Security Policy and Food and Nutrition Security Strategy. The Strategy provides a
mechanism through which the Government will facilitate the implementation of strategic actions to improve and ensure food and nutrition security for the Kenyan population.

- **Malaria is an Important Cause of Anaemia in Primigravidae: Evidence from a District Hospital in Coastal Kenya**

A study was undertaken in order to determine the prevalence and aetiology of anaemia in pregnancy in coastal Kenya, so as to establish locally important causes and enable the development of appropriate intervention strategies. 275 women attending the antenatal clinic at Kilifi district hospital, Kenya, were recruited in November 1993. The prevalence of anaemia (haemoglobin 11 g/dL) was 75.6%, and the prevalence of severe anaemia (7g/dL) was 9.8% among all parities; 15.3% of 73 primigravidae were severely anaemic, compared with 7.9% of 202 multigravidae (P = 0.07). In primigravidae, malaria infection (Plasmodium falciparum) was strongly associated with moderate and severe anaemia (chi 2 test for trend, P = 0.003). Severe anaemia was more than twice as common in women with peripheral parasitaemia as in those who were aparasitaemic, and parasitaemia was associated with a 2.2g/dL decrease in mean haemoglobin level (0.001). In multigravidae, iron deficiency and hookworm infection were the dominant risk factors for anaemia. Folate deficiency and human immunodeficiency virus infection were not strongly associated with anaemia. It is suggested that an intervention that can effectively reduce malaria infection in primigravidae could have a major impact on the health of these women and their infants.

**Indonesia**

**Resources:**

- **Iron and Folic Acid Supplements in Pregnancy Improve Child Survival in Indonesia**

**Background:** Several trials have shown that iron-folic acid supplements during pregnancy protect newborns against preterm delivery and early neonatal death, but the impact beyond the neonatal period is unclear.

**Objective:** We determined whether live-born children <5 y of age born to mothers who used antenatal iron-folic acid supplements had reduced risk of death.
**Design:** Pooled 1994, 1997, 2002?2003, and 2007 Indonesia Demographic and Health Survey data were used to examine the relation between the use of iron-folic acid supplements and child death in 3 cumulative (0?30 d, 0?11 mo, and 0?4 y) and 4 mutually exclusive (first day of life and 1?30 d, 1?11 mo, and 1?4 y of age) time periods. Risk of death was estimated by using Cox regression to control for 19 potential confounders.

**Results:** Survival information for 52,917 singleton live-born infants and 1525 deaths of children <5 y of age was examined. After adjustment for potential confounders, risk of death of children 5 y of age was reduced significantly by 34% if the mother consumed any iron-folic acid supplements [adjusted HR (aHR): 0.66; 95% CI: 0.53, 0.81; P = 0.001]. This protective effect was greatest for deaths on the first day of life (aHR: 0.40; 95% CI: 0.21, 0.77; P = 0.005) but was also shown for neonatal deaths on days 1?30 of life (aHR: 0.69; 95% CI: 0.49, 0.97; P = 0.035) and postneonatal deaths (aHR: 0.74; 95% CI: 0.56, 0.99; P = 0.044). There was a strong dose response of greater protection from death of children <5 y of age with increasing numbers of iron-folic acid supplements consumed.

**Conclusion:** In developing countries increased use of antenatal iron-folic acid supplements will reduce deaths of children <5 y of age, especially in the first year of life.

### Nepal

**Resources:**

- **Success in Delivering Interventions to Reduce Maternal Anemia in Nepal: A Case Study of the Intensification of Maternal and Neonatal Micronutrient Program**

Anemia has been recognized as a serious public health problem in Nepal for many years. Seventy-five percent of pregnant women were found to be anemic in the National Micronutrient Survey of 1998. This finding was used to raise awareness of the problem of maternal anemia and provided the trigger for action to address it. In 2004 the Government of Nepal launched the Intensification of Maternal and Neonatal Micronutrient Program, more commonly called the Iron Intensification Project (IIP), in five districts. The Micronutrient Initiative (MI) and UNICEF were the primary external donor partners supporting the government’s implementation of this program. Over the following seven years, the program was scaled up to cover 70 of Nepal’s 75 districts. Data in 2009 indicated that the program had achieved substantial success in increasing coverage of interventions in pregnant women that are known to reduce maternal anemia: attending antenatal care (ANC) clinics, taking iron-folic acid supplements, and taking deworming medicine.
This case study describes the development of the IIP, its design, the process used to implement it at the district level, the strategy used to scale it up, and the data available to describe coverage. The reduction in maternal anemia in the country between 1998 and 2006 is also described. Last, conclusions are drawn regarding lessons learned for sustaining and strengthening the program in Nepal as well as the usefulness of the program model for translation to other countries.

Nepal Drastically Reduces the Prevalence of Anemia in Pregnant Women in the Past Seven Years

**Background:** Anaemia among pregnant women in Nepal was alarmingly high at 75% in 1998 and coverage of iron/folic acid (IFA) supplementation was only 23% with negligible compliance in 2001. The National Anemia Control Strategy and Iron Intensification Program was developed in 2003, with a key focus to increase the coverage and compliance of iron supplementation along with complementary measures such as deworming of pregnant women and dietary diversification, food fortification and promotion of maternal care practices. The Government started the program with five districts in 2003 and has expanded to 52 districts as of 2008 with the support from Micronutrient Initiative (MI), UNICEF and WHO. The Government Aims to cover all 75 districts by 2010.

**Aims:** The main aim of the program was to increase the coverage and compliance of iron supplementation, thereby reduce Anaemia in pregnant women. As per the policy, pregnant women have to take the supplement from the 2nd trimester of pregnancy to 45 days postpartum.

**Methods:** In order to improve the access, Female Community Health Volunteers (FCHVs) were trained to distribute the iron supplements. With supportive supervision from health system, a strong monitoring system was put in place by using community level micronutrient register to track pregnant women. In five districts, school based monitoring system was also piloted, whereby school children were mobilised for early identification of pregnant women to ensure early initiation of iron supplementation and household tracking for high compliance. Individual compliance card was also provided to pregnant women. FCHVs also promoted issues such as deworming during pregnancy, antenatal care and maternal nutrition.

**Results:** According to the Demographic Health Survey in 2006, the coverage of iron supplementation has increased from 23% to 59% nationally. An evaluation conducted in the intensification districts found increase in coverage from 47% to 86% and compliance from 29% to 76%. The coverage of deworming of pregnant women has also increased from 2% to 52%. Because of these improvements and other complementary measures, Anaemia in pregnant women has been reduced from 75% to 42%.

**Conclusions:** An integrated approach including community based distribution of iron supplements, strong monitoring of pregnant women, awareness creation, improved logistics
supply and promotion of complementary measures has lead to significant reduction in anaemia. School monitoring system has proved to be an effective means to increase early initiation of supplementation and high compliance.

Nicaragua

In Nicaragua (Mora, 2007), the Ministry of Health spearheaded an Integrated Anemia Control Strategy following discouraging results from a 1993 National Micronutrient Survey (NMS-93) that revealed that 27% of children and 34% of non-pregnant women were anemic. The Ministry of Health’s Department of Nutrition launched a sensitization campaign to generate awareness about the need to address micronutrient deficiencies, including iron deficiency, to MOH, politicians, academic institutions, health professionals, NGOs, community groups, media networks, and civil society in order to gain political commitment to address anemia and vitamin A and iodine deficiencies. The strategy encompassed a comprehensive approach to address the most important causes of anemia, including iron, vitamin A and other nutrient deficiencies as well as helminth infections. Although malaria control was underway, it did not become an explicit part of anemia control. The following interventions were included in the strategy: iron folic acid supplementation (IFA) for children < 5 years of age and pregnant women; periodic delivery of deworming to children 2-10 years of age; fortification of wheat flour with iron and B-vitamins; interventions to address vitamin A deficiency, which included vitamin A supplementation, through twice yearly National Health Rallies and routine visits, including immunizations (both were combined with IFA supplements); fortification of table sugar; and behavior change communications (BCCs) on micronutrients. Extensive training of health services personnel was conducted on micronutrient supplementation guidelines and use of BCC materials. Although a largely effective supply chain system was in place to ensure adequate supplies of IFA supplements, new guidelines were developed on forecasting for IFA supplement needs at all levels in the health system and on the use of information for decision-making regarding inventory replenishment at distribution points. Use of community volunteers (?brigadistas?) assisted in IFA supplement delivery and follow-up counseling. As a result of this program, coverage of IFA and vitamin A supplementation and deworming increased dramatically, and anemia rates in non-pregnant women decreased from 33.6% (1990’s) to 23.7% (2000).

Resources:

- Integrated Anemia Control Strategy has Significantly Reduced Anemia in Women and Children in Nicaragua

Anemia was identified as a problem of public health significance in Nicaragua since 1993, when its prevalence amounted to 28.5% in children 1-4 years and 33.6% in non pregnant
women of childbearing age. The average intake and absorption of iron by both children and
the general population was very low, and intake of other nutrients (vitamin A, thiamine,
riboflavin, niacin and folate) was also deficient. Because of the grossly deficient iron intake,
most anemias were attributed to iron deficiency; other possible causal factors were intestinal
parasites (especially hookworms) and systemic infections. Vitamin A deficiency (VAD) was
also significant in children. As part of a National Micronutrient Plan (NMP), an Integrated
Anemia Control Strategy (IACS) was developed by the Ministry of Health (MOH) and
implemented since 2004. The IACS included iron and iron/folic acid supplementation for
pregnant women and children <5 years; periodic delivery of anthelminth medications to
children 2-10 years; fortification of wheat flour with iron and B-vitamins; interventions to
control vitamin A deficiency (supplementation and fortification of table sugar); behavioral
change communications (BCC); comprehensive training of health service personnel,
community health volunteers (CHVs) and non governmental organizations (NGOs);
strengthening of other public health interventions; and a program monitoring and evaluation
(M&E) system. Steps for implementing IACS comprised: clear policies; updated technical
guidelines; incorporation of iron and iron/folic acid supplements in the official list of essential
medicines; addressing supply issues by establishing effective systems for procurement and
logistical management of supply, as well as demand and compliance issues; and conducting
operational research to address key constraints to implementation. The effectiveness of
involving community health volunteers (?)brigadistas?) in supplement delivery, follow up and
counseling, was tested with positive results. Better knowledge and skills of health care
providers and CHVs on anemia, supplementation and counseling improved supplement
demand and compliance with supplementation. The community-based ?brigadista? model for
iron supplementation was gradually extended throughout most of the country.

Thailand

In Thailand (Winichagoon, 2002), the prevalence of anemia among pregnant women was
reduced from 25% to 15% over a ten-year period through the integration of iron supplementation,
deworming, and community based follow-up. Village health volunteers were a critical component
of the program, in terms of identifying and encouraging women to attend ANC services and
operating drug funds in the community, which served as an outlet and supply for iron tablets. The
program notably addressed factors that were barriers to compliance and provided evidence-
based counseling to ensure women knew why, when, and how to take iron supplements, given
by both service providers and community/village health volunteers. Iron tablet supplies were in
place due to funds set aside for tablets, income generated at each health service unit to
purchase them, and support from district hospitals to fill any gap in supplies.

Resources:

- Prevention and Control of Anemia: Thailand Experiences
Thailand has addressed nutrition in national development policy since the mid-1970s, including efforts to reduce iron deficiency anemia. Nutritional improvement has been implemented as an integral part of primary health care and community development extending beyond government services to include community participation. Utilization of village health volunteers has been a crucial feature of the program. Available data indicate that anemia rates have declined among pregnant women and preschool children, although there has been no formal evaluation of the program effect. Universal iron supplementation has been the major strategy for pregnant women, using village health volunteers to encourage continuation of the antenatal care schedule and encouraging a preventive approach by health service providers. Program obstacles have included lack of access to iron tablets by some populations and lack of understanding of the importance of anemia. Women's compliance was complicated by fear of having a large fetus, forgetfulness and side effects. Weekly iron supplementation of school children was piloted in 2000, and is now being extended. Other strategies utilized to address iron deficiency include food fortification, dietary improvement and complementary public health measures. Program monitoring and evaluation require strengthening to assess the effectiveness of intervention strategies and provide proper data for decision-making.

Malaria

Given that anemia stems from multiple causes, it is important to review lessons learned from country programs that incorporated malaria or helminth control, which can also bring about reductions in anemia. Country experiences from Brazil, Eritrea, India, and Vietnam reveal that successful malaria control programs have common elements, including use of multiple technical approaches including balanced case management and prevention, introduction of insecticide treated bednets (ITNs), targeted indoor residual spraying (ITS), and scaling up alternative vector control measures (Barat, 2006). A lead partner agency to provide technical and programmatic support, such as USAID Environmental Health project in Eritrea and PAHO in Brazil, was a key factor in achieving reductions in malaria burden. Although all countries had centrally managed, vertical strategies, significant integration and decentralization of responsibility and resources helped to move forward malaria control. In Eritrea and India, implementation shifted to zonal and state health authorities, while in Vietnam, government and malaria control staff were linked at the provincial, district, and commune levels.

Resources:

- **Malaria and Iron Load at the First Antenatal Visit in the Rural South Kivu, Democratic Republic of the Congo: Is Iron Supplementation Safe or Could It Be Harmful?**
We investigated the relationship between malaria infection and iron status in 531 pregnant women in South Kivu, Democratic Republic of the Congo. Sociodemographic data, information on morbidity, and clinical data were collected. A blood sample was collected at the first antenatal visit to diagnose malaria and measure serum ferritin (SF), soluble transferrin receptor, C-reactive protein, and ?1-acid-glycoprotein. Malaria prevalence was 7.5%. Median (interquartile range) SF (adjusted for inflammation) was significantly higher in malaria-infected (82.9 ?g/L [53.3-130.4]) than in non-infected (39.8 ?g/L [23.6-60.8]) women. Similarly, estimated mean body iron store was higher in malaria-infected women. Malaria was significantly and independently associated with high levels of SF. Efforts to improve malaria prevention while correcting iron deficiency and anemia during pregnancy are warranted.

Maternal Malaria and Malnutrition (M3) Initiative, a Pooled Birth Cohort of 13 Pregnancy Studies in Africa and the Western Pacific

Purpose: The Maternal Malaria and Malnutrition (M3) initiative has pooled together 13 studies with the hope of improving understanding of malaria?nutrition interactions during pregnancy and to foster collaboration between nutritionists and malariologists.

Participants: Data were pooled on 14?635 singleton, live birth pregnancies from women who had participated in 1 of 13 pregnancy studies. The 13 studies cover 8 countries in Africa and Papua New Guinea in the Western Pacific conducted from 1996 to 2015.

Findings to Date: Data are available at the time of antenatal enrolment of women into their respective parent study and at delivery. The data set comprises essential data such as malaria infection status, anthropometric assessments of maternal nutritional status, presence of anaemia and birth weight, as well as additional variables such gestational age at delivery for a subset of women. Participating studies are described in detail with regard to setting and primary outcome measures, and summarised data are available from each contributing cohort.

Future Plans: This pooled birth cohort is the largest pregnancy data set to date to permit a more definite evaluation of the impact of plausible interactions between poor nutritional status and malaria infection in pregnant women on fetal growth and gestational length. Given the current comparative lack of large pregnancy cohorts in malaria-endemic settings, compilation of suitable pregnancy cohorts is likely to provide adequate statistical power to assess malaria?nutrition interactions, and could point towards settings where such interactions are most relevant. The M3 cohort may thus help to identify pregnant women at high risk of adverse outcomes who may benefit from tailored intensive antenatal care including nutritional supplements and alternative or intensified malaria prevention regimens, and the settings in which these interventions would be most effective.
Four Malaria Success Stories: How Malaria Burden was Successfully Reduced in Brazil, Eritrea, India and Vietnam

While many countries struggle to control malaria, four countries, Brazil, Eritrea, India, and Vietnam, have successfully reduced malaria burden. To determine what led these countries to achieve impact, published and unpublished reports were reviewed and selected program and partner staff were interviewed to identify common factors that contributed to these successes. Common success factors included conducive country conditions, a targeted technical approach using a package of effective tools, data-driven decision-making, active leadership at all levels of government, involvement of communities, decentralized implementation and control of finances, skilled technical and managerial capacity at national and sub-national levels, hands-on technical and programmatic support from partner agencies, and sufficient and flexible financing. All these factors were essential in achieving success. If the goals of Roll Back Malaria are to be achieved, governments and their partners must take the lessons learned from these program successes and apply them in other affected countries.

Tools and Resources

A2Z Project:
- http://www.a2zproject.org/
- Anemia reduction: http://www.a2zproject.org/node/8
- Resources for anemia reduction: http://www.a2zproject.org/node/44
- More resources for anemia reduction: http://www.a2zproject.org/node/55

Alive and Thrive:
- https://www.aliveandthrive.org/
- Resources: https://www.aliveandthrive.org/resources/

Feed the Future:

Food and Nutrition Technical Assistance III Project (FANTA):

• https://www.fantaproject.org/

GAIN:

• https://www.gainhealth.org/

Manoff Group:

• https://www.manoffgroup.com/

• Nutrition: https://www.manoffgroup.com/prog_nutrition.html

• Egypt: Preventing and Treating Anemia in School Children: https://www.manoffgroup.com/prog_egypt.html

• Resources page: Iron: https://www.manoffgroup.com/resources.html contains:

PDFs

• Anemia Prevalence Map (2002)

• Communication Strategies to Optimize Commitments and Investments in Iron Programming (2002)


• Egypt's Adolescent Anemia Prevention Program: Program Development, Pilot Efforts, Lessons Learned (2001)


• Ten Steps to Improving Pregnant Women's Compliance With Iron Folate Tablet Supplementation (1993)


President?ś Malaria Initiative
• http://www.pmi.gov/

Strengthening Partnerships, Results and Innovations in Nutrition Globally Project (SPRING):

• http://www.spring-nutrition.org/

• Preventing Anemia page: https://www.spring-nutrition.org/technical-areas/anemia

• SPRING Anemia Resource Review: http://www.spring-nutrition.org/technical-areas/anemia/resource-review

• http://www.micronutrient.org

• Folic acid page: https://www.nutritionintl.org/what-we-do/by-micronutrient/folic-acid/

• Anemia search: https://www.nutritionintl.org/knowledge-centre/knowledge-library/

UNICEF:

• https://www.unicef.org/

• Nutrition: https://www.unicef.org/nutrition/

• Technical and policy documents: https://www.unicef.org/nutrition/index_documents.html

• UNICEF micronutrients page https://www.unicef.org/nutrition/index_iiodine.html

Other:

• CDC https://www.cdc.gov/nutrition/everyone/basics/vitamins/iron.html

• Institute of Health Management, Pachod (India) resources: http://www.ihmp.org/publications/

• Iron deficiency project: http://www.idpas.org/

• Kids health:https://kidshealth.org/en/parents/anemia.html

• MCHIP: https://www.mchip.net/sites/default/files/USAID%20approved%20and%20final%20brief-%20community%20IFA.pdf

• Women?s Health Dot Gov https://www.womenshealth.gov/a-z-topics/iron-deficiency-anemia
Resources:

- Assessment of Knowledge and Practice Towards Prevention of Anemia Among Pregnant Women Attending Antenatal Care at Government Hospitals in West Shoa Zone, Ethiopia

**Background:** Anemia affects 1.62 billion people (24.8%), among which 56 million are pregnant women. It is a major public health problem particularly among poorer segments of the population in developing countries where 95% of the world anemic pregnant women are residing. Anemia is one of the most commonly encountered medical disorders during pregnancy. According to WHO estimates, up to 56% of all women living in developing countries are anemic.

**Objective:** The objective of the study was to assess the knowledge and practice regarding prevention of anemia among pregnant mothers attending ANC in governmental hospitals at West Shoa Zone, Ethiopia.

**Method:** Hospital-based cross-sectional study was employed in three public hospitals found in West Shoa Zone to find out the level of knowledge and practice regarding prevention of anemia during pregnancy among women attending ANC. A total of 286 pregnant mothers were interviewed by using pretested structured questionnaire from three hospitals. Simple random sampling procedure was carried out to attain the required sample size. Data was entered and processed into the computer using SPSS version 20.

**Results:** A total of 286 pregnant women were participated on the study. Among them only 57.3% and 50% were found to have good knowledge and poor practice respectively regarding prevention of anemia during pregnancy. Crude and adjusted odds ratio done revealed that educational status, living in urban, having nuclear family type, previous history of anemia and good practice were significantly associated with knowledge, while educational status and having good knowledge also found to be significantly associated with prevention of anemia during pregnancy.

**Conclusions:** Based on study findings, half of the study participants attending ANC at West Shoa Zone Governmental Hospitals have poor knowledge and poor skills regarding prevention of anemia during pregnancy. Multiple factors such as education, residency, having
nuclear type of family and previous anemia history found to affect knowledge and practice regarding prevention of anemia during pregnancy significantly. Therefore, policy makers would be better consider those factors contributed in prevention of anemia during pregnancy.

**Effect of Iron Fortified Wheat Flour Consumption on the Hemoglobin Status of Adolescent Girls in District Buner**

Food fortification has been defined as the addition of one or more essential nutrients to a food whether or not it is normally contained in the food. Iron acts as an integral part of hemoglobin and is required for the transport of oxygen and carbon dioxide in the blood. Cereal foods can be successfully fortified with iron. Among the cereals, wheat has additional advantage to be used as vehicle. The bioavailability of iron added to wheat is several times greater than other staples such as maize and rice. Ferrous sulphate has excellent bioavailability. It is the fortificant of choice when used in wheat flour and is the best iron source because of its high bioavailability and low cost. In this study the effect of ferrous sulphate fortified wheat flour on the hemoglobin status of adolescent girls was examined in district Buner. A total of 200 adolescent girls were randomly selected and divided into two groups, study and control each group having 100 girls. The subjects of the study group were fed with ferrous sulphate fortified wheat flour while the control group were fed with non-fortified wheat flour as a placebo. The hemoglobin level of both groups was determined 4 times, prior to intervention, after 1st, 2nd and 3rd month of consuming ferrous sulphate fortified wheat flour with the help of Hemo Cue. The mean (± S.D) Hb values (g/dl) of control and study groups prior to intervention, after 1st, 2nd and 3rd month were (11.878 ± 0.46, 11.754 ± 0.61), (11.91 ± 0.50, 11.837 ± 0.60), (11.88 ± 0.53, 11.93 ± 0.65), (11.87 ± 0.66, 12.107 ± 0.63) respectively. The results showed no significant difference between study and control groups by comparing baseline data with the 1st month while showed significant difference by comparing baseline data with 2nd and 3rd month of intervention. The study suggests that the hemoglobin status of adolescent girls was significantly improved by consuming wheat flour fortified with ferrous sulphate.

**Effects of Delayed Umbilical Cord Clamping vs Early Clamping on Anemia in Infants at 8 and 12 Months: A Randomized Clinical Trial**

**Importance:** Delayed umbilical cord clamping has been shown to improve iron stores in infants to 6 months of age. However, delayed cord clamping has not been shown to prevent iron deficiency or anemia after 6 months of age.

**Objective:** To investigate the effects of delayed umbilical cord clamping, compared with early
clamping, on hemoglobin and ferritin levels at 8 and 12 months of age in infants at high risk for iron deficiency anemia.

**Design, Setting, and Participants:** This randomized clinical trial included 540 late preterm and term infants born vaginally at a tertiary hospital in Kathmandu, Nepal, from October 2 to November 21, 2014. Follow-up included blood levels of hemoglobin and ferritin at 8 and 12 months of age. Follow-up was completed on December 11, 2015. Analysis was based on intention to treat.

**Interventions:** Infants were randomized to delayed umbilical cord clamping (?180 seconds after delivery) or early clamping (?60 seconds after delivery).

**Main Outcomes and Measures:** Main outcomes included hemoglobin and anemia levels at 8 months of age with the power estimate based on the prevalence of anemia. Secondary outcomes included hemoglobin and anemia levels at 12 months of age and ferritin level, iron deficiency, and iron deficiency anemia at 8 and 12 months of age.

**Results:** In this study of 540 infants (281 boys [52.0%] and 259 girls [48.0%]; mean [SD] gestational age, 39.2 [1.1] weeks), 270 each were randomized to the delayed and early clamping groups. At 8 months of age, 212 infants (78.5%) from the delayed group and 188 (69.6%) from the early clamping group returned for blood sampling. After multiple imputation analysis, infants undergoing delayed clamping had higher levels of hemoglobin (10.4 vs 10.2 g/dl; difference, 0.2 g/dl; 95% CI, 0.1 to 0.4 g/dl). Delayed cord clamping also reduced the prevalence of anemia (hemoglobin level <11.0 g/dl) at 8 months in 197 (73.0%) vs 222 (82.2%) infants (relative risk, 0.89; 95% CI, 0.81-0.98; number needed to treat [NNT], 11; 95% CI, 6-54). At 8 months, the risk for iron deficiency was reduced in the delayed cord clamping group in 60 (22.2%) vs 103 (38.1%) patients (relative risk, 0.58; 95% CI, 0.44-0.77; NNT, 6; 95% CI, 4-13). At 12 months, delayed cord clamping still resulted in a hemoglobin level of 0.3 (95% CI, 0.04-0.5) g/dl higher than in the early cord clamping group and a relative risk for anemia of 0.91 (95% CI, 0.84-0.98), resulting in a NNT of 12 (95% CI, 7-78).

**Conclusions and Relevance:** Delayed cord clamping reduces anemia at 8 and 12 months of age in a high-risk population, which may have major positive effects on infants' health and development.

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**Effects of Preconceptional Weekly Micronutrient Supplements on Maternal and Child Anemia during the First 2 Years of Life**

**Background:** Anemia remains a major public health problem especially during the first 1000 days of life. Prenatal supplementation with multiple micronutrients (MM) and iron and folic acid (IFA) has been suggested as a potential intervention to reduce anemia in young children but little is known about the benefits of preconception micronutrient interventions. This study
evaluates the impact of preconception weekly MM or IFA supplementation on maternal and child anemia during the first 2 years of age compared to folic acid (FA) alone.

**Methods:** We followed 1,599 offspring born to women who participated in a randomized controlled trial of preconception micronutrient supplementation in Vietnam. A total of 5011 women (18?40 y) received weekly supplements containing either 2800?g FA only, 60mg iron and 2800?g FA, or 15 micronutrients including the same amount of IFA, from baseline until conception; followed by daily prenatal supplements containing 60mg iron and 400?g FA till delivery. Hemoglobin concentrations were measured at different time points (3, 6, 12 and 24 months postpartum) using a portable field B-Hemoglobin Analyzer. Anemia was defined as Hb value <12 g/dL and < 11 g/dL for women and children, respectively. We used ANOVA or chi-square tests to examine group differences for both intention to treat and per protocol analyses (women consumed supplements ?26 weeks before conception). Multivariable logistic regression analyses were used to examine factors associated with child anemia at age 2 y.

**Results:** The prevalence of anemia ranged from 30?40% among women during the postpartum period and decreased from 61.4% to 41.6% among the offspring from age 3 to 24 mo. (n=1476). The groups were similar for baseline maternal and offspring characteristics at birth and there were no significant differences (p>0.05) by intervention group in mean hemoglobin concentrations or the prevalence of maternal and child anemia at various time points during the first 2 years of life in both intent-to-treat and per-protocol analysis. Preconception anemia however remained a significant predictor of the risk of offspring anemia at 24 mo of age (OR: 1.88; 95% CI: 1.44 ? 2.48) even after adjusting for maternal education, socioeconomic status and ethnicity.

**Conclusions:** Weekly supplementation with MM or IFA before conception did not affect the risk of anemia compared to FA in rural Vietnamese women and their offspring at age 2y. Preconception anemia however remained a significant predictor of offspring anemia at age 2y even after adjusting for other known determinants.

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**Small-Quantity Lipid-Based Nutrient Supplements Containing Different Amounts of Zinc Along with Diarrhea and Malaria Treatment Increase Iron and Vitamin A Status and Reduce Anemia Prevalence, but do not Affect Zinc Status in Young Burkinabe Children**

**Background:** We assessed the effects of providing a package of interventions including small-quantity lipid-based nutrient supplements (SQ-LNS) containing 0, 5 or 10 mg zinc and illness treatment to Burkinabe children from 9 to 18 months of age, on biomarkers of zinc, iron and vitamin A status at 18 months and compared with a non-intervention cohort (NIC).
Methods: Using a two-stage cluster randomized trial design, communities were randomly assigned to the intervention cohort (IC) or NIC, and extended family compounds within the IC were randomly assigned to different treatment groups. IC children \( (n = 2435) \) were provided with 20 g SQ-LNS/d containing 0, 5 or 10 mg zinc, 6 mg of iron and 400 ?g of vitamin A along with malaria and diarrhea treatment. NIC children \( (n = 785) \) did not receive the intervention package. At 9 and 18 months, hemoglobin (Hb), zinc, iron and vitamin A status were assessed in a sub-group \( (n = 404) \). Plasma concentrations of zinc (pZC), ferritin (pF), soluble transferrin receptor (sTfR) and retinol-binding protein (RBP) were adjusted for inflammation.

Results: At baseline, 35% of children had low adjusted pZC (<65 ?g/dL), 93% were anemic (Hb <110 g/L), 25% had low adjusted pF (<12 ?g/L), 90% had high adjusted sTfR (>8.3 mg/L) and 47% had low adjusted RBP (<0.94 ?mol/L), with no group-wise differences. Compared with the NIC, at 18 months IC children had significantly lower anemia prevalence (74 vs. 92%, \( p = 0.001 \)) and lower iron deficiency prevalence (13% vs. 32% low adjusted pF and 41% vs. 71% high adjusted sTfR, \( p < 0.001 \)), but no difference in pZC. Mean adjusted RBP was greater at 18 months in IC vs. NIC (0.94 ?mol/L vs. 0.86 ?mol/L, \( p = 0.015 \)), but the prevalence of low RBP remained high in both cohorts. Within the IC, different amounts of zinc had no effect on the prevalence of low pZC or indicators of vitamin A deficiency, whereas children who received SQ-LNS with 10 mg zinc had a significantly lower mean pF at 18 months compared to children who received SQ-LNS with 5 mg zinc (\( p = 0.034 \)).

Conclusions: SQ-LNS regardless of zinc amount and source provided along with illness treatment improved indicators of iron and vitamin A status, but not pZC.

**Multiple-Micronutrient Supplementation for Women During Pregnancy**

Background: Multiple-micronutrient (MMN) deficiencies often coexist among women of reproductive age in low- to middle-income countries. They are exacerbated in pregnancy due to the increased demands, leading to potentially adverse effects on the mother and developing fetus. Though supplementation with MMNs has been recommended earlier because of the evidence of impact on pregnancy outcomes, a consensus is yet to be reached regarding the replacement of iron and folic acid supplementation with MMNs. Since the last update of this Cochrane review, evidence from a few large trials has recently been made available, the inclusion of which is critical to inform policy.

Objectives: To evaluate the benefits of oral multiple-micronutrient supplementation during pregnancy on maternal, fetal and infant health outcomes.

Search Methods: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (11 March 2015) and reference lists of retrieved articles and key reviews. We also contacted experts in the field for additional and ongoing trials.
Selection Criteria: All prospective randomised controlled trials evaluating MMN supplementation with iron and folic acid during pregnancy and its effects on the pregnancy outcome were eligible, irrespective of language or the publication status of the trials. We included cluster-randomised trials, but quasi-randomised trials were excluded.

Data Collection and Analysis: Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. The quality of the evidence was assessed using the GRADE approach.

Main Results: Nineteen trials (involving 138,538 women) were identified as eligible for inclusion in this review but only 17 trials (involving 137,791 women) contributed data to the review. Fifteen of these 17 trials were carried out in low and middle-income countries and compared MMN supplements with iron and folic acid versus iron with or without folic acid. Two trials carried out in the UK compared MMN with a placebo. MMN with iron and folic acid versus iron, with or without folic acid (15 trials): MMN resulted in a significant decrease in the number of newborn infants identified as low birthweight (LBW) (average risk ratio (RR) 0.88, 95% confidence interval (CI) 0.85 to 0.91; high-quality evidence) or small-for-gestational age (SGA) (average RR 0.92, 95% CI 0.86 to 0.98; moderate-quality evidence). No significant differences were shown for other maternal and pregnancy outcomes: preterm births (average RR 0.96, 95% CI 0.90 to 1.03; high-quality evidence), stillbirth (average RR 0.97, 95% CI 0.87, 1.09; high-quality evidence), maternal anaemia in the third trimester (average RR 1.03, 95% CI 0.85 to 1.24), miscarriage (average RR 0.91, 95% CI 0.80 to 1.03), maternal mortality (average RR 0.97, 95% CI 0.63 to 1.48), perinatal mortality (average RR 1.01, 95% CI 0.91 to 1.13; high-quality evidence), neonatal mortality (average RR 1.06, 95% CI 0.92 to 1.22; high-quality evidence), or risk of delivery via a caesarean section (average RR 1.04; 95% CI 0.74 to 1.46). A number of prespecified, clinically important outcomes could not be assessed due to insufficient or non-available data. Single trials reported results for: very preterm birth (20%); results were consistent with the main analysis except for the findings for SGA (average RR 0.91, 95% CI 0.84 to 1.00). We explored heterogeneity through subgroup analyses by maternal height and body mass index (BMI), timing of supplementation and dose of iron. Subgroup differences were observed for maternal BMI for the outcome preterm birth, with significant findings among women with low BMI. Subgroup differences were also observed for maternal BMI and maternal height for the outcome SGA, indicating a significant impact among women with higher maternal BMI and height. The overall analysis of perinatal mortality, although showed a non-significant effect of MMN supplements versus iron with or without folic acid, was found to have substantial statistical heterogeneity. Subgroup differences were observed for timing of supplementation for this outcome, indicating a significantly higher impact with late initiation of supplementation. The findings between subgroups for other primary outcomes were inconclusive. MMN versus placebo (two trials): A single trial in the UK found no clear differences between groups for preterm birth, SGA, LBW or maternal anaemia in the third trimester. A second trial reported the number of women with pre-eclampsia; there was no evidence of a difference between groups. Other outcomes were not reported.

Authors’ Conclusions: Our findings support the effect of MMN supplements with iron and
folic acid in improving some birth outcomes. Overall, pregnant women who received MMN supplementation had fewer low birthweight babies and small-for-gestational-age babies. The findings, consistently observed in several systematic evaluations of evidence, provide a basis to guide the replacement of iron and folic acid with MMN supplements containing iron and folic acid for pregnant women in low and middle-income countries where MMN deficiencies are common among women of reproductive age. Efforts could focus on the integration of this intervention in maternal nutrition and antenatal care programs in low and middle-income countries.

- **Multi-Micronutrient Supplementation During Pregnancy for Prevention of Maternal Anaemia and Adverse Birth Outcomes in a High-Altitude Area: A Prospective Cohort Study in Rural Tibet of China**

Anaemia during pregnancy, characterised by Hb less than 110 g/l, is a specific risk factor for adverse maternal and perinatal outcomes in developing countries. The objective of this study was to determine the effectiveness of daily antenatal supplementation with multiple micronutrients (MMN) compared with folic acid (FA) on the occurrence of anaemia among pregnant women and their infants' health in a high-altitude area. A prospective cohort study was carried out in two rural counties in Tibet from 2007 to 2012. A total of 1149 eligible pregnant women were allocated daily supplementation with FA in one county and MMN containing a recommended allowance of 23 vitamins and minerals in another county starting ≥24 weeks of gestation and continuing until delivery. Compared with the FA group, prenatal supplementation with MMN was significantly associated with reduced odds of anaemia in the third trimester. This was demonstrated in the primary outcome, with an adjusted OR (AOR) of 0.63; 95% CI 0.45, 0.88 and P=0.007 and also reduced odds of preterm delivery (AOR: 0.31; 95% CI 0.15, 0.61; P=0.001). There was no difference between MMN and FA groups in mean birth weight (adjusted mean difference: 36.78; 95% CI -19.42, 92.98 g; P=0.200), whereas MMN supplementation significantly reduced the odds of low-birth weight (LBW) babies (AOR: 0.58; 95% CI 0.36, 0.91; P=0.019). In conclusion, the antenatal MMN supplementation in rural Tibet is associated with a reduction of maternal anaemia in the third trimester, and may potentially decrease the risk of preterm delivery and LBW babies.

- **Determinants of Anemia Among Pregnant Mothers Attending Antenatal Care in Dessie Town Health Facilities, Northern Central Ethiopia, Unmatched Case-Control Study**
Introduction: Anemia affects around 38.2% and 22% of pregnant women at a global and national level respectively. In developing countries, women start pregnancy with already depleted body stores of iron and other vitamins with significant variation of anemia within and between regions.

Objective: To identify the determinants of anemia among pregnant mothers attending antenatal care in Dessie town health facilities, northern central Ethiopia.

Methods: A health facility based unmatched case control study was conducted among 112 cases and 336 controls from January to March 2016 G.C. The sample size was determined by using Epi Info version 7.1.5.2. Study subjects were selected using consecutive sampling technique. Data were collected using a structured questionnaire, entered using Epi Data version 3.1 and analyzed using SPSS version 20. Bivariable and multivariable logistic regression model was used to see the determinants of anemia. Adjusted odds ratio (AOR) with 95% confidence interval (CI) and p-value less than 0.05 were used to see the significant association.

Results: Failure to take dark green leafy vegetables per two weeks (AOR = 5.02, 95% CI: 2.16, 11.71), didn’t take chicken per two weeks (AOR = 2.68, 95% CI: 1.22, 5.86), 1st trimester (AOR = 2.07, 95% CI: 1.12, 3.84), 3rd trimester (AOR = 2.96, 95% CI: 1.53, 5.72), HIV infection (AOR = 6.78, 95% CI: 2.28, 20.18) and medication (AOR = 3.57 95% CI: 1.60, 7.98) were positively associated with anemia.

Conclusions: Inadequate intake of dark green leafy vegetables, inadequate consumption of chicken, trimester of the current pregnancy, HIV infection and medication were the determinants of anemia among pregnant women. Therefore, anemia prevention strategy should include promotion of adequate intake of dark green leafy vegetables and chicken, increase meal pattern during the entire pregnancy and strengthen the prevention of mother to child HIV transmission/antenatal care programs.

Determinants of Iron Status and Hb in the Bangladesh Population: The Role of Groundwater Iron

Objective: Using data from the national micronutrients survey 2011-2012, the present study explored the determinants of Fe status and Hb levels in Bangladesh with a particular focus on groundwater Fe.

Design: Cross-sectional study conducted at the nationwide scale.

Settings: The survey was conducted in 150 clusters, fifty in each of the three strata of rural, urban and slum.

Subjects: Three population groups: pre-school age children (6-59 months; PSAC), school
age children (6-14 years; SAC) and non-pregnant non-lactating women (15-49 years; NPNLW).

**Results:** National prevalence of Fe deficiency was 10.7%, 7.1% and 3.9-9.5% in PSAC, NPNLA and SAC, respectively. Prevalence of anaemia was 33.1% (PSAC), 26.0% (NPNLW) and 17.1-19.1% (SAC). Multivariate regression analyses showed that the area with 'predominantly high groundwater Fe' was a determinant of higher serum ferritin levels in NPNLW (standardized ?=0.19; P=0.03), SAC (standardized ?=0.22; P=0.01) and PSAC (standardized ?=0.20; P=0.03). This area also determined higher levels of Hb in PSAC (standardized ?=0.14; P=0.01).

**Conclusions:** National prevalence of Fe deficiency in Bangladesh is low, contrary to the widely held assumption. High Fe level in groundwater is associated with higher Fe status (all populations) and higher Hb level (PSAC).

#### Diagnosis of Iron Deficiency Anemia Using Density-Based Fractionation of Red Blood Cells

Iron deficiency anemia (IDA) is a nutritional disorder that impacts over one billion people worldwide; it may cause permanent cognitive impairment in children, fatigue in adults, and suboptimal outcomes in pregnancy. IDA can be diagnosed by detection of red blood cells (RBCs) that are characteristically small (microcytic) and deficient in hemoglobin (hypochromic), typically by examining the results of a complete blood count performed by a hematology analyzer. These instruments are expensive, not portable, and require trained personnel; they are, therefore, unavailable in many low-resource settings. This paper describes a low-cost and rapid method to diagnose IDA using aqueous multiphase systems (AMPS) – thermodynamically stable mixtures of biocompatible polymers and salt that spontaneously form discrete layers having sharp steps in density. AMPS are preloaded into a microhematocrit tube and used with a drop of blood from a fingerstick. After only two minutes in a low-cost centrifuge, the tests \(n=152\) were read by eye with a sensitivity of 84% (72?93%) and a specificity of 78% (68?86%), corresponding to an area under the curve (AUC) of 0.89. The AMPS test outperforms diagnosis by hemoglobin alone (AUC = 0.73) and is comparable to methods used in clinics like reticulocyte hemoglobin concentration (AUC = 0.91). Standard machine learning tools were used to analyze images of the resulting tests captured by a standard desktop scanner to 1) slightly improve diagnosis of IDA? sensitivity of 90% (83?96%) and a specificity of 77% (64?87%), and 2) predict several important red blood cell parameters, such as mean corpuscular hemoglobin concentration. These results suggest that the use of AMPS combined with machine learning provides an approach to developing point-of-care hematology.

#### Maternal Anemia and Risk of Adverse Birth and Health
Outcomes in Low- and Middle-Income Countries: Systematic Review and Meta-Analysis

**Background:** Anemia is the leading cause of maternal deaths and adverse pregnancy outcomes in developing countries.

**Objectives:** We conducted a systematic review and meta-analysis to estimate the pooled prevalence of anemia, the association between maternal anemia and pregnancy outcomes, and the population-attributable fraction (PAF) of these outcomes that are due to anemia in low- and middle-income countries.

**Design:** PubMed, EMBASE, CINAHL, and the British Nursing Index were searched from inception to May 2015 to identify cohort studies of the association between maternal anemia and pregnancy outcomes. The anemic group was defined as having hemoglobin concentration <10 or <11 g/dL or hematocrit values <33% or <34% depending on the study. A metaregression and stratified analysis were performed to assess the effects of study and participant characteristics on adverse pregnancy risk. The pooled prevalence of anemia in pregnant women by region and country-income category was calculated with the use of a random-effects meta-analysis.

**Results:** Of 8182 articles reviewed, 29 studies were included in the systematic review, and 26 studies were included in the meta-analysis. Overall, 42.7% (95% CI: 37.0%, 48.4%) of women experienced anemia during pregnancy in low- and middle-income countries. There were significantly higher risks of low birth weight (RR: 1.31; 95% CI: 1.13, 1.51), preterm birth (RR: 1.63; 95% CI: 1.33, 2.01), perinatal mortality (RR: 1.51; 95% CI: 1.30, 1.76, and neonatal mortality (RR: 2.72; 95% CI: 1.19, 6.25) in pregnant women with anemia. South Asian, African, and low-income countries had a higher pooled anemia prevalence than did other Asian and upper-middle-income countries. Overall, in low- and middle-income countries, 12% of low birth weight, 19% of preterm births, and 18% of perinatal mortality were attributable to maternal anemia. The proportion of adverse pregnancy outcomes attributable to anemia was higher in low-income countries and in the South Asian region.

**Conclusion:** Maternal anemia remains a significant health problem in low- and middle-income countries.

Effect of Anthelminthic Treatment on Helminth Infection and Related Anaemia among School-Age Children in Northwestern Ethiopia

**Background:** Information about improvements in the health status of population at-risk of helminth infection after anthelminthic treatment helps to evaluate the effectiveness of the
large scale deworming program. The objectives of this study were to assess the impact of anthelminthic treatment on the prevalence and intensity of intestinal helminth infection, haemoglobin level and prevalence of anaemia among school-age children.

**Methods:** A total of 403 children attending Tikur Wuha Elementary School in Jiga, northwestern Ethiopia were enrolled in this study between February and March 2011. Formol-ether concentration and Kato-Katz methods were used to examine stool for intestinal helminth infections at baseline and one month after anthelminthic treatment. Haemoglobin level was measured using Hemocue machine at baseline and one month after anthelminthic treatment.

**Results:** Out of 403 school children examined, 15.4% were anaemic and 58.3% were infected with intestinal helminths at baseline. Hookworms (46.9%), *Schistosoma mansoni* (24.6%), *Ascaris lumbricoides* (4.2%) and *Trichuris trichiura* (1.7%) infections were common. The odds of anaemia was higher among children infected with helminths (adjusted odds ratio (aOR)=3.83, 95% CI=1.92, 7.62) especially in those infected with hookworm (aOR=2.42, 95% CI=1.34, 4.39) or *S. mansoni* (aOR=2.67, 95% CI=1.46, 4.88) and two or more helminth species (aOR=7.31, 95% CI=3.27, 16.35) than those uninfected with intestinal helminths at baseline. Significant reduction in prevalence of helminth infection (77.0%) and increment in mean haemoglobin level (+3.65 g/l) of children infected with helminths was observed one month after anthelminthic treatment. The increase in haemoglobin level after anthelminthic treatment was significantly positively associated with the age, but negatively associated with the haemoglobin level at baseline. The change in mean haemoglobin level was significantly higher among undernourished than normal children. Percent reduction in the prevalence of anaemia among children infected with helminths was 25.4% after anthelminthic treatment.

**Conclusions:** The present study provides evidence that anthelminthic treatment of school-age children infected with intestinal helminth can improve haemoglobin level in addition to reducing the prevalence and intensity of helminth infections one month after treatment. This suggests that deworming of children may benefit the health of children in sub-Saharan Africa where hookworm and *S. mansoni* infections are prevalent.

*Improved Sanitation Facilities are Associated with Higher Body Mass Index and Higher Hemoglobin Concentration Among Rural Cambodian Women in the First Trimester of Pregnancy*

Multiple factors contribute to undernutrition in Cambodian women. Our aim was to determine if type of household sanitation facility was associated with body mass index (BMI) and hemoglobin (Hb) concentration among pregnant women. Women (*N* = 544) from 75 villages in Kampong Chhnang Province had their height, weight, and Hb measured (HemoCue Hb 201+) in the first trimester. Sociodemographic and household characteristics were collected.
Multivariable linear and logistic regression models were used for analyses. Approximately 40% \((N = 221)\) of women reported primarily using an ?improved? sanitation facility (closed pit latrine) and 60% \((N = 323)\) used ?non-improved? facilities (open defecation). Mean ± standard deviation (SD) BMI was higher among women with improved versus non-improved facilities \((19.9 ± 3.0 \text{ kg/m}^2 \text{ versus } 19.4 ± 2.3 \text{ kg/m}^2; \ P = 0.01)\). Mean ± SD Hb concentration was also higher among women with improved versus non-improved facilities \((118 ± 12 \text{ g/L versus } 114 ± 14 \text{ g/L}; \ P = 0.001)\). Anemia prevalence \((\text{Hb} < 110 \text{ g/L})\) was higher among women with non-improved facilities \((34\% \text{ versus } 25\%; \ P = 0.04)\). An improved sanitation facility was a positive predictor of BMI \((\beta = 0.57 \text{ kg/m}^2; \ 95\% \text{ confidence interval [CI]} = 0.10, 1.04)\) and Hb concentration \((\beta = 2.94 \text{ g/L}; \ 95\% \text{ CI} = 0.53, 5.35)\), adjusting for age, parity, household size, village, gestation week, source of drinking water, and iron folic acid supplementation. Poor sanitation was associated with lower BMI and Hb concentration among pregnant Cambodian women. This warrants multisectoral approaches involving the health, nutrition, water, and sanitation sectors to effectively improve maternal health in Cambodia.

**Translating Formative Research Findings into a Behaviour Change Strategy to Promote Antenatal Calcium and Iron and Folic Acid Supplementation in Western Kenya**

The World Health Organization now recommends integrating calcium supplements into antenatal micronutrient supplementation programmes to prevent pre-eclampsia, a leading cause of maternal mortality. As countries consider integrating calcium supplementation into antenatal care (ANC), it is important to identify context-specific barriers and facilitators to delivery and adherence. Such insights can be gained from women's and health workers' experiences with iron and folic acid (IFA) supplements. We conducted in-depth interviews with 22 pregnant and post-partum women and 20 community-based and facility-based health workers in Kenya to inform a calcium and IFA supplementation programme. Interviews assessed awareness of anaemia, pre-eclampsia and eclampsia; ANC attendance; and barriers and facilitators to IFA supplement delivery and adherence. We analyzed interviews inductively using the constant comparative method. Women and health workers identified poor diet quality in pregnancy as a major health concern. Neither women nor health workers identified pre-eclampsia, eclampsia, anaemia or related symptoms as serious health threats. Women and community-based health workers were unfamiliar with pre-eclampsia and eclampsia and considered anaemia symptoms normal. Most women had not received IFA supplements, and those who had received insufficient amounts and little information about supplement benefits. We then developed a multi-level (health facility, community, household and individual) behaviour change strategy to promote antenatal calcium and IFA supplementation. Formative research is an essential first step in guiding implementation of antenatal calcium supplementation programmes to reduce pre-eclampsia. Because evidence on how to implement successful calcium supplementation programmes is limited,
experiences with antenatal IFA supplementation can be used to guide programme development.

- **Prenatal Anemia Control and Anemia in Children Aged 6-23 Months in Sub-Saharan Africa**

It is unclear whether routine prenatal anemia control interventions can reduce anemia risk in young children. This study examines the associations between prenatal iron supplementation and/or deworming and anemia in children aged 6-23 months in sub-Saharan Africa (SSA). We analyzed data from Demographic and Health Surveys conducted between 2003 and 2014 in 25 SSA countries. The surveys collected data on prenatal iron supplementation and deworming and determined children's hemoglobin levels through blood testing. We assessed the associations between prenatal iron supplementation and/or deworming and anemia using multinomial logistic regression. The study included 31,815 mother-child pairs: 25.0%, 41.4%, and 4.8% of children had mild, moderate, and severe anemia, respectively. Compared with children whose mothers did not take iron and deworming drugs prenatally, the risk of moderate/severe anemia was reduced among children whose mothers took only iron supplements for <6 months (odds ratio [OR]: 0.58; 95% confidence interval [CI]: 0.45-0.76); only deworming drugs (OR: 0.73; 95% CI: 0.56-0.93); deworming drugs plus iron for <6 months (OR: 0.79; 95% CI: 0.67-0.93); and deworming drugs plus iron for ≥6 months (OR: 0.77; 95% CI: 0.59-0.99). Prenatal use of only iron for <6 months was not associated with moderate/severe anemia. Prenatal iron and/or deworming drugs had no effect on mild anemia. Prenatal anemia control interventions are associated with reduced risk of moderate/severe anemia but not with mild anemia in young children in SSA. Iron supplements should be taken for ≥6 months or with deworming drugs prenatally to reduce moderate/severe anemia risk in children.

- **NACs User Guide: How to use a food group questionnaire**

NACS User Guide: How to use a food group questionnaire

- **Guideline: Daily Iron Supplementation in Adult Women and Adolescent Girls**

Globally, one in three non-pregnant women, corresponding to almost 500 million women, were anaemic in 2011. Iron deficiency is thought to contribute to at least half of the global burden of anaemia. Iron deficiency occurs following prolonged negative iron balance, the major causes of which include inadequate intake (owing to insufficient bioavailable iron in the
diet or decreased iron absorption), increased iron requirements (for instance, during periods of growth) and chronic blood loss (from heavy hookworm infection or menstrual bleeding). In adolescent girls, menstrual blood losses, accompanied by rapid growth with expansion of the red cell mass and increased tissue iron requirements, make them particularly vulnerable to iron deficiency compared to male counterparts. This guideline reviews the evidence and updates the recommendation for daily iron supplementation in menstruating adult women and adolescent girls.

• **Tubaramure, a Food-Assisted Integrated Health and Nutrition Program in Burundi, Increases Maternal and Child Hemoglobin Concentrations and Reduces Anemia: A Theory-Based Cluster-Randomized Controlled Intervention Trial**

**Background:** Despite their popularity, food-assisted maternal and child health and nutrition (MCHN) programs have not been evaluated rigorously, and evidence of their impacts on maternal and child outcomes is scant.

**Objective:** This study estimated the impact of *Tubaramure*, a food-assisted MCHN program implemented by Catholic Relief Services and partners in eastern Burundi, on hemoglobin and anemia (primary outcome) in children aged 0–23.9 mo and their mothers and explored the impact pathways. The program targeted women and their children during their first 1000 d of life and included 1) food rations, 2) strengthening and promotion of the use of health services, and 3) behavior change communication.

**Methods:** This was a cluster-randomized controlled study to assess program impact by using cluster fixed-effects double-difference models with repeated cross-sectional data (baseline and follow-up 2 y later). We explored impact pathways by estimating impact on intermediary factors addressed by *Tubaramure* that are known determinants of hemoglobin and anemia and by regressing hemoglobin and anemia on each determinant to assess the plausibility that the effect operated through each determinant.

**Results:** Hemoglobin decreased and anemia increased markedly from baseline to follow-up, but *Tubaramure* had a significant ($P < 0.05$) beneficial effect on both children [6.1 percentage points (pps)] and mothers who had given birth in the previous 3 mo (34.9 pps). The program also had significant ($P < 0.05$) impacts on factors along the hypothesized impact pathways: dietary diversity, consumption of iron-rich foods, morbidity, and fever for child hemoglobin and dietary diversity, consumption of iron-rich foods, and current bed-net use for maternal anemia.

**Conclusions:** We showed, for the first time to our knowledge, that a food-assisted MCHN program had a positive impact on anemia and hemoglobin in both mothers and children. The
Taking dietary history: food frequency questionnaire

Guideline: Daily Iron Supplementation in Infants and Children

Approximately 300 million children globally had anaemia in 2011. Deficiency in iron, a mineral necessary to carry oxygen in haemoglobin, is thought to be the most common cause of anaemia. Iron deficiency can result from inadequate intake or absorption of dietary iron, increased need in periods of growth, increased losses from menstruation in adolescent girls, or infection by intestinal helminths, such as schistosomiasis or hookworm infestation, in areas endemic to these parasites.

Iron is an essential nutrient for development and cell growth in the immune and neural systems, as well as in regulation of energy metabolism and exercise. The economic costs of iron deficiency anaemia from annual physical productivity losses have been calculated to be around US$ 2.32 per capita, or 0.57% of gross domestic product in low- and middle-income countries. The WHO has consistently recommended oral iron supplementation as one of the interventions that can reduce the prevalence of anaemia.

Iron is required for the survival and virulence of many pathogens. Concerns have been expressed on a possible increased risk of malaria with iron interventions in malaria-endemic areas, particularly among iron-replete children. On the other hand, screening to identify iron deficiency in children prior to iron supplementation is not feasible in many malaria-endemic settings. Given the importance and magnitude of anaemia globally, particularly in areas where malaria transmission is intense, an assessment of all available evidence has been carried out, to examine the safety and effectiveness of iron supplementation in children, including in malaria-endemic areas.

Effect of Single-Dose Albendazole and Vitamin A Supplementation on the Iron Status of Pre-School Children in Sichuan, China

The aim of this study was to explore the effect of single-dose albendazole and vitamin A
intervention on the anaemic status and Fe metabolism of pre-school children. This study was a randomised, placebo-controlled and double-blinded intervention trial. All eligible anaemic pre-school children were randomly divided into three groups: group 1 received no intervention, which served as the control group, group 2 received 400 mg single-dose albendazole administration and group 3 received a 60000 ?g vitamin A capsule combined with 400 mg single-dose albendazole at the beginning of the study. The follow-up period was for 6 months. Anthropometry and biochemical index about Fe metabolism were measured before and after intervention. A total of 209 pre-school anaemic children were randomly divided into three intervention groups (sixty-four, sixty-two and sixty for groups 1, 2 and 3, respectively). The mean age of the children in the study was 4.4 (SD 0.7) years and 50.0% of the children were female (94/186). After a follow-up period of 6 months, the levels of serum retinol, ferritin, transferrin receptor-ferritin index and body total Fe content of children in group 3 were significantly higher compared with children in groups 1 and 2 (F<0.05). Moreover, the proportion of vitamin A deficiency, marginal vitamin A deficiency and Fe deficiency among children in group 3 were markedly lower compared with children in groups 1 and 2 (F<0.05). Albendazole plus vitamin A administration showed more efficacy on the improvement of serum retinol and Fe metabolic status.

• Guideline: Iron Supplementation in Postpartum Women

Iron deficiency is one of the most common forms of nutritional deficiencies, particularly among vulnerable groups such as women, children and low-income populations. Iron deficiency often precedes anaemia, and anaemia during pregnancy is one of the strongest predictors of anaemia during the postpartum period, beginning just after childbirth throughout the subsequent 6 weeks. The consequences of iron deficiency and anaemia during the postpartum period can be serious and have long-term health implications for the mother and her infant. This guideline reviews the evidence on the safety and effectiveness of iron supplementation in postpartum women.

• Maternal Haemoglobin Concentrations Before and During Pregnancy and Stillbirth Risk: A Population-Based Case-Control Study

Background: Results of previous studies on the association between maternal haemoglobin concentration during pregnancy and stillbirth risk are inconclusive. It is not clear if haemoglobin concentration before pregnancy has a role. Using prospectively collected information from pre-pregnancy and antenatal visits, we investigated associations of maternal haemoglobin concentrations before and during pregnancy and haemoglobin dilution with stillbirth risk.
Methods: In a population-based case-control study from rural Golestan, a proving in northern Iran, we identified 495 stillbirths (cases) and randomly selected 2,888 control live births among antenatal health-care visits between 2007 and 2009. Using logistic regression, we estimated associations of maternal haemoglobin concentrations, haemoglobin dilution at different stages of pregnancy, with stillbirth risk.

Results: Compared with normal maternal haemoglobin concentration (110-120 g/l) at the end of the second trimester, high maternal haemoglobin concentration (>/= 140 g/l) was associated with a more than two-fold increased stillbirth risk (OR = 2.31, 95% CI [1.30-4.10]), while low maternal haemoglobin concentration (<110 g/l) was associated with a 37% reduction in stillbirth risk. Haemoglobin concentration before pregnancy was not associated with stillbirth risk. Decreased haemoglobin concentration, as measured during pregnancy (OR = 0.61, 95% CI [0.46, 0.80]), or only during the second trimester (OR = 0.75, 95% CI [0.62, 0.90]), were associated with reduced stillbirth risk. The associations were essentially similar for preterm and term stillbirths.

Conclusions: Haemoglobin concentration before pregnancy is not associated with stillbirth risk. High haemoglobin level and absence of haemoglobin dilution during pregnancy could be considered as indicators of a high-risk pregnancy.

Mapping the Global Reach of Biofortified Crops

The number of countries that have adopted biofortified crops continues to grow around the world. Since September 2015, several additional countries have released or tested these nutritious crops. They include Afghanistan, Eritrea, Chad, Gabon, Gambia, Morocco, Lebanon, South Sudan, and Tunisia. More than 50 countries in total have now embraced biofortification.

Sociodemographic and Obstetric Characteristics of Anaemic Pregnant Women Attending Antenatal Clinic in Bolgatanga Regional Hospital

The study determined the sociodemographic and obstetric characteristics of pregnant women which contribute to the risk of developing anaemia. A cross sectional study was conducted among 400 pregnant women attending their first antenatal visit at the Bolgatanga Regional Hospital Antenatal Clinic. Anaemia was significantly associated (p < 0.05) with younger maternal age, parity, gravidity, trimester of pregnancy, and source of drinking water. Multivariate logistic regression identified the following factors with adjusted odds ratios (aOR) and 95% confidence intervals (CI): unemployment (aOR = 4.76 (CI: 2.26-11.33); p < 0.0001), rural dwelling (aOR = 3.10 (CI: 2.16-4.91); p = 0.0071), primigravida (aOR = 2.13 (CI:1.34-3.18); p = 0.0201); nulliparity (aOR = 1.92 (CI: 1.23-2.86); p = 0.0231), first antenatal visit at
second trimester (aOR = 1.71 (CI: 1.33-3.12); p = 0.0149) and first antenatal visit at third trimester (aOR = 2.73 (CI: 1.24-4.35); p = 0.0017), drinking from well and boreholes (aOR = 2.78 (CI: 2.27-5.21); p < 0.0001), and the presence of domestic livestock (aOR = 2.15 (CI: 1.33-3.68); p = 0.0019). This study has shown the various sociodemographic and obstetric factors which significantly contribute to anaemia in pregnancy.

**Senegal: Major Shift for Women and Adolescent Girls' Nutrition**

The ?Right Start Initiative? is a comprehensive program reaching nine countries in Asia and Africa, designed and run by the Micronutrient Initiative (MI) in order to improve the quality of nutrition for 100 million adolescent girls and women of reproductive age. In Senegal, MI will invest $1.7M (CAD) over five years to 2020. The program has two parts: first, there will be a weekly iron and folic acid supplementation offered to more than 1.2M adolescent girls attending school in the regions of Dakar, Kaolack, Kolda, St. Louis, Sédhiou, Thies and Ziguinchor. Secondly, commercial wheat flour will be fortified with iron and folic acid throughout the country in order to reach hundreds of thousands of adolescent girls and women of reproductive age.

**Sociodemographic Factors Influencing Adherence to Antenatal Iron Supplementation Recommendations Among Pregnant Women in Malawi: Analysis of Data from the 2010 Malawi Demographic and Health Survey**

**Background and Aim:** Maternal morbidity and mortality statistics remain unacceptably high in Malawi. Prominent among the risk factors in the country is anaemia in pregnancy, which generally results from nutritional inadequacy (particularly iron deficiency) and malaria, among other factors. This warrants concerted efforts to increase iron intake among reproductive-age women. This study, among women in Malawi, examined factors determining intake of supplemental iron for at least 90 days during pregnancy.
Methods: A weighted sample of 10,750 women (46.7%), from the 23,020 respondents of the 2010 Malawi Demographic and Health Survey (MDHS), were utilized for the study. Univariate, bivariate, and regression techniques were employed. While univariate analysis revealed the percent distributions of all variables, bivariate analysis was used to examine the relationships between individual independent variables and adherence to iron supplementation. Chi-square tests of independence were conducted for categorical variables, with the significance level set at P < 0.05. Two binary logistic regression models were used to evaluate the net effect of independent variables on iron supplementation adherence.

Results: Thirty-seven percent of the women adhered to the iron supplementation recommendations during pregnancy. Multivariate analysis indicated that younger age, urban residence, higher education, higher wealth status, and attending antenatal care during the first trimester were significantly associated with increased odds of taking iron supplementation for 90 days or more during pregnancy (P < 0.01).

Conclusions: The results indicate low adherence to the World Health Organization's iron supplementation recommendations among pregnant women in Malawi, and this contributes to negative health outcomes for both mothers and children. Focusing on education interventions that target populations with low rates of iron supplement intake, including campaigns to increase the number of women who attend antenatal care clinics in the first trimester, are recommended to increase adherence to iron supplementation recommendations.

• Uganda Releases Biofortified Beans to Address Iron Deficiency Anemia

The Government of Uganda released the first five high iron bean varieties that will provide more iron in the diets of millions of Ugandans who eat beans almost every day. Three of the released varieties are bush beans and two are climbers.

• The Prevalence of Anemia and Iron Deficiency is More Common in Breastfed Infants than Their Mothers in Bhaktapur, Nepal
**Background/Objectives:** Iron deficiency anemia is a widespread public health problem, particularly in low- and middle-income countries. Maternal iron status around and during pregnancy may influence infant iron status. We examined multiple biomarkers to determine the prevalence of iron deficiency and anemia among breastfed infants and explored its relationship with maternal and infant characteristics in Bhaktapur, Nepal.

**Subjects/Methods:** In a cross-sectional survey, we randomly selected 500 mother-infant pairs from Bhaktapur municipality. Blood was analyzed for hemoglobin, ferritin, total iron-binding capacity, transferrin receptors and C-reactive protein.

**Results:** The altitude-adjusted prevalence of anemia was 49% among infants 2-6-month-old (hemoglobin (Hb) < 10.8 g/dl) and 72% among infants 7-12-month-old (Hb < 11.3 g/dl). Iron deficiency anemia, defined as anemia and serum ferritin <20 or <12 µg/l, affected 9 and 26% of infants of these same age groups. Twenty percent of mothers had anemia (Hb < 12.3 g/dl), but only one-fifth was explained by depletion of iron stores. Significant predictors of infant iron status and anemia were infant age, sex and duration of exclusive breastfeeding and maternal ferritin concentrations.

**Conclusions:** Our findings suggest that iron supplementation in pregnancy is likely to have resulted in a low prevalence of postpartum anemia. The higher prevalence of anemia and iron deficiency among breastfed infants compared with their mothers suggests calls for intervention targeting newborns and infants.

- **Iron Deficiency Anaemia in Pregnancy: The Role of Parenteral Iron.**

Maternal and perinatal morbidity and mortality remain major challenges in the delivery of safe maternity care worldwide. Anaemia in pregnancy is an important contributor to this dismal picture, especially where blood transfusion services are poorly developed. An early diagnosis and treatment of iron deficiency anaemia in pregnancy using the new generation dextran-free parenteral iron preparations can save lives and reduce morbidity in selected pregnancies. It is time to cast aside the fears associated with the use of the old parenteral iron preparations which were associated with a high incidence of anaphylaxis, and embrace the use of new parenteral iron products which have better side effect profiles and can deliver total dose infusions without the need for dose testing. In selected women, the benefits of this treatment far outweigh any disadvantages.

- **WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience**
This is a comprehensive WHO guideline on routine ANC for pregnant women and adolescent girls. The aim is for these recommendations to complement existing WHO guidelines on the management of specific pregnancy-related complications. The guidance is intended to reflect and respond to the complex nature of the issues surrounding the practice and delivery of ANC, and to prioritize person-centred health and well-being— not only the prevention of death and morbidity—in accordance with a human rights-based approach.

The scope of this guideline was informed by a systematic review of women’s views, which shows that women want a positive pregnancy experience from ANC. A positive pregnancy experience is defined as maintaining physical and sociocultural normality, maintaining a healthy pregnancy for mother and baby (including preventing or treating risks, illness and death), having an effective transition to positive labour and birth, and achieving positive motherhood (including maternal self-esteem, competence and autonomy).

Recognizing that a woman’s experience of care is key to transforming ANC and creating thriving families and communities, this guideline addresses the following questions:

- What are the evidence-based practices during ANC that improve outcomes and lead to a positive pregnancy experience?
- How should these practices be delivered?

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**Amaemia in Adolescent Girls: An Intervention of Diet Editing and Counseling**

**Background:** Though a major public health problem of nutritional anaemia in schoolchildren is being addressed by iron supplementation and/or fortified food, they continue to be anaemic. We aimed to study the effect of fluoride consumption on haemoglobin levels and whether elimination of fluoride from the diet would correct anaemia in children.

**Methods:** Two hundred and fifty adolescent girls, 10-17 years of age, from a government senior secondary girls school in East Delhi, participated in the programme. Only those girls who were dewormed in the school health programme and not on any medication particularly for malaria, were included. The investigations done were (i) haemoglobin level; (ii) fluoride content in urine; and (iii) fluoride content in drinking water both at home and in school. The anaemic students consuming safe drinking water with fluoride level <1.0 mg/L and with urine fluoride >1.0 mg/L were introduced to interventions, viz. diet editing and diet counselling when parents came for the monthly parent-teacher meeting. Besides the parents, their wards and class teachers also attended the counselling session. The students were monitored by re-testing haemoglobin and urine fluoride levels at 1, 3 and 6 months after the start of the intervention.

**Results:** There was an inverse relationship in the levels of urine fluoride and haemoglobin.
Reduction in the level of urine fluoride led to a rise in the haemoglobin level. Following interventions, the haemoglobin level revealed significant improvement from the anaemic (<12.0 g/dl) to the non-anaemic range (12.0-14.4 g/dl). At 6 months of follow-up, of the 244 girls studied, those with severe anaemia decreased from 3% to 1%, with moderate anaemia from 97% to 58% and the non-anaemic girls increased from 0% to 41%.

**Conclusion:** Non-toxic nutritive food and safe water with fluoride level < 1.0 mg/L are useful in improving haemoglobin levels in a high percentage of anaemic schoolchildren. A haemoglobin level of > 12.0-14.4 g/dL is an achievable target in children without iron supplementation.

**Complementary Feeding Diets Made of Local Foods Can Be Optimized, but Additional Interventions Will Be Needed to Meet Iron and Zinc Requirements in 6- to 23-Month-Old Children in Low- and Middle-Income Countries**

**Background:** The question whether diets composed of local foods can meet recommended nutrient intakes in children aged 6 to 23 months living in low- and middle-income countries is contested.

**Objective:** To review evidence of studies evaluating whether (1) macro- and micronutrient requirements of children aged 6 to 23 months from low- and middle-income countries are met by the consumption of locally available foods (observed intake) and (2) nutrient requirements can be met when the use of local foods is optimized, using modeling techniques.

**Methods:** Twenty-three articles were included after conducting a systematic literature search. To allow for comparisons between studies, findings of 15 observed intake studies were compared against their contribution to a standardized recommended nutrient intake from complementary foods. For studies with data on intake distribution, %< estimated average requirements were calculated.

**Results:** Data from the observed intake studies indicate that children aged 6 to 23 months meet requirements of protein, while diets are inadequate in calcium, iron, and zinc. Also for energy, vitamin A, thiamin, riboflavin, niacin, folate, and vitamin C, children did not always fulfill their requirements. Very few studies reported on vitamin B6, B12, and magnesium, and no conclusions can be drawn for these nutrients. When diets are optimized using modeling techniques, most of these nutrient requirements can be met, with the exception of iron and zinc and in some settings calcium, folate, and B vitamins.
Conclusion: Our findings suggest that optimizing the use of local foods in diets of children aged 6 to 23 months can improve nutrient intakes; however, additional cost-effective strategies are needed to ensure adequate intakes of iron and zinc.

Prevalence of Anaemia and Its Associated Risk Factors Among Adolescent Girls of Central Kerala

Introduction: Adolescent age group is the window of opportunity to correct nutritional status of children. If we intervene correctly during this period we can prevent future consequences of nutritional deficiencies. Very few studies have been conducted in Kerala regarding adolescent anaemia.

Aim: To estimate prevalence of anaemia and its associated factors among adolescent girls of central Kerala, India.

Materials and Methods: A cross-sectional study was conducted among 257 adolescent girls of ettumanoor panchayat, the field practice area of Government Medical College, Kottayam. A pre-designed and pre-tested proforma was used to obtain data regarding socio-demographic details and factors associated with anaemia. Relevant clinical examination of participants were done. Blood samples were analysed using an auto-analyser and stool examination for ova or cyst was done under microscopy. Diagnosis of anaemia was established when haemoglobin was less than 12 gm/dl. Data analysis was done using SPSS 16.0. Association between Categorical variables were tested with Chi-square test and continuous variables independent t-test was used. Logistic regression was used to find out independent risk factors. The level of significance was fixed at p-value of < 0.05.

Results: The prevalence of anaemia was 21%. Risk factors associated with anaemia in the univariate analysis were presence of ova or cyst in stool (p = 0.003, OR = 2.94) and number of pads per day during menstruation (p = 0.004). Protective factors were hand washing after toileting (p = 0.021, OR = 0.311), hand washing before food intake (p = 0.026, OR = 0.5), foot wear usage (p = 0.022, OR = 0.25) and jaggery consumption (0.042). The factors which were significant in logistic regression were worm infestation, number of pads per day, washing hands before food intake and foot wear usage.

Conclusion: Worm infestation and number of pads per day during menstruation were found to be risk factors for anaemia. Personal hygiene practices like hand washing and foot wear usage were found to be protective factors.

Consuming Iron Biofortified Beans Increases Iron Status in Rwandan Women after 128 Days in a Randomized
Background: Food-based strategies to reduce nutritional iron deficiency have not been universally successful. Biofortification has the potential to become a sustainable, inexpensive, and effective solution.

Objective: This randomized controlled trial was conducted to determine the efficacy of iron-biofortified beans (Fe-Beans) to improve iron status in Rwandan women.

Methods: A total of 195 women (aged 18-27 y) with serum ferritin <20 μg/L were randomly assigned to receive either Fe-Beans, with 86 mg Fe/kg, or standard unfortified beans (Control-Beans), with 50 mg Fe/kg, 2 times/d for 128 d in Huye, Rwanda. Iron status was assessed by hemoglobin, serum ferritin, soluble transferrin receptor (sTfR), and body iron (BI); inflammation was assessed by serum C-reactive protein (CRP) and serum ? 1-acid glycoprotein (AGP). Anthropometric measurements were performed at baseline and at end line. Random weekly serial sampling was used to collect blood during the middle 8 wk of the feeding trial. Mixed-effects regression analysis with repeated measurements was used to evaluate the effect of Fe-Beans compared with Control-Beans on iron biomarkers throughout the course of the study.

Results: At baseline, 86% of subjects were iron-deficient (serum ferritin <15 mg/L) and 37% were anemic (hemoglobin <120 g/L). Both groups consumed an average of 336 g wet beans/d. The Fe-Beans group consumed 14.5 ± 1.6 mg Fe/d from biofortified beans, whereas the Control-Beans group consumed 8.6 ± 0.8 mg Fe/d from standard beans (P < 0.05). Repeated-measures analyses showed significant time-by-treatment interactions for hemoglobin, log serum ferritin, and BI (P < 0.05). The Fe-Beans group had significantly greater increases in hemoglobin (3.8 g/L), log serum ferritin (0.1 log mg/L), and BI (0.5 mg/kg) than did controls after 128 d. For every 1 g Fe consumed from beans over the 128 study days, there was a significant 4.2-g/L increase in hemoglobin (P < 0.05).

Conclusions: The consumption of iron-biofortified beans significantly improved iron status in Rwandan women. This trial was registered at clinicaltrials.gov as NCT01594359.

Household Food Insecurity in Mexico is Associated with the Co-Occurrence of Overweight and Anemia among Women of Reproductive Age, but Not Female Adolescents

We aimed to determine the association between household food insecurity (HFI) and the co-occurrence of overweight and anemia among women of reproductive age in the Mexican population. We analyzed data on 4,039 nonpregnant female adolescents (15-19 years) and 10,760 nonpregnant adult women of reproductive age (20-49 years) from the 2012 National Health and Nutrition Survey of Mexico. The survey uses a two-stage sampling design,
stratified by rural and urban regions. The Latin American and Caribbean Food Security Scale was used to assess HFI. We assessed overweight and obesity in women based on World Health Organization classifications for body mass index, and BMI-for-age Z-scores for female adolescents, and defined anemia as an altitude-adjusted hemoglobin (Hb) concentration < 120 g/L based on measurement of capillary Hb concentrations. In multiple logistic regression models adjusting for potential confounding covariates, HFI was not associated with the co-occurrence of anemia and overweight among female adolescents. The adjusted odds of women of reproductive age from mildly and moderately food-insecure households, respectively, experiencing concurrent anemia and overweight were 48% (OR: 1.48; 95% CI: 1.15, 1.91) and 49% (OR: 1.49; 95% CI: 1.08, 2.06) higher than among women from food-secure households. Severe HFI was not associated with concurrent overweight and anemia among female adolescents or women. HFI may be a shared mechanism for dual forms of malnutrition within the same individual, simultaneously contributing to overconsumption and dietary inadequacy.

• **Delaying Iron Therapy until 28 Days after Antimalarial Treatment Is Associated with Greater Iron Incorporation and Equivalent Hematologic Recovery after 56 Days in Children: A Randomized Controlled Trial**

**Background:** Iron therapy begun concurrently with antimalarial treatment may not be well absorbed because of malaria-induced inflammation. Delaying the start of iron therapy may permit better iron absorption and distribution.

**Objective:** We compared erythrocyte iron incorporation in children who started iron supplementation concurrently with antimalarial treatment or 28 d later. We hypothesized that delayed iron supplementation would be associated with greater incorporation and better hematologic recovery.

**Methods:** We enrolled 100 children aged 6-59 mo with malaria and hemoglobin concentrations of 50.0-99.9 g/L who presented to Mulago Hospital, Kampala, into a randomized trial of iron therapy. All children were administered antimalarial treatment. Children with zinc protoporphyrin (ZPP) ≥ 80 ?mol/mol heme were randomly assigned to start iron supplementation concurrently with the antimalarial treatment [immediate iron (I) group] or 28 d later [delayed iron (D) group]. All children were administered iron-stable isotope $^{57}$Fe on day 0 and $^{58}$Fe on day 28. We compared the percentage of iron incorporation at the start of supplementation (I group at day 0 compared with D group at day 28, aim 1) and hematologic recovery at day 56 (aim 2).

**Results:** The percentage of iron incorporation (mean ± SE) was greater at day 28 in the D group (16.5% ± 1.7%) than at day 0 in the I group (7.9% ± 0.5%; P < 0.001). On day 56, concentrations of hemoglobin and ZPP and plasma ferritin, soluble transferrin receptor (sTfR), hepcidin, and C-reactive protein did not differ between the groups. On day 28, the
hemoglobin (mean ± SD) and plasma iron markers (geometric mean; 95% CI) reflected poorer iron status in the D group than in the I group at this intervening time as follows: hemoglobin (105 ± 15.9 compared with 112 ± 12.4 g/L; \( P = 0.04 \)), ferritin (39.3 ?g/L; 23.5, 65.7 ?g/L compared with 79.9 ?g/L; 58.3, 110 ?g/L; \( P = 0.02 \)), sTfR (8.9 mg/L; 7.4, 10.7 mg/L compared with 6.7 mg/L; 6.1, 7.5 mg/L; \( P = 0.01 \)), and hepcidin (13.3 ng/mL; 8.3, 21.2 ng/mL compared with 38.8 ng/mL; 28.3, 53.3 ng/mL; \( P < 0.001 \)).

Conclusions: Delaying the start of iron improves incorporation but leads to equivalent hematologic recovery at day 56 in Ugandan children with malaria and anemia. These results do not demonstrate a clear, short-term benefit of delaying iron. This trial was registered at clinicaltrials.gov as NCT01754701.

Maternal Malaria and Malnutrition (M3) Initiative, a Pooled Birth Cohort of 13 Pregnancy Studies in Africa and the Western Pacific

Purpose: The Maternal Malaria and Malnutrition (M3) initiative has pooled together 13 studies with the hope of improving understanding of malaria?nutrition interactions during pregnancy and to foster collaboration between nutritionists and malariologists.

Participants: Data were pooled on 14?635 singleton, live birth pregnancies from women who had participated in 1 of 13 pregnancy studies. The 13 studies cover 8 countries in Africa and Papua New Guinea in the Western Pacific conducted from 1996 to 2015.

Findings to Date: Data are available at the time of antenatal enrolment of women into their respective parent study and at delivery. The data set comprises essential data such as malaria infection status, anthropometric assessments of maternal nutritional status, presence of anaemia and birth weight, as well as additional variables such gestational age at delivery for a subset of women. Participating studies are described in detail with regard to setting and primary outcome measures, and summarised data are available from each contributing cohort.

Future Plans: This pooled birth cohort is the largest pregnancy data set to date to permit a more definite evaluation of the impact of plausible interactions between poor nutritional status and malaria infection in pregnant women on fetal growth and gestational length. Given the current comparative lack of large pregnancy cohorts in malaria-endemic settings, compilation of suitable pregnancy cohorts is likely to provide adequate statistical power to assess malaria?nutrition interactions, and could point towards settings where such interactions are most relevant. The M3 cohort may thus help to identify pregnant women at high risk of adverse outcomes who may benefit from tailored intensive antenatal care including nutritional supplements and alternative or intensified malaria prevention regimens, and the settings in which these interventions would be most effective.
In-Home Fortification with 2.5 mg Iron as NaFeEDTA does not Reduce Anaemia but Increases Weight Gain: A Randomised Controlled Trial in Kenyan Infants

In-home fortification of infants with micronutrient powders (MNPs) containing 12.5 mg iron may increase morbidity from infections; therefore, an efficacious low-dose iron-containing MNP might be advantageous. Effects of iron-containing MNPs on infant growth are unclear. We assessed the efficacy of a low-iron MNP on iron status and growth and monitored safety in a randomised, controlled, double-blind 1-year trial in 6-month-old infants (n = 287) consuming daily a maize porridge fortified with either a MNP including 2.5 mg iron as NaFeEDTA (MNP + Fe) or the same MNP without iron (MNP - Fe). At baseline, after 6 and 12 months, we determined haemoglobin (Hb), iron status [serum ferritin (SF), soluble transferrin receptor (sTfR) and zinc protoporphyrin (ZPP)], inflammation [C-reactive protein (CRP)] and anthropometrics. We investigated safety using weekly morbidity questionnaires asking for diarrhoea, cough, flu, bloody or mucus-containing stool and dyspnoea, and recorded any other illness. Furthermore, feeding history and compliance were assessed weekly. At baseline, 71% of the infants were anaemic and 22% iron deficient; prevalence of inflammation was high (31% had an elevated CRP). Over the 1 year, Hb increased and SF decreased in both groups, without significant treatment effects of the iron fortification. At end point, the weight of infants consuming MNP + Fe was greater than in the MNP - Fe group (9.9 vs. 9.5 kg, \(P = 0.038\)). Mothers of infants in the MNP + Fe group reported more infant days spent with cough \((P = 0.003)\) and dyspnoea \((P = 0.0002)\); there were no significant differences on any other of the weekly morbidity measures. In this study, low-dose iron-containing MNP did not improve infant's iron status or reduce anaemia prevalence, likely because absorption was inadequate due to the high prevalence of infections and the low-iron dose.

Promoting Multi-Micronutrient Powders (MNP) in Peru: Acceptance by Caregivers and Role of Health Personnel

Iron deficiency causes anaemia and other adverse effects on the nutritional status and development of millions of children. Multi-micronutrient powders (MNPs) have been shown to reduce anaemia in young children. In Peru, 50% of children 3-36 months are anaemic. Since 2009, the government has started distributing MNP. This qualitative study explored the acceptability of MNP by caregivers and the role of health personnel (HP) in three regions (Apurimac, Ayacucho and Cajamarca), piloting the MNP programme between 2009 and 2011. Data collection consisted of interviews (35) and observations (13) with caregivers and HP (11). In Cajamarca, 16 families were visited three times in their homes to understand caregivers' use and difficulties. Results showed the critical role HP has in influencing caregiver understanding and use of the MNP, as well as the need for training to avoid
confusing messages and provide counseling techniques that consider cultural sensitivity to optimize HP interactions with caregivers and adapt the recommendations for MNP use to local family feeding routines. There was greater acceptance of MNP by caregivers giving semi-solid foods (e.g. purees) to their children than those who served dilute preparations (e.g. soups). Acceptance was similar across regions, but there were some differences between urban and rural settings. Home visits were shown to be a key in improving the use of MNP by caregivers as misunderstandings on preparation, required consistency and optimum practices were common. These findings can contribute to strategies to enhance acceptability and use.

- **Iron Bioavailability in 8?24-Month-Old Thai Children from a Micronutrient-Fortified Quick-Cooking Rice Containing Ferric Ammonium Citrate or a Mixture of Ferrous Sulphate and Ferric Sodium Ethylenediaminetetraacetic Acid**

The study compared iron absorption by infants and young children fed with micronutrient-fortified quick-cooking rice containing the test iron compounds of FeSO4. Micronutrient-fortified quick-cooking rice prepared as a traditional Thai dessert was fed to two groups of 15 8-24-month health Thai children. The relative bioavailability of FAC and of the FeSO4 + NaFeEDTA was obtained by comparing their iron absorption with that of FeSO4. Mean fractional iron absorption was 5.8% [+-standard error (SE) 1.9] from FAC and 10.3% (+/-SE 1.9) from FeSO4 + NaFeEDTA. The relative bioavailability of FAC was 83% (P = 0.02). The relative bioavailability of FeSO4 + NaFeEDTA was 145% (P = 0.001). Iron absorption from the rice containing FAC or FeSO4 + NaFeEDTA was sufficiently high to be used in its formulation, although iron absorption from FeSO4 + NaFeEDTA was significantly higher (P = 0.00001).

- **Adding Multiple Micronutrient Powders to a Homestead Food Production Programme Yields Marginally Significant Benefit on Anaemia Reduction among Young Children in Nepal**

Anaemia affects 46% of preschool-aged children in Nepal. A cluster-randomised study was conducted in rural Nepal to test whether providing micronutrient powders (MNP) in addition to enhanced homestead food production (EHFP) programme, consisting of home gardens, poulty and nutrition education, could lead to a higher reduction in anaemia compared with providing only EHFP. This sub-study enrolled 335 children aged 6-9 months into one of three
groups: (1) EHFP + MNP; (2) EHFP; or (3) control. Mean +/- SE haemoglobin concentration increased significantly in all groups, with a slightly higher but non-significant increase in the EHFP + MNP and EHFP compared with control (difference-in-differences: 4.1 g/L for EHFP + MNP vs. control; 3.6 g/L for EHFP vs. control; 0.5 g/L for EHFP + MNP vs. EHFP). Anaemia decreased at a slightly higher magnitude in the EHFP + MNP [51.5 percentage points (PP)] than the EHFP (48.6 PP) and control (39.6 PP), with adjusted odds ratios (95% CI) at post-supplementation of 0.52 (0.25-1.12) for EHFP + MNP and 0.69 (0.35-1.36) for EHFP, compared with control. There was no impact on child growth. Combining EHFP and MNP programmes yielded a marginally significant reduction in anaemia among children.

• Caterpillar Cereal as a Potential Complementary Feeding Product for Infants and Young Children: Nutritional Content and Acceptability

To avoid micronutrient deficiency, the World Health Organization recommends complementary feeding with animal-source foods. However, animal-source foods are not readily available in many parts of the Democratic Republic of Congo (DRC). In such areas, caterpillars are a staple in adult diets and may be suitable for complementary feeding for infants and young children. We developed a cereal made from dried caterpillars and other locally available ingredients, measured its macro- and micronutrient contents and evaluated for microbiologic contamination. Maternal and infant acceptability was evaluated among 20 mothers and their 8-10-month-old infants. Mothers were instructed in the preparation of the cereal and asked to evaluate the cereal in five domains using a Likert scale. Mothers fed their infants a 30-g portion daily for 1 week. Infant acceptability was based on cereal consumption and the occurrence of adverse events. All infants consumed more than 75% of the daily portions, with five infants consuming 100%. We conclude that a cereal made from locally available caterpillars has appropriate macro- and micronutrient contents for complementary feeding, and is acceptable to mothers and infants in the DRC.

• Anaemia Prevalence may be Reduced among Countries that Fortify Flour

The effectiveness of flour fortification in reducing anaemia prevalence is equivocal. The goal was to utilise the existing national-level data to assess whether anaemia in non-pregnant women was reduced after countries began fortifying wheat flour, alone or in combination with maize flour, with at least Fe, folic acid, vitamin A or vitamin B12. Nationally representative anaemia data were identified through Demographic and Health Survey reports, the WHO Vitamin and Mineral Nutrition Information System database and other national-level nutrition surveys. Countries with at least two anaemia surveys were considered for inclusion. Within countries, surveys were excluded if altitude was not consistently adjusted for, or if the blood-
draw site (e.g. capillary or venous) or Hb quantification method (e.g. Hemocue or Cyanmethaemoglobin) differed. Anaemia prevalence was modelled for countries that had pre- and post-fortification data (n 12) and for countries that never fortified flours (n 20) using logistic regression models that controlled for time effects, human development index (HDI) and endemic malaria. Among countries that never fortified, no reduction in the odds of anaemia prevalence over time was observed (PR 0.999, 95% CI 0.997, 1.002). Among both fortification and non-fortification countries, HDI and malaria were significantly associated with anaemia (P < 0.001). Although this type of evidence precludes a definitive conclusion, results suggest that after controlling for time effects, HDI and endemic malaria, anaemia prevalence has decreased significantly in countries that fortify flour with micronutrients, while remaining unchanged in countries that do not.

- **Evidence of the Effectiveness of Flour Fortification Programs on Iron Status and Anemia: A Systematic Review**

**Context:** More than 80 countries fortify flour, yet the public health impact of this intervention on iron and anemia outcomes has not been reviewed.

**Objective:** The objective of this systematic review was to review published and gray literature pertaining to the impact of flour fortification on iron and anemia.

**Data Sources:** A systematic review was conducted by searching 17 databases and appealing for unpublished reports, yielding 1881 documents.

**Study Selection:** Only studies of government-supported, widely implemented fortification programs in which anemia or iron status was measured prior to and ?12 months after initiation of fortification were included.

**Data Extraction:** Details about the design, coverage, compliance with national standards, and evaluation (e.g., anemia prevalence before and after fortification) of flour fortification programs were extracted from the reports.

**Data Synthesis:** Thirteen studies describing 26 subgroups (n?=14 for children ?15y, n?=12 for women of reproductive age) were included. During the period from pre- to postfortification (and as difference-in-difference for those studies that included a control group), there were statistically significant decreases in the prevalence of anemia in 4 of 13 subgroups of children and in 4 of 12 subgroups of women of reproductive age as well as significant decreases in the prevalence of low ferritin in 1 of 6 subgroups of children and in 3 of 3 subgroups of women of reproductive age.
Conclusions: Evidence of the effectiveness of flour fortification for reducing the prevalence of anemia is limited; however, evidence of effectiveness for reducing the prevalence of low ferritin in women is more consistent.

Multiple-Micronutrient Supplementation for Women During Pregnancy

Background: Multipl-micronutrient deficiencies often coexist in low- to middle-income countries. They are exacerbated in pregnancy due to the increased demands, leading to potentially advers effects on the mother. Substantive evidence regarding the effectiveness of multiple-micronutrient supplements (MMS) during pregnancy is not available.

Objectives: To evaluate the benefits to both mother and infant of multiple-micronutrient supplements in pregnancy and to assess the risk of adverse events as a result of supplementation.

Search Methods: We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (17 February 2012) and reference lists of retrieved articles and key reviews. We also contacted experts in the field for additional and ongoing trials.

Selection Criteria: All prospective randomised controlled trials evaluating multiple-micronutrient supplementation during pregnancy and its effects on the pregnancy outcome, irrespective of language or publication status of the trials. We included cluster-randomised trials but quasi-randomised trials were excluded.

Data Collection and Analysis: Two review authors independently assessed trials for inclusion and trial quality. Two review authors independently extracted the data. Data were checked for accuracy.
Main Results: Twenty-three trials (involving 76,532 women) were identified as eligible for inclusion in this review but only 21 trials (involving 75,785 women) contributed data to the review. When compared with iron and folate supplementation, MMS resulted in a statistically significant decrease in the number of low birthweight babies (risk ratio (RR) 0.89; 95% confidence interval (CI) 0.83 to 0.94) and small-for-gestational age (SGA) babies (RR 0.87; 95% CI 0.81 to 0.95). No statistically significant differences were shown for other maternal and pregnancy outcomes: preterm births RR 0.99 (95% CI 0.96 to 1.02), miscarriage RR 0.90 (95% CI 0.79 to 1.02), maternal mortality RR 0.97 (95% CI 0.63 to 1.48), perinatal mortality RR 0.99 (95% CI 0.84 to 1.16), stillbirths RR 0.96 (95% CI 0.86 to 1.07) and neonatal mortality RR 1.01 (95% CI 0.89 to 1.15). A number of prespecified clinically important outcomes could not be assessed due to insufficient or non-available data. These include placental abruption, congenital anomalies, including neural tube defects, premature rupture of membranes, neurodevelopmental delay, very preterm births, cost of supplementation, side-effects of supplements, maternal well being or satisfaction, and nutritional status of children.

Authors’ Conclusions: Though multiple micronutrients have been found to have a significant beneficial impact on SGA and low birthweight babies, we still need more evidence to guide a universal policy change and to suggest replacement of routine iron and folate supplementation with a MMS. Future trials should be adequately powered to evaluate the effects on mortality and other morbidity outcomes. Trials should also assess the effect of variability between different combinations and dosages of micronutrients, keeping within the safe recommended levels. In regions with deficiency of a single micronutrient, evaluation of each micronutrient against a placebo in women already receiving iron with folic acid would be especially useful in justifying the inclusion of that micronutrient in routine antenatal care.

Introducing a New Monitoring Manual for Home Fortification and Strengthening Capacity to Monitor Nutrition Interventions

Lack of monitoring capacity is a key barrier for nutrition interventions and limits programme management, decision making and programme effectiveness in many low-income and middle-income countries. A 2011 global assessment reported lack of monitoring capacity was the top barrier for home fortification interventions, such as micronutrient powders or lipid-based nutrient supplements. A Manual for Developing and Implementing Monitoring Systems for Home Fortification Interventions was recently disseminated. It is comprehensive and describes monitoring concepts and frameworks and includes monitoring tools and worksheets. The monitoring manual describes the steps of developing and implementing a monitoring system for home fortification interventions, including identifying and engaging stakeholders; developing a programme description including logic model and logical framework; refining the purpose of the monitoring system, identifying users and their monitoring needs; describing the design of the monitoring system; developing indicators; describing the core components of a comprehensive monitoring plan; and considering factors
related to stage of programme development, sustainability and scale up. A fictional home fortification example is used throughout the monitoring manual to illustrate these steps. The monitoring manual is a useful tool to support the development and implementation of home fortification intervention monitoring systems. In the context of systematic capacity gaps to design, implement and monitor nutrition interventions in many low-income and middle-income countries, the dissemination of new tools, such as monitoring manuals may have limited impact without additional attention to strengthening other individual, organisational and systems levels capacities.

**Double-Blind Cluster Randomised Controlled Trial of Wheat Flour Chapatti Fortified with Micronutrients on the Status of Vitamin A and Iron in School-Aged Children in Rural Bangladesh**

Food fortification is a cost-effective and sustainable strategy to prevent or correct micronutrient deficiencies. A double-blind cluster (bari) randomised controlled trial was conducted in a rural community in Bangladesh to evaluate the impact of consumption of chapatti made of micronutrient-fortified wheat flour for 6 months by school-aged children on their vitamin A, haemoglobin and iron status. A total of 43 bars (group of households) were randomly selected. The bars were randomly assigned to either intervention or control group. The intervention group received wheat flour fortified with added micronutrients (including 66 mg hydrogen-reduced elemental iron and 3030 µg retinol equivalent as retinyl palmitate per kilogram of flour), while the control group received wheat flour without added micronutrients. A total of 352 children were enrolled in the trial, 203 in the intervention group and 149 in the control group. Analyses were carried out on children who completed the study (191 in the intervention group and 143 in the control group). Micronutrient-fortified wheat flour chapatti significantly increased serum retinol concentration at 6 months by 0.12 µmol/L [95% confidence interval (CI): 0.06, 0.19; P < 0.01]. The odds of vitamin A deficiency was significantly lower for children in the intervention group at 3 months [odds ratio (OR) = 0.26; 95% confidence interval (CI): 0.07, 0.89; P < 0.05] and 6 months (OR = 0.21; 95% CI: 0.06, 0.68; P < 0.01). No demonstrable effect of fortified chapatti consumption on iron status, haemoglobin levels or anaemia was observed. Consumption of fortified chapattis demonstrated a significant improvement in the vitamin A status, but not in iron, haemoglobin or anaemia status.

**The Role of Folate in Malaria ? Implications for Home Fortification Programmes Among Children Aged 6-59 Months**
Folic acid and iron supplementation has historically been recommended as the preferred anaemia control strategy among preschoolers in sub-Saharan Africa and other resource-poor settings, but home fortification of complementary foods with multiple micronutrient powders (MNPs) can now be considered the preferred approach. The World Health Organization endorses home fortification with MNPs containing at least iron, vitamin A and zinc to control childhood anaemia, and calls for concomitant malaria control strategies in malaria endemic regions. Among other micronutrients, current MNP formulations generally include 88 µg folic acid (corresponding to 100% of the Recommended Nutrient Intake). The risks and benefits of providing supplemental folic acid at these levels are unclear. The limited data available indicate that folate deficiency may not be a major public health problem among children living in sub-Saharan Africa and supplemental folic acid may therefore not have any benefits. Furthermore, supraphysiological, and possibly even physiological, folic acid dosages may favour Plasmodium falciparum growth, inhibit parasite clearance of sulfadoxine-pyrimethamine (SP)-treated malaria and increase subsequent recrudescence. Even though programmatic options to limit prophylactic SP use or to promote the use of insecticide treated bed nets may render the use of folic acid safer, programmatic barriers to these approaches are likely to persist. Research is needed to characterise the prevalence of folate deficiency among young children worldwide and to design safe MNP and other types of fortification approaches in sub-Saharan Africa. In parallel, updated global guidance is needed for MNP programmes in these regions.

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## Association of Maternal Anemia with Other Risk Factors in Occurrence of Great Obstetrical Syndromes at University Clinics, Kinshasa, DR Congo

**Background:** Maternal anemia, a common situation in developing countries, provokes impairment of nutrients/oxygen supply to the placenta-fetus unit that leads to Great obstetrical syndromes (GOS). In our setting, however, occurrence of GOS has been found also depending on variables existing prior to pregnancy such as diabetes in family, hypertension in family, previous macrosomia, stillbirth, SGA and pre-eclampsia as well as overweight/obesity. Our study thus aimed to determine the magnitude of maternal anemia and its association with these pre-pregnancy high-risk variables in occurrence of GOS.

**Methods:** This is a cross-sectional study including women delivered at the University Clinics of Kinshasa, DR Conge 12. during 18 months. Anemia was stated at hemoglobin blood concentration <10 g/dL. Sampled women were checked for pregnancy high-risk factors and pregnancy complications. Odds ratios (95% confidence intervals) were calculated to establish associations of anemia with various variables. Multivariate calculations aimed to isolate variables influencing these associations. The p<0.05 was considered significant.

**Results:** The study sample included 412 women, among whom 220 (53.4%) were diagnosed anemic. Anemia was found significantly linked to malaria, urinary infection, cesarean section,
prematurity, SCA and stillbirth whose risk was 1.6 - 6.1 times augmented. Anemia was also found linked to pre-pregnancy high-risk factors such as age < 18 and ≥ 35 years, previous miscarriage, grand multiparity, diabetes in family, previous prematurity, overweight/obesity, previous cesarean section and previous pre-eclampsia, all of them enhancing the link of maternal anemia with complications.

**Conclusion:** Maternal anemia is very prevalent among pregnant women of our setting. It strongly contributes to worsening of morbidities that act with pregnancy high-risk factors in raising the risk of cesarean section, prematurity, SGA and stillbirth.

- **Global Nutrition Targets 2025: Anaemia Policy Brief**

In 2012, the World Health Assembly Resolution 65.6 endorsed a Comprehensive implementation plan on maternal, infant and young child nutrition, which specified six global nutrition targets for 2025. This policy brief covers the second target: a 50% reduction of anaemia in women of reproductive age. The purpose of this policy brief is to increase attention to, investment in, and action for a set of cost-effective interventions and policies that can help Member States and their partners in reducing the rates of anaemia among women of reproductive age.

- **IRON AND FOLIC ACID SUPPLEMENTATION (IFAS) Dialogue guide for health care providers.**

- **Guideline: Use of Multiple Micronutrient Powders for Home Fortification of Foods Consumed by Pregnant Women**

This guideline provides global, evidence-informed recommendations on the use of multiple micronutrient powders for home fortification of foods consumed by pregnant women. The guideline will help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Millennium Development Goals, in particular, the eradication of extreme poverty and hunger (MDG 1), reduction of child mortality (MDG 4) and improvement of maternal health (MDG 5). The guideline is intended for a wide audience including policy-makers, their expert advisers, and technical and programme staff at organizations involved in the design, implementation and scaling-up of
nutrition actions for public health.

**School Feeding Programs and Development: Are We Framing the Question Correctly?**

School feeding programs are politically popular interventions. They are, nevertheless, difficult to assess in terms of effectiveness since their impact is partially on education and partially on school health. They are, additionally, a means to augment consumption by vulnerable populations. The authors look at recent evidence from in-depth studies and argue that while school feeding programs can influence the education of school children and, to a lesser degree, augment nutrition for families of beneficiaries, they are best viewed as transfer programs that can provide a social safety net and help promote human capital investments.

**What Health Policymakers Can Do**

- Anemia is one of the most widely prevalent disorders, affecting the lives of almost half a billion women of reproductive age.
- Iron deficiency anemia (IDA), alone, contributes to over 100,000 maternal and almost 600,000 perinatal deaths each year. Inter-generational impacts include increased risk of infant mortality, pre-term delivery, low birth weight, and reduced cognitive development in children.
- Anemia results in reduced energy levels which affect productivity, earning power and even maternal caring practices. Economic losses due to IDA alone are estimated at approximately $0.32 per capita or 0.6% of GDP.
- Anemia has multiple causes: increased iron requirements during pregnancy, inadequate intake of micronutrients, particularly iron, and malaria, hookworm, HIV, diarrhea and other infections.

**Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, Controlled Community Trial**

**Background:** The long-term benefits of antenatal iron supplementation in child survival are not known.

**Methods:** In 1999-2001, 4,926 pregnant women in rural Nepal participated in a cluster-randomized, double-masked, controlled trial involving 4 alternative combinations of micronutrient supplements, each containing vitamin A. The authors examined the impact on birth weight and early infant mortality in comparison with controls, who received vitamin A
only. They followed the surviving offspring of these women at approximately age 7 years to study effects of in utero supplementation on survival. Of 4,130 livebirths, 209 infants died in the first 3 months and 8 were lost to follow-up. Of those remaining, 3,761 were followed, 150 died between ages 3 months and 7 years, and 152 were lost to followup.

**Results:** Mortality rates per 1,000 child-years from birth to age 7 years differed by maternal supplementation group, as follows: folic acid, 13.4; folic acid-iron, 10.3; folic acid-iron-zinc, 12.0; multiple micronutrients; 14.0; and controls, 15.2. Hazard ratios were 0.90 (95% confidence interval (CI): 0.65, 1.22), 0.69 (95% CI: 0.49, 0.99), 0.80 (95% CI: 0.58, 1.11), and 0.93 (95% CI: 0.66, 1.31), respectively, in the 4 supplementation groups.

**Conclusions:** Maternal iron-folic acid supplementation reduced mortality among these children by 31% between birth and age 7 years. These results provide additional motivation for strengthening antenatal iron-folic acid programs.

**What Works? Interventions for Maternal and Child Undernutrition and Survival**

We reviewed interventions that affect maternal and child undernutrition and nutrition-related outcomes. These interventions included promotion of breastfeeding; strategies to promote complementary feeding, with or without provision of food supplements; micronutrient interventions; general supportive strategies to improve family and community nutrition; and reduction of disease burden (promotion of handwashing and strategies to reduce the burden of malaria in pregnancy). We showed that although strategies for breastfeeding promotion have a large effect on survival, their effect on stunting is small. In populations with sufficient food, education about complementary feeding increased height-for-age Z score by 0·25 (95% CI 0·01?0·49), whereas provision of food supplements (with or without education) in populations with insufficient food increased the height-for-age Z score by 0·41 (0·05?0·76).

Management of severe acute malnutrition according to WHO guidelines reduced the case-fatality rate by 55% (risk ratio 0·45, 0·32?0·62), and recent studies suggest that newer commodities, such as ready-to-use therapeutic foods, can be used to manage severe acute malnutrition in community settings. Effective micronutrient interventions for pregnant women included supplementation with iron folate (which increased haemoglobin at term by 12 g/L, 2·93?21·07) and micronutrients (which reduced the risk of low birthweight at term by 16% (relative risk 0·84, 0·74?0·95). Recommended micronutrient interventions for children included strategies for supplementation of vitamin A (in the neonatal period and late infancy), preventive zinc supplements, iron supplements for children in areas where malaria is not endemic, and universal promotion of iodised salt. We used a cohort model to assess the potential effect of these interventions on mothers and children in the 36 countries that have 90% of children with stunted linear growth. The model showed that existing interventions that were designed to improve nutrition and prevent related disease could reduce stunting at 36 months by 36%; mortality between birth and 36 months by about 25%; and disability-adjusted life-years associated with stunting, severe wasting, intrauterine growth restriction, and
micronutrient deficiencies by about 25%. To eliminate stunting in the longer term, these interventions should be supplemented by improvements in the underlying determinants of undernutrition, such as poverty, poor education, disease burden, and lack of women's empowerment.

- **Association between Anaemia during Pregnancy and Blood Loss at and after Delivery among Women with Vaginal Births in Pemba Island, Zanzibar, Tanzania**

  **Background:** The study sought to identify determinants of blood loss at childbirth and 24 hours postpartum. The study was nested in a community-based randomized trial of treatments for anaemia during pregnancy in Wete Town, Pemba Island, Zanzibar, United Republic of Tanzania. Status of anaemia during pregnancy, nutritional information, obstetric history, and socioeconomic status were assessed at enrollment during routine antenatal care.

  **Methods:** Pregnant women presented for spontaneous vaginal delivery, and nurse-midwives collected information on labour and delivery via partograph. Blood-stained sanitary napkins and pads from childbirth and 24 hours postpartum were quantified using the alkaline hematin method. Moderate- to-severe anaemia (Hb <90 g/L) at enrollment was strongly associated with blood loss at delivery and the immediate postpartum period, after adjusting for maternal covariates and variables of biological relevance to blood loss.

  **Results:** Greater blood loss was associated (p<0.10) with duration of the first stage of labour, placental weight, receipt of oxytocin, preterm birth, and grand multiparity.

  **Conclusions:** The findings provide unique evidence of a previously-suspected link between maternal anaemia and greater blood loss at childbirth and postpartum. Further research is needed to confirm these findings on a larger sample of women to determine whether women with moderate-to-severe anaemia are more likely to experience postpartum haemorrhage and whether appropriate antenatal or peripartum care can affect the relationships described here.

- **Impact of Micronutrient Supplementation during Pregnancy on Birth Weight, Duration of Gestation, and Perinatal Mortality in Rural Western China: Double Blind Cluster Randomized Controlled Trial**

  **Objective:** To examine the impact of antenatal supplementation with multiple micronutrients
or iron and folic acid compared with folic acid alone on birth weight, duration of gestation, and maternal haemoglobin concentration in the third trimester.

**Design:** Cluster randomised double blind controlled trial. Setting Two rural counties in north west China. Participants 5828 pregnant women and 4697 live births. Interventions Villages were randomised for all pregnant women to take either daily folic acid (control), iron with folic acid, or multiple micronutrients with a recommended allowance of 15 vitamins and minerals. Main outcome measures Birth weight, length, and head circumference measured within 72 hours after delivery. Neonatal survival assessed at the six week follow-up visit.

**Results:** Birth weight was 42 g (95% confidence interval 7 to 78 g) higher in the multiple micronutrients group compared with the folic acid group. Duration of gestation was 0.23 weeks (0.10 to 0.36 weeks) longer in the iron- folic acid group and 0.19 weeks (0.06 to 0.32 weeks) longer in the multiple micronutrients group. Iron-folic acid was associated with a significantly reduced risk of early preterm delivery (<34 weeks) (relative risk 0.50, 0.27 to 0.94, P=0.031). There was a significant increase in haemoglobin concentration in both iron-folic acid (5.0 g/l, 2.0 to 8.0 g/l, P=0.001) and multiple micronutrients (6.9 g/l, 4.1 to 9.6 g/l, P<0.001) groups compared with folic acid alone. In post hoc analyses there were no significant differences for perinatal mortality, but iron- folic acid was associated with a significantly reduced early neonatal mortality by 54% (relative risk 0.46, 0.21 to 0.98).

**Conclusion:** In rural populations in China antenatal supplementation with iron-folic acid was associated with longer gestation and a reduction in early neonatal mortality compared with folic acid. Multiple micronutrients were associated with modestly increased birth weight compared with folic acid, but, despite this weight gain, there was no significant reduction in early neonatal mortality. Pregnant women in developing countries need sufficient doses of iron in nutrient supplements to maximise reductions in neonatal mortality.

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**Anaemia Prevention Badge Project**

**Background:** FANTA and the Regional Center for Quality of Health Care (RCQHC), in partnership with the African Regional Office of the World Association of Girl Guides and Girl Scouts (WAGGGS), designed the Girl Guides Anemia Prevention Badge Project, a program to reach adolescent girls in East and Southern Africa with information and activities on anemia prevention and control.

**Methods:** Under the program, Girl Guides (ages 7-18) can earn a badge in anemia prevention through educational programs and community involvement in anemia control. FANTA and RCQHC developed an Anemia Prevention Badge Handbook and Workbook for the Girl Guides as well as a training manual for Girl Guide leaders.
Results: Anemia and iron deficiency remain at epidemic levels among women and children in many nations. Iron deficiency anemia (IDA) is associated with 22% of maternal deaths and 24% of perinatal deaths, according to a recent meta-analysis.

Conclusions: Correcting anemia of any severity reduces the risk of death, the analysis also showed. These estimates of the maternal and perinatal deaths associated with IDA underscore the importance of implementing a package of interventions, such as the Girl Guides badge project, to address the multiple causes of anemia.

Both the English and French versions are available for download via the link below. Due to file size, the English version of the Guiders’ Training Manual is also available for download by section.

• Maternal Anemia: A Preventable Killer

This brief, of collaboration among USAID’s A2Z Micronutrient and Child Blindness Project, ACCESS Program, and Food and Nutrition Technical Assistance (FANTA) Project, is aimed towards policy makers and summarizes the causes and consequences of anemia, the recommendations for proven anemia interventions and discusses 6 priorities for consideration to make anemia control a reality.

• How to Add Deworming to Vitamin A Distribution

This manual is written for health planners and aims to promote the deworming of preschool children where vitamin A distribution campaigns are conducted. In this manual, preschool children are defined as all children older than 1 year who are not yet attending school.

Attention is focused on this group because while school-age children (classified from the age of around 6 years onwards) are normally dewormed through school health programmes, preschool children are often not reached by deworming interventions.

In recognition of the constant demands made on health planners to prioritize health interventions, often with limited financial and human resources, this manual describes some of the advantages of combining two programmes which are often delivered separately: vitamin A distribution and deworming.

The manual is divided into three main sections that describe:

- The benefits of deworming preschool children;
- Practical information about deworming drugs;
- Experiences from three countries where deworming has been added to existing vitamin A distribution programmes.
Anemia Prevention and Control: What Works. Program Guidance, Parts I and II

This document provides program and project managers background information on the causes and consequences of anemia and guidance on formulating and monitoring anemia prevention and control programs.

• Effects of Alternative Maternal Micronutrient Supplements on Low Birth Weight in Rural Nepal: Double Blind Randomised Community Trial

Objective: To assess the impact on birth size and risk of low birth weight of alternative combinations of micronutrients given to pregnant women. Design Double blind cluster randomised controlled trial.

Setting: Rural community in south eastern Nepal.
Participants: 4926 pregnant women and 4130 live born infants.

Interventions: 426 communities were randomised to five regimens in which pregnant women received daily supplements of folic acid, folic acid-iron, folic acid-iron-zinc, or multiple micronutrients all given with vitamin A, or vitamin A alone (control).

Main Outcome Measures: Birth weight, length, and head and chest circumference assessed within 72 hours of birth. Low birth weight was defined < 2500 g.

Results: Supplementation with maternal folic acid alone had no effect on birth size. Folic acid-iron increased
mean birth weight by 37 g (95% confidence interval: 16 g to 90 g) and reduced the percentage of low birthweight babies (< 2500 g) from 43% to 34% (16%; relative risk = 0.84, 0.72 to 0.99). Folic acid-iron-zinc had no effect on birth size compared with controls. Multiple micronutrient supplementation increased birth weight by 64 g (12 g to 115 g) and reduced the percentage of low birthweight babies by 14% (0.86, 0.74 to 0.99). None of the supplement combinations reduced the incidence of preterm births. Folic acid-iron and multiple micronutrients increased head and chest circumference of babies, but not length.

Conclusions: Antenatal folic acid-iron supplements modestly reduce the risk of low birth weight. Multiple micronutrients confer no additional benefit over folic acid-iron in reducing this risk.

• Low Hemoglobin Level is a Risk Factor for Postpartum Depression

The role of maternal anemia in the development of postpartum depression (PPD) is unclear. PPD is a serious disorder that may negatively affect the physical and emotional health of a new mother and her infant. Although psychosocial factors that increase the risk of developing PPD are known, few studies have identified physiologic factors that predispose a woman to PPD. New mothers were visited at home on d 7, 14 and 28 after an uncomplicated labor and delivery. Hemoglobin (Hb) concentration was measured via finger-prick blood at each visit, and the women completed the Center for Epidemiological Studies-Depressive Symptomatology Scale (CES-D) on d 28. There was a negative correlation between Hb concentration on d 7 postpartum and depressive symptoms on d 28 ($r = -4.26; P = 0.009$).

CES-D scores (means ± sem) on d 7 of women with normal Hb levels (> 120 g/L (12 g/dL)) were significantly lower (6.90 ± 1.04) than those of women with Hb levels ≤ 120 g/L (12 g/dL) [16.36 ± 3.34; $t(35) = -3.632$, $P = 0.001$]. Thus, women suffering early postpartum anemia may be at increased risk of developing PPD.

• Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia

While the main focus of these guidelines is on iron supplementation programs and parasite
control, these guidelines acknowledge the beneficial role food fortification and dietary diversification can have in controlling iron deficiency anemia. Further information on these approaches can be found in other INACG documents as well as those of other organizations. It is hoped that these guidelines, which reflect our current state of knowledge, will be useful to those charged with planning and implementing iron supplementation programs. Please feel free to send your comments regarding these guidelines, so that they might be improved at a future date.

- **Micronutrient Powder Toolkit**

  This MNP Toolkit is a systematically organized collection of tools and resources relevant to Micronutrient Powder (MNP) programs focusing on planning and implementation stages. It complements the MNP implementation manual.

  Tools are job aids that assist in completing a task and resources may include "how to manuals" or other resources that are related to operationalizing or using the tools. The tools provided here are examples for MNP programs for children 6-23 months (or 6-59 months), even though many also apply for other at-risk groups.

  The starting point for the Toolkit assumes that a decision has already been made to implement an MNP program.

  This Toolkit is organized such that it goes through the major steps in the program planning cycle: planning, implementation, and monitoring with consideration of other key parts of an MNP program.

- **Burkina Faso National Anemia Profile**

  Anemia has substantial negative effects on the health and economic wellbeing of nations and communities. Children with anemia experience irrevocable cognitive and developmental delays and exhibit decreased worker productivity as adults. Globally, maternal anemia increases the risk of pre-term delivery and low birth weight, and iron-deficiency anemia underlies 115,000 maternal deaths and 591,000 perinatal deaths each year.

**Policies, Strategies and Plans**

**Resources:**
Guideline: Daily Iron Supplementation in Adult Women and Adolescent Girls

Globally, one in three non-pregnant women, corresponding to almost 500 million women, were anaemic in 2011. Iron deficiency is thought to contribute to at least half of the global burden of anaemia. Iron deficiency occurs following prolonged negative iron balance, the major causes of which include inadequate intake (owing to insufficient bioavailable iron in the diet or decreased iron absorption), increased iron requirements (for instance, during periods of growth) and chronic blood loss (from heavy hookworm infection or menstrual bleeding). In adolescent girls, menstrual blood losses, accompanied by rapid growth with expansion of the red cell mass and increased tissue iron requirements, make them particularly vulnerable to iron deficiency compared to male counterparts. This guideline reviews the evidence and updates the recommendation for daily iron supplementation in menstruating adult women and adolescent girls.

Guideline: Daily Iron Supplementation in Infants and Children

Approximately 300 million children globally had anaemia in 2011. Deficiency in iron, a mineral necessary to carry oxygen in haemoglobin, is thought to be the most common cause of anaemia. Iron deficiency can result from inadequate intake or absorption of dietary iron, increased need in periods of growth, increased losses from menstruation in adolescent girls, or infection by intestinal helminths, such as schistosomiasis or hookworm infestation, in areas endemic to these parasites.

Iron is an essential nutrient for development and cell growth in the immune and neural systems, as well as in regulation of energy metabolism and exercise. The economic costs of iron deficiency anaemia from annual physical productivity losses have been calculated to be around US$ 2.32 per capita, or 0.57% of gross domestic product in low- and middle-income countries. The WHO has consistently recommended oral iron supplementation as one of the interventions that can reduce the prevalence of anaemia.
Iron is required for the survival and virulence of many pathogens. Concerns have been expressed on a possible increased risk of malaria with iron interventions in malaria-endemic areas, particularly among iron-replete children. On the other hand, screening to identify iron deficiency in children prior to iron supplementation is not feasible in many malaria-endemic settings. Given the importance and magnitude of anaemia globally, particularly in areas where malaria transmission is intense, an assessment of all available evidence has been carried out, to examine the safety and effectiveness of iron supplementation in children, including in malaria-endemic areas.

**Global Nutrition Targets 2025: Anaemia Policy Brief**

In 2012, the World Health Assembly Resolution 65.6 endorsed a Comprehensive implementation plan on maternal, infant and young child nutrition, which specified six global nutrition targets for 2025. This policy brief covers the second target: a 50% reduction of anaemia in women of reproductive age. The purpose of this policy brief is to increase attention to, investment in, and action for a set of cost-effective interventions and policies that can help Member States and their partners in reducing the rates of anaemia among women of reproductive age.

**Kenya's National Iron Folic Acid Policy Guideline**

This is a poster size version of Kenya's National Policy Guideline on Combined Iron and Folic Acid (IFA) Supplementation for Pregnant Women in Kenya. This version of the policy is meant for display in a health care facility and serve as easy reference for health care providers. It includes information about the purpose of IFA supplementation, composition, dosage, duration, target group, administration, possible side effects and the recommended action to take if they occur.


The purpose of the 2012-2017 National Nutrition Action Plan (NNAP) is to provide a framework for coordinated implementation of nutrition intervention activities by the government and nutrition stakeholders. The Plan has been developed at a time when the government of Kenya is stepping up efforts to realize Millennium Development Goals through implementation fo High impact Nutrition initiatives (HiNi). The HiNi include: exclusive breastfeeding, timely complementary feeding, iron folate, vitamin A and zinc supplementation, hand washing, deworming, food fortification and management of moderate
and severe acute malnutrition. The NNAP was a collaborated effort of a task force through the supplementation sub-committee, compromised of members from the Division of Nutrition, Division of Child and Adolescent Health, Division of Reproductive Health, in the Ministry of Health (MoH) as well as multiple partners.


The National Iron and Folic Acid Supplementation programme is guided by different Policy and National action frameworks. These policy documents include the Kenya Food and Nutrition Security Policy (2011) and the Kenya National Nutrition Action Plan (2011-2017). These documents provide a platform for National and County response to addressing Iron and Folic Acid deficiencies through, among other interventions, supplementation programmes. The Kenya National Health Policy (2012-2030) and the Kenya Health Sector Strategic Plan 2012-2017 provide clear policy objectives and strategies that are supportive of nutrition. The Constitution of Kenya guarantees that every person has the right to health, which includes healthcare services. The Government of Kenya developed the Vision 2030 as its new long-term development plan for the country. To improve the overall livelihoods of Kenyans, the country aims to provide an efficient integrated and high quality affordable health care system. Under the nutrition sector, the Health Strategy aims to strengthen collaboration in order to ensure adequate nutrition for the whole population, through avoiding and managing over or under nutrition and micronutrient deficiencies. Iron and Folic Acid Supplementation was made a flagship project under the MTP 11 under Vision 2030.

According to World Health Organization it is estimated that 41.8% of pregnant women worldwide are anaemic. In Kenya the most recent micronutrient survey in the country indicated the prevalence of anaemia among pregnant women to be 55.1% and 46.4% among non-pregnant women. Anaemia is the leading indirect cause of high maternal and neonatal deaths. Iron and Folic Acid Supplementation (IFAS) for pregnant women is one of the interventions that has been recommended by WHO and implemented by the Ministry of Health to reduce anaemia levels. IFAS has been implemented through Focused Antenatal Care (FANC) and although this is the case, there have been challenges which have resulted in sub-optimal IFAS coverage rates and very low adherence rates.

This strategy provides a road map that is aimed at improving ANC attendance and IFAS coverage and utilization rates among pregnant women in Kenya in alignment with National IFAS plan targets. We call upon all partners and stakeholders to collaborate and ensure good coordination in the implementation of IFAS interventions to improve the chances of maternal and child survival.

Kenya's National Nutrition Action Plan (NAP), is derived principally from the Food and Nutrition Security Policy and Food and Nutrition Security Strategy. The Strategy provides a mechanism through which the Government will facilitate the implementation of strategic actions to improve and ensure food and nutrition security for the Kenyan population.

- **National Strategy for Anaemia Prevention and Control in Bangladesh**

The magnitude of anaemia, together with the associated adverse health, development and economic consequences, highlights the need for intensified action to address this serious public health problem in Bangladesh. Based on existing health and nutrition, this national strategy identifies comprehensive interventions aimed at high risk groups, in particular infants and young children, adolescent girls, newly wed women and pregnant and breastfeeding women.

The overall goal of the National Strategy is to reduce by one quarter the prevalence of anaemia among high-risk groups in Bangladesh by 2015. The objectives to be achieved by 2015 are:

- Provide a package of interventions to prevent and control anaemia in 60% of high-risk groups, including micronutrient supplementation, parasitic diseases control, and promotion of key dietary behaviours known to improve micronutrient intake.
- Fortify at least one food vehicle with iron and other micronutrients needed for anaemia prevention.
- Increase the availability of affordable micro-nutrient rich foods through household food production, crop diversification, biotechnology and biofortification.

**Frequently Asked Questions**

**Q: Should we be worried about giving iron to young children in African countries?**

**A:** There are currently concerns about both giving iron and not giving it to young children where malaria is endemic. There is some evidence that giving iron to children who don't need it may increase malaria and other infections. There is a body of literature about the role that iron plays in neurodevelopment. Giving iron may have implications for survival in young children while withholding it may have consequences for both individual and national development. The World Health Organization recommends giving iron to children living in malaria-endemic areas in the context of malaria prevention and treatment activities. Click here for a more extensive review of giving iron to young children in malaria areas.
Q: Does mass treatment for worms lead to drug resistance?

A: Repeated mass treatment of helminths can lead to drug resistance, which has been shown to develop as a result of repeated treatment (Albonico et al, 2003). To avoid or delay drug resistance, the World Health Organization (WHO, 2002) recommends alternating drugs and assessing the efficacy of treatment periodically at sentinel sites during mass treatment programs. The frequency of tracking drug resistance depends on the frequency of the mass campaigns (WHO, 2002).

Q: Shouldn’t all women be screened for anemia before they receive iron?

A: No. Where anemia prevalence is high, all pregnant women should receive iron-folic acid supplements whether they have had screening test or not. In malaria- and hookworm-endemic areas, pregnant women also should receive anthelminthic and malaria (IPTp) treatment without screening for anemia or these infections. While screening for anemia is a best practice and a policy in most developing countries, the supplies for anemia testing are not always available. Ideally, if resources allow, screening would identify women with anemia who would then receive additional iron and be tested for malaria and helminth infections. When screening supplies are not available, all health workers should be trained to check for clinical signs of anemia (e.g., pallor) which identifies about 70% of severe anemia cases. Pregnant women and young children with severe anemia can then be treated and, if they do not respond to treatment, referred. In low resource settings where anemia prevalence is high, the cost of screening needs to be balanced with the cost of getting the integrated package (IFA, IPTp, and deworming) to all pregnant women. If the budget does not allow for purchasing both screening supplies and commodities for the integrated package, the public health approach would be to put available resources into ensuring the commodities for the integrated package are available to 80% of women.

Q: Who is the target group for deworming? In many countries school-age children appear to be receiving deworming medication while other groups are not?

A: Pregnant women and young children are the most vulnerable groups to the iron deficiency anemia caused by hookworm infection. Anemia in school-children has effects on educational outcomes such as attention span and educability, so many Ministries of Education are implementing, often with the Ministries of Health, programs to deworm children in school. There is some evidence that decreasing the burden of hookworm disease in school-children reduces transmission and also benefits the rest of the population. Click here for more information on deworming (Components of the Integrated Package tab/Helminths sub-tab).

Q: Isn’t anemia prevalence high because women do not take their iron-folic acid pills?

A: No. Available information from Demographic and Health Surveys show that coverage of the integrated package to control anemia (IFA supplements, IPTp, and deworming) is still low, suggesting that the commodities in the package, including IFA, are just not available. Because IPTp and deworming are administered only several times during ANC visits, it is unlikely that non-compliance is a problem for these interventions. The compliance literature, mainly from Western countries, shows that adherence to a daily regimen, like IFA, may be challenging. Side effects from taking iron (e.g., black stools, gastric upset) are often touted as the main reason women do
not take IFA. However, from the literature about compliance with IFA, the evidence supports that lack of supplies is still the major reason women do not take all their 180 IFA supplements. Women take IFA supplements if they are counseled that side effects may occur and how to manage them. Click here for more information about how to improve IFA supplementation programs.

Q: Does folic acid increase malaria?

A: Large doses of folic acid interfere with the treatment of malaria using sulfadoxine-pyrimethamine (SP). WHO recommends that doses below 5 mg of folic acid are safe to use. Most iron-folic acid tablets, including those available through UNICEF, contain 60 mg of iron and 400 mcg of folic acid, which is a low dose of folic acid and safe to give with SP treatment. Click here for more information on the Malaria sub-tab.

Pregnancy, IFA supplementation, and anti-folate malaria treatment:

Several studies, including a 2008 study following 467 pregnant women in western Kenya, found that women receiving high-dose folate supplementation (5 mg/day) had an increased risk of sulfadoxine-pyrimethamine (SP) treatment failure for malaria. Low doses of 0.4 mg/day or even 1.5 mg/day were not shown to have a negative effect on SP treatment (Van Eijk et al, 2008). The 2009 WHO position statement regarding weekly iron-folic acid supplementation (WIFS) in women of reproductive age addresses that weekly iron alone may need provided in two situations: 1) where mandatory folic acid fortification of staple foods has been introduced and shown to be effective; and 2) in anti-folate malaria treatment regions (WHO position paper, 2009). Click here to learn more.

Q: IFA and multi-micronutrients?

A: There have been studies comparing multi-micronutrients (MMNs) with iron and iron-folic acid supplements alone. In many developing countries, diets are not diverse, so giving an MMN to supplement these diets held promise for improving pregnancy and newborn outcomes. So far, these studies giving MMNs have not shown an overwhelming increase in benefits compared to IFA supplements alone. The 2013 Lancet Maternal and Child Nutrition series recommended replacement of iron-folate with multiple micronutrient supplements in pregnancy might have additional benefits for reduction of SGA (small-for-gestational-age) in at-risk populations, although further evidence from effectiveness assessments might be needed to guide policy change. If MMNs do prove to have a comparative advantage over IFA, the cost-benefit of providing MMN over IFA needs to be considered. The cost of MMN supplements is $16.37 per pregnancy compared with the cost of IFA supplements, which is $5.23 per pregnancy.

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