

**THE EVIDENCE ON MICRONUTRIENT PROGRAMS:
A SELECTED REVIEW**

OMAR DARY
PHIL HARVEY
ROBIN HOUSTON
JEE RAH

AUGUST 2008



USAID
FROM THE AMERICAN PEOPLE



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID) under the terms of Cooperative Agreement No. GHS-A-00-05-00012-00. The contents are the responsibility of the Academy for Educational Development and do not necessarily reflect the views of USAID or the United States Government.

Micronutrient Forum
A2Z, The USAID Micronutrients and Child Blindness Project
Academy for Educational Development
1825 Connecticut Avenue, NW
Washington, DC 20009
mnforum@aed.org
www.micronutrientforum.org

August 2008

Contents

1. Executive Summary	4
2. Vitamin A Supplementation of Preschool Children	10
3. Maternal Iron Supplementation	21
4. Zinc Supplementation as Adjunct Treatment for Diarrhea	33
5. Salt Fortified with Iodine	36
6. Sugar Fortified with Vitamin A	48
7. Flours Fortified with Folic Acid.....	58
8. Foods Fortified with Iron	66
9. Operational Components of Mass-Food Fortification Programs.....	75
10. Complementary Feeding Interventions	78
11. Breastfeeding.....	86

Tables

Table 2.1. Summary description of the key vitamin A supplementation program implementation components	13
Table 2.2. Coverage and impact of vitamin A supplementation for children.....	15
Table 2.3. Data quality for coverage, compliance and impact of vitamin A supplementation programs for children.....	17
Table 3.1. Summary description of the key implementation components of iron supplementation programs.....	26
Table 3.2. Coverage, compliance, and impact of maternal iron supplementation programs	27
Table 3.3. Quality of available data on coverage, compliance, and impact of maternal iron supplementation programs	28
Table 3.4. Summary description of the key implementation components of a weekly multiple micronutrient supplementation program in Peru.....	29
Table 3.5. Coverage, compliance, and impact of a weekly multiple micronutrient supplementation program in Peru	30
Table 3.6. Quality of available data on coverage, compliance, and impact of a weekly multiple micronutrient supplementation program in Peru.....	31
Table 5.1. Coverage and impact of iodine fortification of salt programs	39
Table 5.2. Data quality for coverage and impact of iodine fortification of salt programs	42
Table 5.3. Summary description of the key implementation components of iodine fortification of salt programs.....	44
Table 6.1. Coverage and impact of vitamin A fortification of sugar programs	50
Table 6.2. Data quality for coverage and impact of vitamin A fortification of sugar programs	52
Table 6.3. Summary description of the key implementation components of vitamin A fortification of sugar programs	54
Table 7.1. Coverage and impact of folic acid fortification of cereal flour programs	59
Table 7.2. Data quality for coverage and impact of folic acid fortification of cereal flour programs	61
Table 7.3. Summary description of the key implementation components of folic acid fortification of cereal flour programs.....	62
Table 8. 1. Coverage and impact of iron fortification programs	67
Table 8.2. Data quality for coverage and impact of iron fortification of food	69

Table 8.3. Summary description of the key implementation components of iron fortification programs.....	71
Table 10.1. Summary description of the key implementation components of Sprinkles Programs....	81
Table 10.2. Coverage, compliance, and impact of Sprinkles programs	82
Table 10.3. Quality of available data on coverage, compliance, and impact of Sprinkles programs...	83

Figures

Figure 1. Prevalence of anemia in children 0-5 years old, pregnant and lactating women from National Nutrition Surveys, Thailand (P Winichagoon, personal communication)	23
--	----

1. Executive Summary

Background and rationale

After more than a decade of implementation, micronutrient (MN) programs have been established in many countries, based on the efficacy trials that have shown impact under controlled research situations. The evidence on efficacy of MN interventions provided in the Lancet Series on Maternal and Child Undernutrition and confirmed by Ten Year Strategy Group meeting late January, 2008, is well accepted. However, there is less information available about whether programs, implemented and assessed under real life settings, are achieving the expected impact, and on the strength of the evidence confirming this progress. Examination of the strength of the evidence supporting reported progress of large-scale and national programs and identification of good practices will further assist in advocating for the inclusion of MN interventions in national programs, and in strengthening their implementation. This literature review was undertaken to guide the discussion of the evidence at the Innocenti Micronutrient Program Meeting. Data and information were critically analyzed using an approach outlined in a Program Assessment Tool that was developed as part of the Innocenti meeting.

The selected literature review identified case studies through discussions with a range of global partners, a review of the published and unpublished literature, and finally a Call for Expressions of Interest, with responses used to help identify successful program and the evidence supporting their success. The case studies reviewed included:

- Supplementation interventions: vitamin A supplementation of children, iron supplementation of pregnant women, zinc supplementation for the management of diarrhea
- Fortification interventions: Salt fortified with iodine; sugar fortified with vitamin A; flour fortified with folic acid; various food vehicles fortified with iron
- Other interventions: complementary feeding interventions including home fortification using MN powder; breastfeeding

For each selected country program implementing one of these interventions, a summary of the progress to date was done using a series of tables, in part derived from the Assessment Tool. These tables allowed for a review of program components; coverage, compliance and impact; and the quality of the data presented. Following document review and completion of the tables, a narrative summary was developed. Tables and narrative summaries for each case study are provided below.

Results

Vitamin A supplementation (VAS) of preschool children

Six country programs were reviewed, all of which used primarily a twice-yearly event for VAS distribution. All programs have achieved high coverage, as measured by both aggregated reports from distribution sites, and periodic surveys at various geographic levels. For most countries, there has been reasonable consistency in coverage achieved, although not all countries reported regional or district coverage over time. In Nepal and Indonesia, there are data showing improved serum retinol following program introduction, and these two plus the Bangladesh report show

improvement in functional indicators. Functional indicators did not improve in a small sample in Ghana. All countries have shown a decline in under-5 mortality over time. In Nepal and Tanzania, thorough reviews of these declines and factors contributing to them have provided plausible evidence of attribution to the VAS programs.

These results suggest that countries are able to achieve high VAS coverage, twice-yearly. The available evidence suggests that this is associated with improved levels of serum retinol, and reduced functional effects of vitamin A deficiency. In addition, it appears likely, but not provable, that the programs have contributed to the decline in mortality—suggesting that countries can achieve the results predicted by efficacy trials. The main limitations are the difficulties with collection and interpretation of serum retinol, and the difficulty in demonstrating causality between the program and mortality decline.

Iron supplementation of pregnant women

The national iron and iron folic acid (IFA) supplementation programs in Thailand and Nicaragua and a large-scale weekly multiple-micronutrient (MMN) effectiveness study in Peru were reviewed. The two national programs were well implemented, and had high coverage and compliance and good evidence for other measures of program implementation. The programs had good political support, and have evidence from a number of sources on both implementation and outcomes, including reduction of anemia prevalence.

Significant reductions in anemia rates were observed among women of reproductive age in Nicaragua and Peru, and among pregnant women in Thailand. However, the relationship between these reductions and the program achievements is less clear. In Nicaragua, there was reduction in anemia in women of reproductive age, but the IFA supplementation targeted only pregnant women who represent only 10% of that group, thus making it difficult to attribute all of the improvement to the supplementation program. Nevertheless, it is highly plausible that this program did contribute to the reduction. In Thailand, the substantial reduction in anemia observed from 1986 to 1995 did not continue through the period from 1995-2003 in spite of good program implementation, and this suggests that other factors, including socio-economic improvement, may have been a key contributing factor. The report of the operational research studies in Peru highlighted the importance of partnership building, timely provision of supplies, essentiality of mobilizing communities, and particularly, the challenges of applying a rigorous evaluation design in an operational setting.

The multiple causes of anemia make attributing observed reductions in its prevalence to a particular program or program component remarkably difficult. Regardless of these findings, maternal iron supplementation should remain a high priority because during pregnancy, the iron intake of very few women is sufficient to meet their requirements and there is increasingly compelling evidence of serious, adverse and broad ranging effects resulting from the deficiency.

Zinc supplementation in the management of diarrhea

There is compelling evidence from efficacy studies that zinc supplementation reduces the duration and severity of diarrhea. The Lancet Series on Maternal and Child Undernutrition concluded that incorporating therapeutic zinc supplementation into the management of diarrhea was a highly cost-effective child survival intervention warranting a top priority in efforts to achieve the MDG 4.

In spite of this, there have been very few countries that have initiated this intervention at scale, and only Bangladesh has done so for long enough to report on progress, which will be done at the Innocenti meeting. In this document we present a brief review of global efforts to roll out this intervention. The challenges in initiating this intervention have been described in an unpublished manuscript (Fisher-Walker, personal communication). These authors identified five major barriers including: 1) ensuring supplies and registration of a zinc product, 2) adapting policy, 3) financing start-up activities, 4) creating demand, and 5) developing delivery strategies. Underlying these barriers is the low priority on efforts to enhance the management of diarrhea, particularly in the face of greater emphasis on other programs, such as HIV/AIDs and malaria. Given the continued large contribution of diarrhea to child mortality, addressing the identified barriers and accelerating initiation of zinc programs is important.

Salt fortification with iodine

Five country salt iodization programs were reviewed. Each program has been established for over a decade, and most have achieved high household use rates for salt with iodine. The programs have data on household coverage trends, iodized salt quality, urinary iodine values (mostly for schoolchildren), and trends in goiter rates. Some programs also have information on pregnant women, who represent a group at particular risk because of increased iodine requirements during pregnancy.

The evidence suggests a clear relationship between iodized salt quality (and the achievement of an adequate average iodine content) and household coverage, with measures of impact, primarily median urinary iodine. In instances where coverage is lower, urinary iodine values remained marginal or low. There is a need for more data on pregnant women, because their requirements may be larger than the iodine supplied by programs aimed at the general population

The review demonstrates that programs can achieve high coverage, and that salt used at the household level can contain adequate iodine so that iodine intakes improve—as assessed by urinary iodine. Although there is no new programmatic information on the impact of this achievement on IQ or other measures of intellectual capacity, the decrease in iodine deficiency suggests that programs can achieve what efficacy trials have suggested.

Concerns remain about ensuring adequacy among pregnant women, although depending on estimated consumption, an average iodine content in salt of 20-40 mg/kg should be adequate for pregnant women while safely avoiding exceeding the recommended safe upper limit of intake of iodine for other segments of the population.

Sugar fortification with vitamin A

Three countries with well-established sugar fortification programs were reviewed. For each, there was reasonable government support and implementation, but both coverage and fortificant levels varied.

In Guatemala and Nicaragua, the coverage was high (over 75%), and the fortificant level was calculated to provide, on average, over 150% of the estimated average requirement (EAR). At this level of coverage and fortification, the population intake was adequate to address vitamin A

deficiency, and this was demonstrated by marked decrease in xerophthalmia in Guatemala, and in reduction in the prevalence of low serum retinol in pre-school age children in Nicaragua. Both countries also have vitamin A supplementation for preschool children, which contributes to these improvements in that target group. Both countries monitor household use and quality, and Nicaragua periodically reviews serum retinol.

In Zambia, the situation differs, in that both coverage and fortification levels are lower. Coverage is estimated to be 25%, fortificant levels are smaller and vitamin A intakes are three to nine times lower than in Guatemala or Nicaragua. As a result, only 26-52% of the EAR was met. In addition, high levels of infection likely contribute to the difficulty in measuring small improvements in serum retinol that might occur from fortification or the VAS program.

These programs demonstrate that with high coverage and adequate intakes matched to adequate fortificant levels, sugar fortification can improve vitamin A status, and thus have the impact expected from controlled efficacy trials. The difficulty with programs is achieving adequate coverage, and in understanding that additional intakes of nutrient provided will depend upon the usual dietary patterns of populations, which vary substantially.

Flour fortified with folic acid

Three mature folic acid flour fortification programs were reviewed. Reports from the programs in both Chile and South Africa showed a decrease in neural tube defects (NTDs) following the introduction of fortified flours, with a concurrent rise in serum and red blood cell folate, although in South Africa the biochemical indicators were available for only one province.

An analysis of the estimated intake suggested that in Chile, 227% of the EAR of Dietary Folate Equivalents¹ was met. In South Africa is difficult to make a similar estimation because of the uncertainty of the information for the national level. Nevertheless, the additional intake due to this program is between 25 and 190% of the folate EAR.

In Guatemala, the probable impact of this program in poor and rural segments of the population is lessened by the fact that wheat flour consumption is very low in these communities compared with that of non-poor and urban communities.

As with sugar fortified with vitamin A, these studies demonstrate that programs to fortify flours with folic acid can achieve adequate coverage and intake, and are plausibly associated with reductions in a clinical indicator, in this case NTDs.

Various vehicles fortified with iron

Fortification of various vehicles with iron is common. Two mature programs (maize and wheat flour in Venezuela and South Africa) and a large-scale effectiveness study (soy sauce in China) were reviewed. The findings from Venezuela and China indicated substantial reductions in anemia but the strength of the evidence that these reductions were attributable to the interventions is not strong. Efficacy trials have demonstrated improvement in anemia and other indicators associated to

¹ One microgram of folic acid is equivalent to 1.7 micrograms of Dietary Folate Equivalents because the higher bioavailability of folic acid over the dietary sources of folate.

iron status, but commonly use iron levels much higher than programs, often 60-110% of EAR. The estimated additional intakes in the Chinese and Venezuelan cases were much lower than this (25-35% of EAR). The South Africa program, which demonstrated improvement related to folic acid fortification, did not show any improvement on iron status, and this finding is easy to explain because of the very low estimated intake for iron (8-10% of EAR).

The monitoring of these mature programs has not been sufficient to ensure compliance with government standards, and thus the magnitude of the additional intakes provided through the program is uncertain. Without evidence of additional intake, it is difficult to fully attribute any change in anemia to the programs alone.

These studies suggest that iron fortification programs may not achieve adequate intake levels, and thus may be unable to replicate the conditions of success observed in the efficacy trials.

Home fortification of complementary foods with MN powders

Adequate complementary feeding is essential to optimal growth, health and development of infants and young children. Thus, the review included discussion on interventions aiming to improve the quality and quantity of complementary foods. Interventions conducted in developing countries included nutrition education, complementary foods providing additional energy, MN fortification of complementary foods, and improving the energy density of complementary foods.

The evidence from efficacy and effectiveness trials and large-scale programs combined showed a somewhat mixed picture for each of these interventions. Nutrition education for mothers improved iron and zinc intakes from complementary foods, but showed mixed findings regarding iron status and anemia prevalence. Provision of centrally processed fortified complementary foods increased iron, zinc and vitamin A intakes in some efficacy studies and improved iron and vitamin A status in both efficacy studies and large-scale programs.

Home-based fortification using MN powders have consistently shown equal efficacy in improving iron status and reducing anemia when compared to iron drops in a number of studies in different parts of the world. Smaller effectiveness trials in Haiti, Bangladesh, Benin and Vietnam have all demonstrated improvements in anemia rates when MN powders were provided for 2 or more months. Few large-scale programs of home fortification have been launched. The first large-scale implementation of MN powder in Mongolia achieved high coverage and compliance, and a reduction in anemia rates from 46% to 25% in 6-59 month old children, with a concurrent reduction in stunting. However, there was no improvement in the prevalence of rickets, which may be attributable to the low vitamin D content of the MN powder. An emergency program in Indonesia also achieved high coverage, and demonstrated a significant reduction in anemia prevalence.

To date, few large-scale mature programs distributing MN powders at a countrywide level have been carried out and the programs reviewed can not easily rule out secular changes or other factors affecting anemia rates. Given that both efficacy and effectiveness trials have suggested MN powders as a promising strategy for the prevention of anemia, efforts need to be made to strengthen the scale-up process of the program.

Breastfeeding

The Lancet series includes breastfeeding as a high priority intervention of proven efficacy, but notes that coverage remains low. As such, this intervention is critical in improving infant and child nutrition, but requires programmatic strengthening. As an indirect program affecting micronutrient status, a full literature review for this intervention was not undertaken as part of the direct intervention review.

A recent program review covering 15 studies outlined a variety of program practices that have been critical to scaling up exclusive breastfeeding programs. This review provides guidance for improving breastfeeding programs to increase coverage, and their ability to have their maximum indirect impact on micronutrient status.

2. Vitamin A Supplementation of Preschool Children

Overview

As with the other literature reviews, a number of reports were selected based on communication with various program managers and partners and web searching. Reports were selected based on their reflection of current or recent reviews of progress for programs known to be mature and implemented at scale.

For each report, the data presented was reviewed with respect to the level of progress achieved, but also with regard to the strength of the evidence for progress. This process of data review was facilitated by the use of a number of tables on data consistency and quality, and on other factors that might affect findings and influence the plausible association of the intervention and the outcomes and impact.

The mechanism for distribution of vitamin A capsules has been debated, and has changed over time. Several mechanisms have been used, including:

- Distribution during routine health facility visits, including inclusion with EPI visits
- Distribution through monthly outreach visits, usually established for immunization
- Distribution through National Immunization Days (NIDs)
- Distribution through some twice yearly event, such as child health days.

Most countries reviewed distribute through a twice-yearly mechanism. Coverage achieved through routine visits was historically disappointing, because of the limitations in visits beyond 1 year of age, when immunization visits end. Distribution through routine monthly immunization outreach has been more successful, but similarly limited. Distribution through NIDs was immediately successful, with high coverage achieved, but NIDs have been phased out, or have become sub-national in most countries. The highest coverage has been through establishing a twice-yearly event, and mobilizing for a variety of interventions provided during this event. The programs included here all distribute through this mechanism.

Coverage is commonly assessed as reported coverage—being an aggregate of the reported doses given for different distribution sites. Reported coverage estimates are complemented by survey coverage estimates, either from district-level surveys, or periodic national surveys. While coverage optimally describes the cohort of children fully protected (i.e. those individual children receiving 2 doses, 6 months apart), it is generally not possible to measure this because of difficulties with recording and maintenance of child health cards beyond the immunization period, and practical difficulties with register management that would permit tracking individual children for the 2 rounds. Thus, coverage is commonly reported by distribution round.

Coverage would best be described in terms of ‘effective’ coverage. Effective coverage is determined by access, utilization and effectiveness. Access incorporates availability, accessibility, affordability and acceptability. Utilization relates to population characteristics and behaviors, while effectiveness includes efficacy, quality of service delivery and inclusiveness. For VAS programs, the current distribution mechanisms have helped to address access issues, and for most countries reviewed, awareness was high, with high motivation to receive the supplements. For VAS, efficacy is well

accepted, except for some recent concerns related to studies in India. However, there remain concerns about inclusiveness, and whether those in greatest need are those more commonly missed.

For vitamin A supplementation of children 6-59 months old, monitoring of program progress has focused on coverage. Unlike iron/folate, compliance is of limited concern because most programs have health workers or volunteers actively give the dose. The impact of VAS programs has been difficult to measure. Measures of vitamin A status have been debated, and a variety of methods can be used, including retinol binding protein, modified relative dose response, and serum retinol. Among these, serum retinol remains the most commonly used. All measures have significant limitations, which have made assessing program progress with regard to reducing measured vitamin A deficiency difficult. Most countries with significant deficiency also have high rates of infection, which hampers the ability to interpret measures of vitamin A status. Including biochemical measures of infection is recommended, but not always done. For these reasons, interpretation of vitamin A status as a measure of the impact of a VAS program is difficult.

Functional measures of impact are also difficult, mostly because of the low prevalence of functional deficiencies. Eye findings (xerophthalmia, Bitot spots) and nightblindness can be used, but large sample sizes are needed. The strong impact of VAS on mortality is well demonstrated in efficacy trials. However, at the programmatic level, it is difficult to measure mortality, and even more difficult to demonstrate causality between mortality reduction and VAS. Furthermore, many countries are undergoing a secular trend showing decreasing infant and under-5 mortality that may or not be associated with achievement in high VAS coverage. Thus mortality is a difficult measure of VAS impact.

In spite of these limitations, the analysis of a selection of VAS programs that have achieved high coverage does suggest that programs can achieve the results suggested by efficacy trials.

For this literature review, 6 country programs were reviewed. These included:

- Tanzania
- Nepal
- Ghana
- Cambodia
- Indonesia
- Bangladesh

Results

All countries had data on household coverage, including both reported and survey coverage. Three have information on trends in serum retinol, two have information on functional indicators, and four have reports discussing a concurrent decline in under-5 mortality, including two comprehensive reviews of factors contributing to the decline. For most countries, there was consistency in the findings reported, with limited evidence for weak data quality, missing data, or other concerns about the evidence presented. The following general conclusions can be drawn from the reports reviewed:

1. Programs have been able to demonstrate achievement of high VAS coverage, currently using a twice-yearly approach.

2. Programs have been able to demonstrate some consistency in coverage estimates between reported and survey coverage, with survey coverage generally slightly lower.
3. Regional variation in coverage remains, and there is concern that even with high coverage, those not dosed may represent the most vulnerable
4. Programs achieving high coverage have demonstrated reductions in the % of children with low serum retinol, although the magnitude of this change is not as high as might be expected.
5. Programs with high coverage also demonstrated improvements in functional indicators, though these were mostly assessed in small studies.
6. Two studies demonstrated a plausible association between VAS and mortality decline, showing a lack of other health program progress that would explain the decline. However, secular trends in socio-economic or other factors cannot be ruled out.

Among the reports reviewed, Nepal and Tanzania have had thorough assessments of disaggregated coverage trends over time, and Tanzania has undergone an assessment of the sustainability of the program through a comprehensive review of program elements at the district level. Both have shown a plausible association between the VAS program and the decline in under-5 mortality, without any other clear explanation with respect to indicators for other health programs, or strong changes in socio-economic measures. In Nepal, a striking decline in fertility may be contributing.

In the aggregate, the reports suggest that the programmatic evidence supports the findings of efficacy trials with respect to limited biochemical and functional improvement, and a possible contribution to documented reduction in under-5 mortality.

The analysis would be stronger if there were better indicators for vitamin A status, and more assessment of retinol status adjusted for infection (although in the absence of a stronger measure of vitamin A status, results will continue to be difficult to interpret). More information is also needed on regional or district variation in coverage over time.

The analysis would also be stronger if there were more information on the characteristics of children not dosed, and whether a selected cohort is repeatedly missed. Two studies from Indonesia suggest that the household characteristics (including immunization rates) among children not dosed differ from those dosed, with those missed being of lower SES, with lower immunization rates and lower education levels in parents. In addition, these studies suggest that the children missed also had worse nutritional status and higher rates of diarrhea—though this could be interpreted as an effect of VAS rather than a difference in the characteristics of those missed. Anecdotal reports from Nepal have suggested that the SES of children missed is higher than among those dosed, although the number of children missed is low because of consistent high coverage.

Table 2.1. Summary description of the key vitamin A supplementation program implementation components

Country / Scale	Program Description / Target Group	Policy & political support	Logistics	Training	Quality Control & Monitoring	BCC & Communication
Tanzania (1,2,3,4)	VAS for children 6-59 mo. distributed twice-yearly Integrated w/ EPI, IMCI and other programs	1997 Policy defined need and supplementation intervention National Health Policy mentions VAD National Task Force exists and meets, and helps with intersectoral coordination 89% of 119 districts include VAS distribution in annual planning	Procured from MI through UNICEF to Medical Stores Department, and to councils—generally received on time District needs predetermined at national level; first in, first out practiced Variability in color and shape of capsules in past 82% of districts felt to have non-vulnerable logistics supply systems	Training materials developed in 1996, and became outdated, and little used. Modifications undertaken in 2004 Some weakness in human resources for VAS at district level: 53% felt human resources inadequate	HMIS includes routine clinic distribution; Reporting form used for twice yearly distribution Good stock management w/ minimal expiration or losses, but weak forecasting of needs	Strong community mobilization strategy for twice yearly events; No written strategy, most materials prepared at national level
Nepal (5,6,7)	Twice yearly VAS distribution 6-59 months done by female community health volunteers Phased in over 10 years Implementation oversight for government, by Nepali NGO NTAG	Strong political support; strong support in medical community. Early studies showed mortality impact in Nepal	Capsules procured by UNICEF from MI/CIDA Period program self-assessment surveys suggest limited stockouts, but no routine data VAS distribution assisted by NTAG	Extensive orientation done at district-community levels with phased introduction of program	Initially no FCHV activities included in HMIS, thus no VAS monitoring. Monitoring done by district level periodic surveys done by NTAG Several national surveys complement program surveys (DHS, Karnali Zone-New Era survey, UNICEF BCHIMES and MICS)	Strong community level promotion prior to first initiation; support for community mobilization for 2 nd round, then done by districts. Multiple modalities used to increase awareness: Awareness high among community members. Strong recognition of vitamin A as a program, but sometimes seen as independent of government health programs
Ghana (8)	Evaluation based on initiation of program in 3 Northern Regions	Strong political support	Logistic supply felt to be adequate, based on small scale assessment; no strong evidence for stockouts	Training of HW prior to each twice yearly distribution	Monitoring based on tally and mini-survey, complemented by periodic national surveys Periodic qualitative surveys for awareness, compliance and BCC measures	NVAP developed materials; Multiple methods used, including town criers and community meetings; BCC efforts assessed using qualitative surveys

Country / Scale	Program Description / Target Group	Policy & political support	Logistics	Training	Quality Control & Monitoring	BCC & Communication
Cambodia (9)	Primarily twice yearly distribution via routine outreach sites; some facility based distribution	Multiple agencies including MOH support VAS program in 72 of 77 operational districts Coordination remains an issue Strong and ongoing support by external partners for most districts	Central Medical Supply not involved in VAS forecasting (but is for other essential drugs) Central level procurement varies, and source not clear after 2007	VAS included in minimum package of training materials for HF workers Extensive training in multiple districts, but dependent on partner support Concerns over CHW motivation and turnover rates	One episode of poor QA for capsules (similar color for both doses) Discrepancies between Med. stores forecasting and district requests	Some inconsistency in IEC messaging (due to poor coordination)
Indonesia (10,11,12)	1975: VAS adopted as a national program 1991: Twice-yearly approach initiated	Strong government support, with strong partner assistance	No apparent major logistics supply issues	2004-05: HKI focus on capacity building for VAS program, as programs decentralized	Some reporting problems uncovered during 2005 assessment Strength of monitoring system not clear	2000-04: HKI focus on BCC to increase VAS coverage Extensive work with focus districts to improve funding and BCC efforts
Bangladesh (13,14)	1972: Nutritional Blindness Prevention Program launched, included VAS for children 6-72 mo.—distributed through HH visits, w/ first dose done through EPI contacts at age 9 mo. Other interventions included (education and dietary approaches) 1990s: Bangladesh Integrated Nutrition Project improved coverage; 1995: Vitamin A Weeks established Currently program done through NNP (National	Strong policy and political support Partnerships and coordination across different government institutions and programs, and with partners are strong National Core Committee coordinates efforts Program costs divided between government and partners	Government purchases VAC, with procurement done by MI and UNICEF EPI calculates based on population targets and previous coverage Districts do similar population based estimates No evidence for major stockouts	Basic training for community nutrition promoters includes VAS, as does basic HF staff training Pre distribution orientation of field workers done at sub-district level	Standard aggregate reporting of capsules distributed. No evidence presented on quality assurance measures for this Fixed and extra distribution sites supervised through microplanned supervisory system from district downward	1994 and 1995: Large awareness campaign launched (in response to low coverage)—stated to increase coverage, and helped ‘institutionalize’ VAS twice yearly approach Annual promotion done prior to each distribution, managed by districts, using a variety of approaches

Country / Scale	Program Description / Target Group	Policy & political support	Logistics	Training	Quality Control & Monitoring	BCC & Communication
	Nutrition Program) with 9-11 mo. done through EPI outreach, and 12-59 mo. done twice yearly through Vitamin A Plus campaigns					

Table 2.2. Coverage and impact of vitamin A supplementation for children

Country / Scale	Composition and target group	Coverage	Awareness, knowledge, attitudes	Impact: Biochemical	Impact: Functional
Tanzania	100,000 IU for 6-12 mo children 200,000 IU for 12-59 mo. children Given through twice yearly event	1992: 63% coverage for disease-targeted VAS for children at facilities 1997: 55% coverage for universal distribution through EPI (measles) contacts for children 6-24 mo. 2000: 99% coverage during sub-national measles campaign 2004 HKI survey: 85% national coverage, coverage presented by region, minimal variation 2005 DHS: 46% coverage w/ regional variation 2006: 83% of districts achieved >80% coverage for last 5 rounds. Only 8% showed inconsistent coverage from round to round	High awareness of VAS program among health staff (89% include in district plans) High community appreciation (92% of districts reported that communities would be upset if program stopped)	1997 National survey: 24% of children (6-71 mo.) had low serum retinol levels (less than 20 micrograms/dL) and 69% of lactating women had low vitamin A levels (< 30 micrograms/dL) No further retinol assessment	Striking decline in infant and under-5 mortality plausibly associated with achievement of high VAS coverage, though cause not known
Nepal	100,000 IU for 6-12 mo children 200,000 IU for 12-59 mo. children Given through twice yearly event	1998: National Micronutrient Survey: 87% coverage among program districts (program was being phased in by district) Mini surveys (district level) consistently find coverage >85%	High awareness of importance of VAS, and of female community health volunteer's role in distributing it	1998: Lower (but not significant) rates of low serum retinol in children receiving capsules—Program conferred a 14% protective effect. Confirmed 1996 finding of lower RR for low serum retinol w/ capsule and nutrition education	1998: Program participation conferred a 59% protective effect for nightblindness (XN); 51% for Bitot spots (X1B) 2005: Assessment of 2001 DHS showed a reduction in odds of dying reduced by slightly more than half with 100% community coverage with VAS
Ghana	100,000 IU for 6-12 mo children	Program began in N. part of country in 1997; biannual distribution since 1999	Good community mobilization campaign	No recent national data available for serum retinol	No change in nightblindness—based on likely insufficient sample

Country / Scale	Composition and target group	Coverage	Awareness, knowledge, attitudes	Impact: Biochemical	Impact: Functional
	<p>200,000 IU for 12-59 mo. children</p> <p>Given through twice yearly event</p> <p>Model of child-to-child and outreach distribution tested (2000), and had lower coverage</p>	<p>Mortality association study examined only 3 regions in Northern part of country</p> <p>High coverage reported for most rounds (9 rounds from 1997-2001) for all 3 regions: range 63%-130%</p> <p>1998 DHS (combined 3 regions): 50%</p> <p>2002: IHNS: 78%</p> <p>1999-2001 program mini-surveys: all >80%</p>	<p>Lower than expected recognition of vitamin A, but high attendance at VAS event.</p>		<p>among small geographic area</p> <p>NVAP likely has contributed to documented improvement in child mortality, though direct association not proven</p>
Cambodia	<p>100,000 IU for 6-12 mo children</p> <p>200,000 IU for 12-59 mo. children</p> <p>Given through twice yearly event and at outreach sites and through routine facility visits</p>	<p>1996: Integration with NIDs, single round: >90% coverage</p> <p>2000: Cambodia National MN survey: 29% coverage through routine EPI</p> <p>2002: Pilot in 3 districts: 75% and 72% (two rounds)</p> <p>2005: 65% coverage</p> <p>2006: Average coverage round 1: 77% and round 2: 87% (National Nutrition Program reported figures)</p>	<p>Extensive IEC and community mobilization effort (data on awareness not presented)</p>	<p>No recent national data available for serum retinol</p>	<p>IMR reduced from 95 to 65 per 1000 live births in 2000 and 2005 respectively (CDHS 2000 and 2005)</p> <p>U5 mortality rate has decreased from 124 to 83 per 1000 live births in 2000 and 2005 respectively</p>
Indonesia	<p>100,000 IU for 6-12 mo children</p> <p>200,000 IU for 12-59 mo. children</p>	<p>HH coverage increased from <50% in 1999 to >80% in 2003, with mostly consistent upward trend</p>	<p>2000-04 Awareness campaign launched w/ HKI assistance, and reported to increase awareness (data not presented)</p> <p>2005: 90% of districts conducted some VAS promotion</p>	<p>2000: Study in 2 sub-districts w/ coverage of 60% showed decrease in low serum retinol from 19% to 15% following supplementation</p>	<p>1977 survey in 15 provinces: xerophthalmia prevalence of 1.3%; 1986 survey of 5 showed decrease from 1.16% to 0.67%; 1992-3: National survey showed decrease to 0.34%</p>
Bangladesh	<p>Initially 6-72 mo old, reduced to 6-59 mo. <12 mo covered</p>	<p>1982-3: 45% coverage</p> <p>1987-88: 37% coverage</p> <p>1989: 35% coverage</p>	<p>High awareness in general population bolstered by awareness campaigns and</p>	<p>No recent serum retinol</p> <p>1997: 22% of pre-school children had levels below 20ug;</p>	<p>Currently nightblindness below 1% since 1997</p> <p>2002: Nightblindness in pre-school</p>

Country / Scale	Composition and target group	Coverage	Awareness, knowledge, attitudes	Impact: Biochemical	Impact: Functional
	through expanded EPI at 9 months; remainder done	1990s: steady increases from 50% to 85% 2003: 89% coverage 2004-2005: > 80% coverage all rounds (note: 69% coverage for 6-11 mo. old done through EPI contacts)	promotion prior to each distribution		children 0.2% Decreased from 3.7% in 1982-83 in schoolchildren, and 2.7% of pregnant women Strong secular trend in declining under-5 mortality, from 133 in 1993 to 65 in 2007

Table 2.3. Data quality for coverage, compliance and impact of vitamin A supplementation programs for children

Country / Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors / Enabling factors / Unintended results
Tanzania	2004: Survey in 5 districts 2004 HKI survey: 85% national coverage, coverage presented by region, minimal variation 2005 DHS: 46% coverage w/ regional variation 2006: District reported coverage >80% for 83% of districts for previous 5 rounds	2004: Qualitative survey on awareness and behavior primarily Consistently high coverage for majority of districts, consistent with HKI program survey data (2 surveys); Inconsistent DHS coverage data, w/ possible problems with VAS question and presenting capsules	Minimal non-reporting by district distribution sites	District reported data reflects self-assessment, and may be affected by inaccurate census figures	Variability in coverage too small to make comparisons; Districts felt to be vulnerable with respect to coverage also vulnerable with respect to finances, and other program factors HKI survey and district reported coverage very consistent; DHS lower and inconsistent by region w/ other data	Strong public response to health facility interventions at the district level; decentralized outreach Significant decline in IMR and U5 mortality from 1996 to 2005 DHS (IMR: 100 to 68 deaths/1000 live births) No evidence of fertility decline
Nepal	1996 DHS: 32% (national, without differentiating program districts) 1996 Karnali Zone survey: 88% coverage (all districts in zone in program)	Remarkable coverage consistency assessed by different surveys Weaker reduction in serum retinol Plausibly associated	1998: program not implemented in all districts, impairing national estimate No recent retinol levels	Program surveys reflect self-assessment. DHS, Karnali zone and MN survey are independent	Program participation conferred a 59% protective effect for nightblindness (XN); 51% for Bitot spots (X1B) and 14% for low retinol Plausible mortality effect	High infection rates complicate interpretation of serum retinol levels Concurrent striking trend in reduction in fertility; large IMR decline-but only half would be affected by VAS)

Country / Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors / Enabling factors / Unintended results
	1998: National Micronutrient Survey: 87% coverage among program districts 1998 to present: Multiple district level surveys show >80% coverage	reduction in mortality			higher than expected, suggesting influence of other factors	FCHV is unique health worker cadre
Ghana	1998 DHS (combined 3 regions): 50% 2002: IHNS: 78% 1999-2001 program mini-surveys: all >80%	District tally reports consistent with program mini-survey results; compatible w/ IHNS survey results	Confidence interval for mini-surveys likely to be wide; Data not available by survey for all years (to compare w/ reported tally data) Small sample size for regions for 1998 DHS; DHS may underestimate because of restricting response to mothers stating receipt in last 6 months	Mini surveys done by program thus potentially biased	Coverage data internally consistent for Northern Region No ability to review relationship to serum retinol Mortality decline for 1-4 y/o less for region w/ lowest coverage Small reductions in % of admissions for diarrhea and measles	Ongoing trend showing decreasing child mortality; decline began before NVAP, but accelerated in Northern region after NVAP and more so for 1-4 y/o than IMR No contributing influence for EPI, nutrition or other factors affecting mortality; some increase in piped water, but only for 1 region of 3; no change in women's education level Some improvement in measures of SES, but changes small, and less likely to affect N. regions
Cambodia	2006: Average coverage round 1: 77% and round 2: 87% (National Nutrition Program reported figures) Survey (HKI) in 33 of 34 districts showed >80% coverage in 22, with the lowest being 52%	Some consistency with recent coverage figures between reported and survey figures	Some evidence for missing reports for reported data system	Reporting done by program thus potentially biased	No evidence available	Highest child mortality rates for region; recovering from civil disturbance Undernutrition rates have declined: 45.2% in 2000 to 35.9% in 2005
Indonesia	1977-79: National impact and coverage assessment for VAC program (HKI)	Some reversal of upward HH coverage trend between Aug	District specific data limited—trends improving, but variability from round	Recent coverage data from program reports and potentially subject to bias.	Caretaker knowledge about importance of VAS correlated w/ participation,	Review of Nutrition Surveillance System data w/ over 300,000 children

Country / Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors / Enabling factors / Unintended results
	<p>1977 survey in 15 provinces: xerophthalmia prevalence of 1.3%; 1986 survey of 5 showed decrease from 1.16% to 0.67%; 1992-3: National survey showed decrease to 0.34%</p> <p>Nutrition and Health Surveillance System (NSS) established</p> <p>HH coverage increased from <50% in 1999 to > 80% in 2003, with mostly consistent upward trend</p> <p>HKI documented dietary consumption confirming failure to meet RDA for vitamin A</p>	<p>2002 and Feb 2003 rounds</p> <p>Several studies (sub-district level) found association between program awareness and higher regular program participation</p>	<p>to round not provided</p> <p>Strong provincial variation (~50%-95%)</p>	<p>However, independent small studies show similar coverage estimates.</p>	<p>and % low serum retinol</p> <p>Coverage from several small studies consistent with national estimates</p>	<p>showed an association between VAS receipt and reduced diarrhea morbidity, better anthropometry measures, lower history of < 1 mortality. These results suggest either an effect of VAS, or that the VAS program is not reaching the more vulnerable.</p>
Bangladesh	<p>1990-1994: 42-55% coverage (HKI report)</p> <p>2004-2005: > 80% coverage all rounds (note: 69% coverage for 6-11 mo. old done through EPI contacts)</p>	<p>Limited external confirmation of coverage, but trends and reported estimates appear consistent</p>	<p>1994: External support for capsules decreased and coverage dropped to 31%</p>	<p>Reported coverage potentially subject to bias or poor data quality; no recording of missed reports from distribution sites</p>	<p>No evidence available</p>	<p>Secular trend in mortality could be associated with many other factors</p>

References

1. Report on a rapid assessment of vitamin A supplementation to young children and postpartum women in mainland Tanzania, HKI, USAID/MOST, TFNC. 2004
2. Assessing the Sustainability of the Tanzania National Vitamin A Supplementation Program: Results of a sustainability analysis. UNICEF, USAID/A2Z, HKI and TFNC. 2006.
3. Tanzania DHS 2004-5r
4. Mugyabuso, J et al, personal communication. Presentation to USAID by HKI on HKI VAS Surveys. 2004
5. Gorstein J, Shreshtra R, et al. *Current status of vitamin A deficiency and the National Vitamin A Control Program in Nepal: results of the 1998 National Micronutrient Status Survey*, Asia Pacific J Clin Nutr 2003; 12 (1):96-103.
6. Pant CR, Pokharel GP, et al. *Impact of nutrition education and mega-dose vitamin A on the health of children in Nepal*, Bulletin of the WHO, 1996, 74 (5) 533-545.
7. Thapa S, Choe MK, et al. *Effects of vitamin A supplementation on child mortality: evidence from Nepal's 2001 Demographic and Health Survey*, Tropical Medicine and International Health, volume 10 no 8 pp 782–789 August 2005.
8. David, Patricia: *Evaluating the Vitamin A Supplementation Programme in Northern Ghana: Has it contributed to improved child survival?* Micronutrient Initiative and JSI, 2003
9. *Review of the Vitamin A Supplementation (VAS) program for children aged 6-59 months & postpartum women in Cambodia*. National Nutrition Program (NNP), National MCH Center Ministry of Health, Royal Government of Cambodia & Helen Keller International, 2007.
10. *Summary and Accomplishments of the HKI/GOI Collaboration for Vitamin A, 1999–2005*. Final Report; Helen Keller International / Indonesia, 2006.
11. Pangaribuan R, Erhardt JG et al. Vitamin A capsule distribution to control vitamin A deficiency in Indonesia: effect of supplementation in pre-school children and compliance with the programme. *Public Health Nutrition*: 6(2), 209–216 DOI: 0.1079/PHN2002418
12. Berger S, de Pee, S, et al. *Malnutrition and Morbidity Are Higher in Children Who Are Missed by Periodic Vitamin A Capsule Distribution for Child Survival in Rural Indonesia*. *J. Nutr.* 137: 1328–1333, 2007.
13. Bloem M, Hye A, et al. *The Role of Universal Distribution of Vitamin A Capsules in Combating Vitamin A Deficiency in Bangladesh*, *American Journal of Epidemiology*, Vol. 142, No. 8, 1995.
14. *A Review of the Vitamin A Supplementation Program in Bangladesh*. Institute of Public Health Nutrition, MOHFW Bangladesh and MI, December 2007.

3. Maternal Iron Supplementation

Anemia in women and young children remains highly prevalent in many high-need countries. The adverse consequences are well recognized. Anemia has many preventable causes which vary in importance across regions, countries, and even within countries. Iron deficiency is generally accepted as the most common cause, with malaria and intestinal worms being particularly important in certain environments. This review focuses on maternal iron supplementation programs which address only that portion of the anemias resulting from iron deficiency.

The efficacy of daily iron supplementation for pregnant women and weekly supplementation for women of reproductive age (WRA) is clear (1, 2) but many believe that iron supplementation programs are not effective (3). Several authors have argued that large-scale maternal iron and/or iron folic acid (IFA) supplementation programs have rarely if ever had substantial impact on anemia prevalence because they have only rarely been implemented as designed (4). Reviews of the national iron supplementation programs from Nicaragua and Thailand are presented in Tables 1a, 2a, and 3a, along with a large-scale effectiveness study of weekly multiple micronutrient supplementation program from Peru in Tables 1b, 2b, and 3b. The findings are used to highlight issues related design, implementation, and evaluation these programs.

Nicaragua

Anemia in Nicaraguan women was identified as a priority public health problem in 1993 and addressed through an Integrated Anemia Control Strategy (IACS). Results from nationally representative surveys in 1993, 2000, and 2003-5 indicate that the prevalence of anemia in WRA decreased by about two-thirds during the period that the IACS was implemented (34% to 24% to 11%). An evaluation was undertaken to determine the extent to which the observed trends in anemia rates could be attributed to IACS programs (5).

The IFA supplementation protocol for pregnant women who are non-anemic or untested is a preventive weekly supplementation (two tablets, 120 mg Fe + 500 ug FA), and for those with anemia, therapeutic daily supplements (60 mg Fe + 250 ug FA) for 4 months, followed by a preventive schedule. This policy of weekly rather than daily supplementation in pregnancy is inconsistent with WHO recommendations and its introduction was reportedly contentious. The policy has not been embraced by many health professionals. Coverage of pregnant women with IFA was reported to be >80% with an average supplementation period of 4 months. Other interventions that are likely to have contributed to reducing the prevalence of anemia included increasing use of modern contraceptives, declining fertility, consuming sugar fortified with vitamin A and to a lesser extent in urban populations wheat flour fortified with iron.

The evaluators concluded that supplies of IFA were adequate, although the data presented on this were inconsistent. Other strengths of the IFA supplementation program included: intensive training of health workers that resulted in documented increase in knowledge of anemia; BCC strategy implemented and increased knowledge of and demand for IFA documented among pregnant women; strong community support for IFA, as a component of preventive ANC services that was mobilized through health volunteers known as 'brigadistas'.

Other interventions addressing anemia were implemented concurrently with the IFA program. Mandatory wheat flour fortification will have increased intakes of absorbable iron, although wheat flour is consumed by a lower proportion of households in rural areas and the estimated contribution

of fortified wheat flour to iron intake is “modest”. Ferrous fumarate replaced reduced iron as the fortificant in 2002 to increase absorption of iron. Sugar was fortified with vitamin A in 2000 and this is likely to have contributed to reduced anemia in the population.

The program evaluators concluded that *“adequacy and plausibility assessment support the contention that the consistent reduction in anemia rates in Nicaraguan women and children may to a large extent be related to the IACS implementation.”* A significant consideration in this conclusion in assessing the contribution of the IFA component of the IACS is that the outcome variable available is anemia in women of reproductive age (WRA) and the IFA program targeted only pregnant women. The evaluators estimated that pregnant women constitute about 10% of the WRA and that *“even a relatively high coverage >80% and duration achieved during pregnancy may not fully account for the large reduction in anemia rates in all women. The increased use of modern contraceptives (particularly iron containing oral contraceptives) and reduced fertility were likely to have contributed to the reduction.”*

The reduction of prevalence of anemia in children < 5years noted between 2000 and 2005 was associated with an increase in coverage of IFA supplementation from 37% to 63% after the child’s component of the program began in 2000. There was no decrease in anemia prevalence in children noted between 1993 and 2000 when vitamin A supplementation had increased substantially but no iron supplementation was implemented.

Thailand

Since the early 1980’s universal iron supplementation for pregnant women has been an integral component of Thailand’s Food and Nutrition Policy, a policy that is incorporated into the national Social and Economic Development Policy (6, 7). The supplements are delivered through antenatal services which are part of the community-based Primary Health Care strategy. A cadre of approximately 500,000 village health volunteers provides the backbone of community involvement and support for primary health services. Volunteers identify women in their communities who become pregnant and encourage them to attend ANC services. Through ANC, pregnant women receive iron tablets, possibly also multivitamins depending on the service site, and other ANC services. Sufficient iron supplements are given for daily use until the follow-up appointment, usually monthly until the third trimester when appointments may be more frequent. Iron supplies are adequate to support this. Volunteers are trained to provide support to women for a range of preventive services including consuming the iron supplements. Communication messages and materials were developed through formative research that identified specific concerns women held in relation to IFA supplementation, promoted the benefits of iron supplementation, used memory aids, and information on coping with any side-effects.

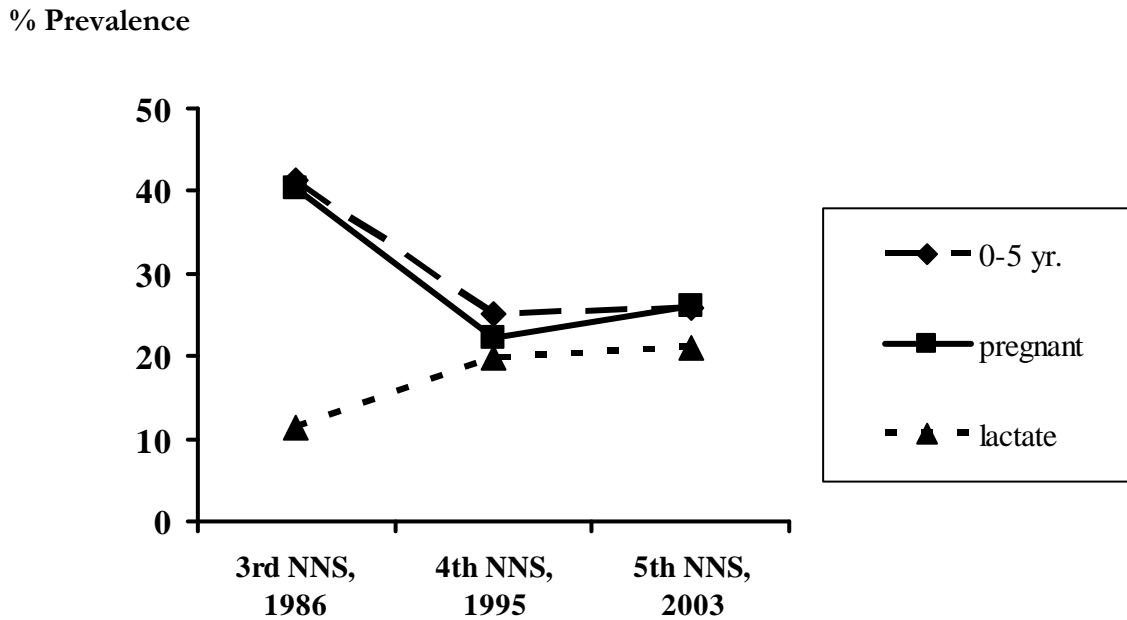
Information on both the implementation and the impact of the iron supplementation program are available through two series of surveys (National Nutrition Surveys, NNS, conducted approximately every 10 years since 1963; National Health Examination Survey, NHES, conducted every five years since 1991) and Health Management Information System (HMIS). As yet, there has been no explicit coordination between the two surveys. All data implementation suggest a very successful program with very high attendance at ANC services and compliance with iron supplementation. Supplies are reported to be adequate.

The results for pregnant women from the NNS and women of reproductive age from NHES are consistent in describing a decrease in prevalence of anemia from the late 1980’s to the mid-1990’s and no further decrease to last surveys that were undertaken in 2003 (Figure 1). There has been no

formal evaluation of the anemia program in Thailand and specific comparisons between the results between the two surveys are difficult to make. Information from the HMIS system confirm a substantial decrease in anemia prevalence from 1988 to 1999, but to our knowledge, data from more recent years have not yet been incorporated into this investigation.

Winichagoon (2002) described this IFA program and contextual factors associated with the decrease in prevalence of anemia through the 1990s. She described the maternal iron supplementation program as the major strategy for addressing anemia in pregnant women and considered that, in the context of improved services via primary health care, this program was likely to have contributed to the decrease. That this trend for decreasing prevalence was not seen in the results of 2003 surveys warrants further investigation. ANC coverage and compliance with IFA supplementation remained high and has been strengthened further through broadening accessibility to health insurance coverage for these preventive services. Changes in parity and child spacing have been ruled out as explanations (P. Winichagoon, personal communication).

Figure 1. Prevalence of anemia in children 0-5 years old, pregnant and lactating women from National Nutrition Surveys, Thailand (P Winichagoon, personal communication)



Determining the extent to which the IFA program contributed to the decreasing anemia prevalence in Thailand is difficult with available data and highlights the need for additional information. Perhaps the simplest explanation for the decrease in prevalence of anemia reported in both pregnant women and children under five is the concurrent improvement in economic conditions and associate increase in consumption of animal foods. That no further decreases in anemia were seen in 2003 survey support this explanation. The increase in prevalence of anemia in lactating women during the 1990's is difficult to explain.

The NHES survey results show differences across four regions in the country between 1991 and 2003. Decreases in both males and females were substantial in the North and South, but were little changed in the North-East and Central. Anemia prevalence increased in both men and women over 60 years of age. The lack of any reported statistical analyses on these trends in prevalence make conclusions difficult to make.

Peru: weekly multiple micronutrient supplementation of WRA

The need to improve iron status of women, and particularly adolescents, before they become pregnant is well recognized. An increasingly favored approach to achieving this goal is weekly IFA supplementation (WIFS), and a number of large-scale operational research and effectiveness studies describing this approach have been reported (8,9). At the time this review was being developed for the Innocenti meeting, WHO (WPRO) had commissioned a comprehensive review of the implementation and impact of the large-scale WIFS programs (T. Cavalli-Sforza, personal communication). The findings of the WHO review will synthesize the available evidence on this approach. In order to avoid duplicating effort, and still identify issues of implementation and evaluation in the weekly approach, this review described a large-scale effectiveness study of multiple-micronutrient (MMN) weekly supplementation undertaken in Peru (10-14).

The reports of this operational study describe comprehensively the planning, implementation and evaluation of a weekly supplementation program. The challenges highlighted include those of partnership building, timely provision of supplies, essentiality of mobilizing communities, and particularly, those of applying a rigorous evaluation design in an operational setting. The program was designed to target communities in highest need and the criterion for this was a prevalence of stunting higher than average in a baseline survey. Four supplements were distributed monthly. Supplements contained approximately two RDAs of iron, (30 mg - lower than most weekly supplements), zinc (20 mg), vitamin A as retinol (4 mg), vitamin C (60 mg), and folic acid (0.7 mg). Ninety percent of beneficiaries who received the tablets took more than 75% of the distributed supplements, but coverage was less than 50%. A significant and positive impact on anemia prevalence from the weekly supplementation was observed after 8 weeks of intervention (12 weeks for some). This impact resulted from an increase in prevalence in the comparison group rather than a reduction in the supplemented group. That the comparison groups were established on the basis of prevalence of stunting creates uncertainty about potentially unknown differences between the groups that might have affected the impact of the supplements (e.g. intestinal worms). Further, that the endline survey was undertaken after only 8 or 12 weeks of the intervention precludes findings related to sustainability of this intervention.

Conclusions

- There is strong evidence of efficacy of iron supplementation reducing iron deficiency anemia in pregnant women.
- There is strong evidence that the national supplementation programs in Nicaragua and Thailand were implemented effectively. Each was based upon: clear policy; enjoyed strong political support; delivered through well attended, high quality ANC services; ensured sufficient supplies were available; utilized community support through active volunteers; and, created solid demand through effective BCC programs.
- Substantial reductions in anemia have been observed at national levels in Nicaragua among women of reproductive age, and in Thailand among pregnant women, and it has been suggested these reductions may be attributable to the IFA or iron supplementation programs.
- The evidence that maternal iron supplementation programs contributed substantially to the reduction in anemia observed in Nicaragua is plausible, but it is weaker for the program in Thailand. The multiple causes of anemia make attributing observed reductions in prevalence to a particular program or program component remarkably difficult.

- The weekly MMN program in a high-need urban population in Peru showed that weekly supplementation can achieve high compliance for women that receive the supplements if staff are trained adequately, the community is engaged and supportive, demand for the supplement is created, and the implementation is carefully monitored. Availability of supplies was a limiting factor.
- Applying a rigorous evaluation framework in the context of implementing programs is enormously challenging, but without it, firm conclusions from such research are difficult to make.
- The potential benefits of reducing the adverse consequences associated with iron deficiency anemia warrant investing in strong monitoring and evaluation studies and these components of programs.

Table 3.1. Summary description of the key implementation components of iron supplementation programs

Country	Program Description	Policy Political Support	Logistics	Health Worker Training	BCC & Mother's Awareness
Thailand (6,7)	<ul style="list-style-type: none"> • Universal iron supps delivered to pregnant women through ANC services, in some places multiple MNs supps also distributed • 60 mg Fe as sulfate (no folic acid), MNs (not described and likely vary in composition) • Community mobilization, Cadre of 500,000 Village Health Volunteers identify preg women, encourage them to ANC, and then support iron supp & other preventive services • Fe distributed at monthly follow-up ANC visits • Weekly iron supps through schools introduced in 2000 as part of a universal coverage package, but have since been discontinued 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Strong policy for universal iron supplementation as part of Food & Nutrition Policy, this in turn is part of Social and Economic Development Policy. • Iron supplementation Integral part of Community-based nutrition program and ANC, both components part of Primary Health Care (PHC) strategy • From around 1990, nutrition in general receives strong support from Royal Family 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Iron supplies funded thru central MOH, procurement based upon prevalence of anemia and potential pregnancies • As for other medicines, local funds/district hospitals are available to cover shortfalls in peripheral centers if/when these are identified • "...scarcity of iron tablet supplies has not been a major problem." <p><u>Limitations</u></p> <ul style="list-style-type: none"> • No specific data on stock-outs available 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Village Health Volunteer (VHV) selected from communities and trained in "essential health knowledge" and assigned specific preventive tasks. • Manuals for anemia programs were produced in 1997 <p><u>Limitations</u></p> <ul style="list-style-type: none"> • No specific training in anemia reported • Anemia reported as low priority among health workers 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Formative research studies identified 3 primary barriers (fear bigger baby, forgetfulness, side effects) and developed messages to help address them • "respected senior women" from villages support program
Nicaragua (5)	<ul style="list-style-type: none"> • Pregnant women: as component of ANC services <ul style="list-style-type: none"> - <i>Preventive</i>-(all non-anemia and untested) 120 mg Fe + 500 ug FA weekly - <i>Therapeutic</i>-(Hb < 11g/dL or palor) 60 mg Fe + 250 Ug FA daily for 4 months, followed by preventive schedule • Since 1994, IFA included in twice annual National Health Rallies (NHR) • Community support from volunteers (brigadistas) 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Clear policy in place, updated protocols and guidelines; supporting infrastructure; good political support, no opposition <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Health professionals dispute weekly Fe for pregnant women results in "non-standard" protocols 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Procurement procedures in place & functional • Minimal stockouts (although only 54% health centers reported adequate iron supplies by a 2000 survey; adequate supplies reported in 98% MOH local health units and 93% private services by 2001 survey) 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • High level of intensity of training and supervision initially • Part of basic training; extensive focused training; community component added. Two-thirds of health workers trained by 2002; • Improved knowledge and commitment among HW; • Increased distribution during ANC visits. • Limited information on specifics of supervision, and how this will be sustained 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Aggressive awareness and sensitization effort initiated in 1993-1996 and continued to present; • >90% of mothers aware of risk of anemia and importance of iron/folate per survey 2001 • HW provide information: 77% of women taught about anemia from HW • Strong support from (brigadistas) • Successful social mobilization through NHRs

Table 3.2. Coverage, compliance, and impact of maternal iron supplementation programs

Country	Source of Data	Coverage	Compliance	Impact
Thailand (6,7)	<ul style="list-style-type: none"> National Nutrition Surveys (NNS): data reported for 1986, 1995, 2003 (pregnant/lactating /young children; urban-rural comparisons) National Health Examination Surveys (NHES) 1991, 1996, 2003 (15 y + males, females; by regions & age group comparisons) HMIS: national ANC data anemia data reported for 1986 thru 1999 (pregnant only) Health Promotion Bureau, Ministry of Public Health, 1995 Survey 	<p>ANC attendance</p> <p><i>NNS 2003</i></p> <ul style="list-style-type: none"> 92% 'ever attend', urban rural areas similar 70% attend 1st trimester 83% attend 4+ times <p><i>MOPH 1995</i></p> <ul style="list-style-type: none"> 98% 'ever attend' 65% attend 1st trimester 83% attend 4+ times <p>No data on coverage or impact of weekly Fe supps available</p>	<p><i>NNS '03</i></p> <ul style="list-style-type: none"> 80% preg women regularly take Fe 'regularly' 15% 'irregular' (mainly forgetfulness) 5% 'never' (mainly bec not prescribed) 	<p><u>NNS</u></p> <ul style="list-style-type: none"> Pregnant* <ul style="list-style-type: none"> '86 - 40% n=354 '95 - 16% n=245 '03 - 26% n= ? Lactating* <ul style="list-style-type: none"> '86 - 13% n=760 '95 - 15% n=698 '03 - 21% n= ? <p>*'86 and '95 combined numbers & prevalence for urban and rural (Table 4 Winichagoon 2000)</p> <p><u>NHES 2003</u> (n=21,421) Females, anemia by severity Mild - 18% Mod - 2.5% Severe - 0.6%</p> <p><u>HMIS</u> '88 27%, yearly to '99 13%</p>
Nicaragua (5)	<ul style="list-style-type: none"> National surveys by various groups describe coverage, compliance, and anemia rates Surveillance system (SIVIN) data for ANC attendance, IFA distr, anemia rates 	<ul style="list-style-type: none"> Pregnant women received any IFA, 70% in 2000, increased to 85% in 2003-5 when 76% consumed IFA for at least 4 mo, 58% for at least 6 mo. IFA proved to be the most difficult component of IACS to implement and monitor 	<ul style="list-style-type: none"> "Reportedly, side-effects... have not disturbing enough to affect compliance" 	<p><i>Impact:</i></p> <p>% anemia in WRA</p> <ul style="list-style-type: none"> '93 34% '00 24% '05 11%

Table 3.3. Quality of available data on coverage, compliance, and impact of maternal iron supplementation programs

Country	Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors	Contextual factors
Thailand (6,7)	<ul style="list-style-type: none"> • HMIS data available only for pregnant women, consistent with NNS 	<ul style="list-style-type: none"> • No indicators of iron status, small studies indicate high prevalence of abnormal hemoglobin • NNS, small sample size, particularly for urban in 1995 • Categorization of 'urban' varied across surveys and time • HMIS & NHES No control for gestation age of pregnancy 	<ul style="list-style-type: none"> • Three sources of data use different sampling frames, different analyses reported • Results not weighted for popn. • No statistical tests of trends available • HMIS: more urban than rural women; first ANC visit where Hct/Hb available; large sample, but not consistent districts/HCs 	<ul style="list-style-type: none"> • Reports of high ANC attendance and iron supp distribution and consumption is consistent with decrease in anemia • Decrease in prevalence of anemia from late '80s for pregnant women but not lactating women, nor men • In NHES, mat anemia prevalence decreased across 4 regions 	<p><u>Positive</u></p> <ul style="list-style-type: none"> • '86-'95 SES improved, expect increased consumption of animal foods (although anemia prevalence in men increased over same period) • increased access to many ANC services • no info on use of modern contraceptive methods/fertility 	<p><u>Positive</u></p> <ul style="list-style-type: none"> • Strong policy support, existing cadre VHVs • improved transport has increased access to health c • other interventions expected to reduce anemia e.g. fortification, deworming <p><u>Negative</u></p> <ul style="list-style-type: none"> • % anemia attributable to iron not known • anemia not a priority for HWs • yet to verify SES change '95 to '03
Nicaragua (5)	<ul style="list-style-type: none"> • Previous regional survey w/ similar results 	<ul style="list-style-type: none"> • Main outcome is anemia in pregnancy, data available only for anemia in Women Reproductive Age (WRA) 	<ul style="list-style-type: none"> • Integrated Surveillance System (SIVIN) provides nationally representative, time series data on wide range of nutrition information • Good, systematic data checks 	<ul style="list-style-type: none"> • BCC monitored and reported effective in 2001 • Higher anemia rates among those w/ poor compliance 	<ul style="list-style-type: none"> • Secular trend for improving in general health indicators, e.g. maternal nutrition, use of modern contraceptive, decline in fertility, consumption of wheat flour fortified with iron and sugar/vit A; • Neg. confounders, not known 	<ul style="list-style-type: none"> • High ANC rates • Strong donor support

Table 3.4. Summary description of the key implementation components of a weekly multiple micronutrient supplementation program in Peru

Country	Program Description	Policy Political Support	Logistics	Health Worker Training	BCC & Mother's Awareness	Program Monitoring & Evaluation
• Peru (10-13)	<ul style="list-style-type: none"> • Weekly multiple micronutrient (MM) supplementation program implemented as part of the Integrated Food Security Program (PISA) <ul style="list-style-type: none"> - designed & implemented by governments of Peru & Germany - goal was to develop & implement policy & programs to reduce food insecurity & malnutrition in an urban area of Peru - a baseline survey identified MN deficiencies as main nutritional problems in an urban population, in north of Peru - weekly MM supplementation program was designed & implemented targeting geographic areas in highest need (higher than average % stunting in baseline), 26 low-income communities • Weekly MM Supplementation <ul style="list-style-type: none"> - 20,000 adolescent girls & women of reproductive age (12-44 y) and to 8,000 children under 5 y - 2 types of MMNs: capsules for adolescent girls & women, “foodlet” for children - supplements contained <u>2 RDAs</u> of key micronutrients (included 30 mg Fe) - distribution accompanied by nutrition education 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • A memorandum of understanding (MOU) was signed between PISA & Ministry of Health (DIRESA) to implement a joint supplementation campaign: DIRESA had planned to be responsible for supplement distribution, training, & program monitoring • To achieve strong governmental support, two other governmental institutions were contacted for collaboration <p><u>Limitations</u></p> <ul style="list-style-type: none"> • There was a delay in signing MOU between PISA & DIRESA • Due to the delay in signing the MOU between PISA & DIRESA, health staff of DIRESA did not comply with all of their responsibilities: resulted in overburdening of the limited number of health & nutrition professionals in PISA 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Supplements were manufactured in country with imported premix • A systematic supplement distribution cascade involving local health staff & supplementation committee (including facilitators) was developed <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Supplement delivery by the manufacturer was delayed at the early stage of the program: activities had to be delayed • The program ran out of supplements due to error of manufacturer 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Health professionals were first trained on the supplementation campaign • Trained health professionals developed educational materials for the facilitators • Facilitators were trained by the health professionals using the developed educational materials • Training of facilitators focused on the supplementation campaign, how to take the supplements, side effects, etc • Training was participatory & based on pre-developed manual • A post-test was conducted to evaluate the increase in knowledge of facilitators: re-training conducted if training was unsatisfactory • A post-test evaluation showed a significant improvement in facilitators’ knowledge 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Before the supplement distribution began, information on the benefits of MM supplement & where/when to receive supplements was disseminated • Information disseminated by loudspeakers, posters, T-shirts & interpersonal communication • Supplement distribution was accompanied by communication strategy addressing the importance of taking the supplements: cartoons, logo, printed materials were used <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Due to the delay in supplement delivery, only 2 weeks available to promote the campaign (too short) • Dissemination of information overlapped with the presidential election campaign: target audience distracted & many activities were restrained 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Each program step was monitored by small groups of participants • PISA had its own internal monitoring system: 1) tracking administrative sheets filled out by health staff & facilitators 2) assess increase of knowledge of program beneficiaries • External monitoring by independent group: small samples of women, adolescent girls and caregivers selected monthly to evaluate compliance & knowledge about the campaign <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Comparison group comprised communities not targeted by program (i.e. % stunting lower than average) • study design modified twice due to logistics problems • Initial & final evaluations were conducted only during the 4th campaign between June & August 2002, initial campaigns not evaluated

Table 3.5. Coverage, compliance, and impact of a weekly multiple micronutrient supplementation program in Peru

Country	Coverage	Compliance	Impact	Knowledge Attitude
<ul style="list-style-type: none"> Peru (12-14) 	<ul style="list-style-type: none"> Women & adolescent girls: 47% Children: 88% 	<ul style="list-style-type: none"> Among the beneficiaries who received MM supplements, 90% reported taking at least 9 supplements out of 12 	<p><u>Women & Adolescent Girls</u></p> <ul style="list-style-type: none"> Groups had similar Hb level & anemia prevalence at baseline Intervention group: No change in mean Hb level & anemia prevalence after 8 wks of supplementation (P=.65) Comparison group: mean Hb level declined from 126.4 to 123.9 g/L after 8 wks (P=0.04), anemia prevalence increased from 29% to 36% (P=.054) Anemia prevalence after 12 wks was higher in the comparison vs. intervention group (36% vs. 30%) (P=.06) No impact on BMI (P=.54) (as expected) <p>• Multivariate analyses identified positive association of MM supplementation on anemia prevalence (P=.01)</p> <p><u>Children</u></p> <ul style="list-style-type: none"> Intervention & comparison groups had similar Hb level & anemia prevalence at baseline Intervention group: mean Hb level & anemia prevalence did not change after 8 & 12 wks of supplementation Comparison group: mean Hb level significantly declined from 113.2 to 108.5 g/L after 8 wks, while anemia prevalence significantly increased from 35% to 50% Final Hb level after 12 wks was significantly higher in the intervention group (111.7 vs. 108.5 g/L) Anemia prevalence after 12 wks was significantly higher in the comparison vs. intervention group (50% vs. 40%) No impact on anthropometry (as expected) <p>• Multivariate analyses identified positive association of MM supplementation on anemia prevalence (P=.01)</p>	<ul style="list-style-type: none"> 60% of women & adolescent girls named liver & meat as food sources with high micronutrient content 61% of women & adolescent girls & 72% of caretakers reported increased appetite of themselves or their children The caregivers reported an acceptability rate of 90% 80% of women & adolescent girls & 90% of the mothers reported no negative side effects

Table 3.6. Quality of available data on coverage, compliance, and impact of a weekly multiple micronutrient supplementation program in Peru

Country	Source of Data	Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors	Other Determinants of Data Quality
<ul style="list-style-type: none"> • Peru (12-14) 	<ul style="list-style-type: none"> • Initial & final survey & assessments conducted in the intervention & comparison groups • HH were chosen using a randomized cluster method 	<ul style="list-style-type: none"> • Prevalence of child malnutrition & anemia found during the baseline survey was similar to the national estimates • Not enough information to evaluate consistency of findings across studies regarding the impact of MM supplementation on anemia prevalence in urban poor population in Peru 	<ul style="list-style-type: none"> • Precise data; Indicator used is a good proxy for coverage, compliance and impact; 	<ul style="list-style-type: none"> • Evaluation was conducted an independent academic institutions • No information on data quality assurance measures, however, data error rates assumed to be low 	<ul style="list-style-type: none"> • Coverage rate among women & adolescent girls was low, but compliance was high • Coverage & compliance were both high among young children • Increase in anemia prevalence in the comparison group & no change in anemia prevalence in the intervention group found among both women & children • Not enough information to assess dose-response relationship 	<ul style="list-style-type: none"> • Potential confounding factors were controlled for in the multivariate analysis: multivariate analyses showed similar results as the univariate analyses • Establishing comparison groups on basis of prevalence of stunting creates uncertainty about potential unknown differences between the groups that can not be controlled for in analysis (e.g. intestinal worms) 	<ul style="list-style-type: none"> • Due to the short supply of supplements, final evaluation was conducted after 8 wks of supplementation in some households

References

1. Institute of Medicine. Prevention of micronutrient deficiencies: tools for policymakers and public health officials. National Academy Press, Washington DC, 1998.
2. Kulier et al. De Onis M, Gülmezoglu A. M., Villar J. Nutritional interventions for the prevention of maternal morbidity. *Int J Gyn Obs* 1998 ; 63(3): 231-246.
3. Sloan NL, Jordan E, Winikoff B. Effects of iron supplementation on maternal hematologic status in pregnancy. *Am J Publ Health* 2002; 92(2):288-293
4. Yip, R. Iron supplementation: Country level experiences and lessons learned. *J Nutr* 2002; 132: 895S-861S.
5. Mora JO, Boy E. Integrated anemia control strategy (IACS) has significantly reduced anemia in women and children in Nicaragua. Micronutrient Initiative, Ottawa, 2007.
6. Winichagoon P, Prevention and control of anemia: Thailand experiences. *J Nutr* 2002; 132: 862S-866S.
7. Winichagoon P, Policy and program of prevention and control of iron deficiency an anemia in Thailand: A cases study. Micronutrient Initiative, Ottawa, 2000.
8. Dwivedi A, Schultink W. Reducing anemia among Indian adolescent girls through once-weekly supplementation with iron and folic acid. *SCN News* #31.
9. Cavalli-Sforza T, Berger J, Smitasiri S, Viteri F. Weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans, and contributions toward achievement of the millennium development goals. *Nutr Rev.* 2005 Dec; 63: S152-8.
10. Gross R, Gross U, Lechtig A, Lopez de Romana D. We know much about what to do but little about how to do it: experiences with a weekly multimicronutrient supplementation campaign. *Food Nutr Bull* 2006; 27: S111-4.
11. Gross R, Lechtig A, Lopez de Romana. Baseline evaluation of nutritional status and government feeding programs in Chiclayo, Peru. *Food Nutr Bull* 2006; 27: S115-21.
12. Gross U, Valle C, Diaz MM. Effectiveness of distribution of multimicronutrient supplements in children and in women and adolescent girls of childbearing age in Chiclayo, Peru. *Food Nutr Bull* 2006; 27: S122-9.
13. Gross U, Diaz MM, Valle C. Effectiveness of the communication program on compliance in a weekly multimicronutrient supplementation program in Chiclayo, Peru. *Food Nutr Bull* 2006; 27: S130-42.
14. Lopex de Romana, Verona S, Aquino Vivanco O, Gross R. Protective effect of multimicronutrient supplementation against anemia among children, women, and adolescent girls in lower-income areas of Chiclayo, Peru. *Food Nutr Bull* 2006; 27: S143-50.

4. Zinc Supplementation as Adjunct Treatment for Diarrhea

In 2004 WHO and UNICEF recommended a new strategy to improve diarrhea management: incorporate zinc supplementation for 10-14 days as an adjunct treatment together with low-osmolarity oral rehydration salts (ORS), and continued child feeding (WHO/UNICEF 2004). In 2008, both the Lancet Series on Maternal and Child Undernutrition and the recent update of the Copenhagen Consensus (Horton et al. 2008) concluded that incorporating therapeutic zinc supplementation into the management of diarrhea was a highly cost-effective child survival intervention that should be assigned a top priority in efforts to achieve the MDG 4.

Diarrhea remains one of the leading causes of death among infants and young children and accounts for 18% of under-five mortality (Bryce et al. 2005). Coverage rates for treatment of diarrhea with ORS/ORT remain at less than 40% and have improved little over the last few years (Bryce et al. 2008). Incorporating zinc supplementation into diarrhea management presents an important opportunity to revitalize a key child survival intervention. The findings of Bhandari et al. (2008) highlighted this opportunity in the report of a large randomized study in India that compared care seeking behaviors when diarrhea was managed in primary health care facilities with either therapeutic zinc plus ORS or with ORS alone. After 6 months of intervention, adding therapeutic zinc resulted in diarrhea being treated far more often (60% Vs 10%) and more effectively. Confirming previous published findings, adding the zinc also reduced the use of drugs of unknown identity and antibiotics in treating diarrhea, and also reduced the incidence of diarrhea.

Despite ample evidence of efficacy and increasingly strong evidence of effectiveness, this intervention has only been rolled out at national scale in Bangladesh. The Bangladesh program was developed and managed by the Scaling Up Zinc for Young Children (SUZY) project. An important enabler of this initiative was the relatively high use of ORS/ORT that already existed in the country and SUZY was able to build upon that. *A review of this initiative will be presented during the Innocenti meeting.*

Fisher Walker et al. (unpublished manuscript) described the substantial efforts invested to date at the global level in rolling out the new recommendations for managing diarrhea. The authors lamented the slow progress that has been made to date and highlighted the urgent need to accelerate that progress. They concluded that the underlying cause of the slow progress in adopting the new recommendations was primarily that diarrhea treatment was no longer an international priority. Winch et al. (2008) have described the challenges in moving forward with the adaptation of policies in the current context of donor focus on HIV, malaria, and TB.

The focus of global efforts to promote the new approach to managing diarrhea have addressed five major barriers, mostly within countries: 1) ensuring supplies and registration of a zinc product, 2) adapting policy, 3) financing start-up activities, 4) creating demand, and, 5) developing delivery strategies (Fisher Walker et al. unpublished manuscript). These authors have estimated that in 2008, four years after the new recommendations were launched, only 43 countries had changed policies regarding low-osmolarity ORS and 53 had included therapeutic zinc. They estimated that fewer than 30 countries had begun the formative research and/or pilot programs needed to develop context-specific mechanisms to deliver the intervention.

Possibly the most direct obstacle to rolling out the intervention has been the lack of an appropriate zinc product in sufficient quantities to support large-scale programs. The product must be in the form of a dispersible tablet or syrup that does not contain other micronutrients that may compete with zinc for absorption. The specifications of Good Manufacturing Practices (GMP) required of products being procured by WHO and UNICEF were finalized in 2007 by United States Pharmacopeia Drug Quality Information Program. Fisher Walker et al. noted that in 2008, zinc products were being produced in at least eight developing countries but that most did not yet have this GMP certification. These authors further estimated that by mid-2008, only 20 countries had an appropriate zinc product available to enable the intervention to be introduced at large scale.

The advantage of producing appropriate zinc products locally was demonstrated clearly in Nepal. Promoting several local zinc products and working closely with the MOH, the Zinc Social Marketing (POUZN) project launched a private sector initiative alongside the public sector zinc introduction. The program began in three districts surrounding the capital city and has been now scaled-up to reach more than half the country's population. Generic promotional messages are being aired through mass media targeting both public and private sector providers, pharmacists and child caregivers in order to increase the use of ORS and zinc and reduce the use of unnecessary diarrhea treatments. Distribution of zinc to rural areas is being undertaken by the public sector with volunteer female health workers carrying zinc into hard-to-reach rural communities (V. MacDonald, personal communication).

The importance of the private sector to improving access to appropriate diarrhea treatment products is well recognized. The POUZN project has promoted the marketing opportunities of zinc products to support this intervention to pharmaceutical manufacturers, distributors, detailers and retailers in India, Indonesia, and Tanzania and provided/facilitated technical assistance. The project has also raised awareness of the intervention and availability of product with medical practitioners and other health workers in both the formal and non-formal sectors, and also NGOs (C. Winger, personal communication). A diarrhea treatment kit (DTK), created by packaging together zinc tablets and ORS and delivered through both commercial retail outlets and NGOs, has been piloted successfully in Cambodia and is being introduced in both Benin and Madagascar. Packaging the two products together was found to be an effective means of marketing them, encouraging their combined use, and increasing the access and use of the treatment in rural communities (V. MacDonald, personal communication).

Since diarrhea causes almost one-fifth of child deaths, achieving MDG 4 by 2015 will require that Ministries of Health and donors assign a far higher priority to rolling out the new approach to managing diarrhea than it currently receives. The evidence of efficacy and cost-effectiveness is compelling but to date appears to have been insufficient to enable the required modification in global funding priorities.

References

1. Bhandari N, Mazumder S, Taneja S, et al. Effectiveness of zinc supplementation plus oral rehydration salts compared with oral rehydration salts alone as a treatment for acute diarrhea in a primary health care setting: A cluster randomized trial. *Pediatrics* 2008; 21; e1279-e1285.
2. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. *Lancet* 2005; 365(9465): 1147-52.

3. Bryce J, Daelmans B, Dwivedi A, et al. Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet* 2008; 371(9620): 1247-58
4. Horton S, Alderman H, Rivera J. Hunger and malnutrition. Copenhagen Consensus Center. Copenhagen Consensus 2008 - Results. 2008, Denmark
5. Fischer Walker CL, Fontaine O, Young MW, Black RE. Zinc and low-osmolarity ORS for diarrhea: A call to action 4 years after the WHO/UNICEF global recommendation. (unpublished manuscript).
6. WHO/UNICEF. Joint Statement: Clinical Management of Acute Diarrhoea (WHO/FCH/CAH/04.07). Geneva and New York: World Health Organization, Department of Child and Adolescent Health and Development, and United Nations Children's Fund, Programme Division, 2004.
7. Winch P, Gilroy K, Fischer Walker C. Effect of HIV/AIDS and malaria on the context for introduction of zinc treatment and low-osmolarity ORS for childhood diarrhoea. *J Health Popul Nutr* 2008; 26: 1-11.

5. Salt Fortified with Iodine

Overview

A number of reports were selected based on communication with various program managers and partners and web searching. Reports were selected based on their reflection of current or recent reviews of progress for programs known to be mature and implemented at scale.

For each report, the data presented was reviewed with respect to the level of progress achieved, but also with regard to the strength of the evidence for progress. This process of data review was facilitated by the use of a number of tables on data consistency and quality, and on other factors that might affect findings and influence the plausible association of the intervention and the outcomes and impact.

For salt iodization, the core indicators of program progress are well accepted, and include:

- % of HH using iodized salt (salt containing any iodine, usually measured by rapid test kit or RTK)
- % of HH using ‘adequately’ iodized salt (optimally measured by titration, and reflecting a minimum of 15 mg/kg, or reflecting the current government standard for the iodine content at the household level)
- Median urinary iodine (UI), commonly measured in schoolchildren, preferably also measured in pregnant women
- Total tonnage of iodized salt produced or imported as a % of total estimated need
- % of salt meeting government standard (usually >30ppm) at production level
- Trend analysis for HH coverage and median UI
- Discussion of regional variation in the above indicators

Salt iodization programs were strongly promoted as early as 1950, with momentum gaining in most countries by the mid 1980’s. Thus most countries have relatively mature salt iodization programs, and reasonable data with which to judge progress. Some countries initiated iodized oil injections (lasting 5 years) or iodized oil supplements (lasting 1 year) for selected target populations, and these programs contribute to improved UI values, yet usually the contribution is difficult to separate out from the impact of salt iodization.

UNICEF, MI and ICCIDD (and the Network) have a process for ‘certifying’ achievement of universal salt iodization and IDD elimination goals, and several countries have undergone this external evaluation.

For this literature review, 5 country programs were reviewed (in addition to the review of the Nigeria program using the full Assessment tool). These included:

- Cambodia
- Tibet Autonomous Region
- Bhutan
- Indonesia
- Thailand

All countries had data on household coverage, urinary iodine and production/import level quality assurance, and some trend data.

Results

The following general conclusions can be drawn from the reports reviewed:

1. Iodine deficiency, as evidenced by goiter rates initially, and later by median urinary iodine excretion, can be reduced to levels below the WHO levels felt to represent a public health problem.
2. Using median UI as a population measure of iodine intake, iodized salt can provide adequate levels of intake when household use is high, and there is an adequate food control system
3. Functional measures of IDD are limited to goiter rates at the programmatic level—no programmatic data are available on changes in IQ, stillbirth rates or other functional consequences of iodine deficiency. Goiter rates consistently decline initially, but following introduction of iodized salt or iodized oil, become less reliable as measures of current iodine intake.

Among the reports reviewed, the success in Bhutan was achieved early, and is supported by good evidence. It appears likely that iodized salt is providing adequate iodine for the full population, recognizing that there is variability in consumption, and that the level may not be fully adequate to meet the needs of pregnant women.

Similarly, for Cambodia, there has been a solid trend toward lower goiter rates in schoolchildren, followed by a high UI. Calculations based on iodized salt coverage and quality suggest that the population is receiving adequate iodine through iodized salt, with an unknown contribution from use of fish sauce made with iodized salt.

Indonesia presents a similar situation as Cambodia, but with some inconsistency in coverage data from different sources, significant provincial variability (but based on a small number of clusters per province), and some potential confounding from continued use of iodized oil supplements.

The programs in both Tibet Autonomous Region and Thailand show progress, but failure to achieve USI or IDD elimination goals at present, based primarily on lower household coverage. However, these programs do show the same relationship between household coverage, salt quality, and median UI. Their lower percentages for use and quality are reflected in lower median UI values, and a lower estimated population intake—inadequate to meet needs, particularly for pregnant women.

In the aggregate, the reports suggest that the programmatic evidence supports the findings of efficacy trials with respect to biochemical improvement in iodine status accompanied by reduction in goiter. There is no program evidence pertaining to mental status improvement.

The analysis would be stronger if there were more data on titration. This would make calculations of estimated population intake (and the ability of the salt program to meet daily needs) stronger.

The analysis would also be stronger if there were more information on the contribution to daily intake from consumption of foods made with iodized salt. It is not known to what degree

consumption of salty foods (such as fish sauce) cause a decrease in the use of table salt. There are also few data that quantify the consumed amount of food made with iodized salt. Thus, while the measures of household coverage for use of iodized salt are consistent with improvements in measures of iodine intake, the contribution of food made with iodized salt is not known.

Operational components of iodine fortification are discussed in the section “Operational Components of Mass-Food Fortification Programs,” starting on page 74.

Table 5.1. Coverage and impact of iodine fortification of salt programs

Country / Scale Population	Provision		Utilization - Food Intake (g/day)	Coverage (% homes w/ <u>fortified</u> product)	Micronutrient Intake (% EAR)			Biological Indicators of Impact		
	Food Supply	Additional Amount (mg/kg)			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (metabolic biomarker)	Tertiary (Clinical or Functional)
Cambodia: (1,2,3) National Population 14 million	Iodization of salt mandated in 2004 100% of estimated annual need for iodized salt is met by local production. Current standards: 20-40 mg/kg iodine content at production.	Measured: 25 and 32 mg/kg (median among coarse and refined samples with iodine, respectively)	General: Estimated salt consumption 15-17 g/person/day	2005: 73-74% of HH use iodized salt 2000: 12%	N.A.	448 ug ² / person / day = 418%	448 ug ³ / person / day = 418%	2005: Median UI in 8-10 y/o schoolchildren was 222 ug/L	Not available	Not available
Tibet Autonomous Region (4) Population: 2.7 million	USI legislation enacted in 1993 An estimated 6000 MT ² produced against an estimated need of 13,700 MT (44%) in 2003 Standard: 20-40 mg/kg at production level Iodized oil capsules used	Measured: 91% of salt tested met standard	Estimated salt consumption 10 g / person / day Iodized oil capsules for 3-12 y/o children, schoolchildren, women of reproductive age	2003: 54% of HH used 'quality' iodized salt 1997: 6.2% 2001: Iodized oil capsule coverage: 18% for 3-12 y/o children, 98% for schoolchildren, 100% for women of reproductive age, (2003)	Iodized oil: 18% for 3-12 y/o 98% for school children 100% for women (assumes iodized oil provides 100% of EAR for 1 year)	Salt: 200 ug/ person/day ⁴ = 187%	Population: 187% plus oil contribution Pregnant women: 43% for salt, or 100% including iodized oil	2003: Median UI of 125 ug/L in schoolchildren and 96 ug/L in women of reproductive age Increased from median UI 55ug/L in schoolchildren in 1997	Not available	2003: TGR of 12% in school children Decreased from 29% in 1997

² Using a national average of 28 mg I/kg, and 16 g salt/day..

³ Using a national average of 28 mg I/kg, and 16 g salt/day..

⁴ Using the minimum value of the required standard; i.e. 20 mg/kg.

Country / Scale Population	Provision		Utilization - Food Intake (g/day)	Coverage (% homes w/ <u>fortified</u> product)	Micronutrient Intake (% EAR)			Biological Indicators of Impact		
	Food Supply	Additional Amount (mg/kg)			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (metabolic biomarker)	Tertiary (Clinical or Functional)
Bhutan (5,6) Population: 650,000 (1996)	Salt iodization introduced in 1985—all salt imported and iodized in-country Est. annual need is 5000 MT, met by import quota of 7000MT. Standard: 60ppm factory; 25 ppm retail, and 15ppm HH level	Measured: Retail samples (n=137): 0% w/ no iodine; 74% ≥ 25ppm; 84% ≥ 15ppm ; which means that the average content is probably 50 ppm	Estimated salt consumption 10 g / person / day	95% HH coverage 1996: 100% of HH samples with iodine; 82% with ≥15mg/kg; 74% ≥ 25mg/kg (n=333) 1992: 95% HH coverage w/ 'adequately' iodized salt	NA	Salt: 475 ug/ person / day ⁵ = 444%;	Salt: 475 ug/ person / day ⁶ = 444%;	1996: Median UI 230 ug/L	Not available	2001: TGR 5% Decreased from 14% (1.2% grade 2-visible goiter) in 1996 Decreased from 65% with cretinism reported commonly in 1983
Indonesia (7) Population: 235 million	Early initiation of salt iodization (1976) Iodized oil capsules used in some parts of country Standard: 30ppm at production level; 30ppm at point of consumption (HH level)	Measured: 61% met std at HH level, (which means that average is above 30 mg/kg)	Consumption 10g/person /day	2003 (multiple sources): 86-100% of HH w/ iodine 5-94% variable iodized oil capsule coverage Population: 100% Pregnant women: 100%	Not available ? contribution of Iodized oil	Salt: 300 ug/ person / day = 280% based on 10g / person / day consumption;	Salt: 300 ug/ person / day = 280% based on 10g / person / day consumption;	2003: Median UI: 229 ug/L	Not available	2003: TGR 11% Decreased from 10% TGR in 1998 and 37% TGR (26 province survey) in 1982

⁵ Assuming that the household average was $50 \times 0.95 = 47.5$ mg/kg.

⁶ Assuming that the household average was $50 \times 0.95 = 47.5$ mg/kg.

Country / Scale Population	Provision		Utilization - Food Intake (g/day)	Coverage (% homes w/ <u>fortified</u> product)	Micronutrient Intake (% EAR)			Biological Indicators of Impact		
	Food Supply	Additional Amount (mg/kg)			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (metabolic biomarker)	Tertiary (Clinical or Functional)
Thailand (8) Population: 65 million	1991: Iodized salt and water, plus iodized oil capsules included in program Estimated annual iodized salt need is 237,000 MT/yr; estimated iodized salt production: 196,000MT (83% of need) Noodles, fish sauce, eggs currently iodized Standard: 30ppm at production level; HH level not specified	Measured: 51% met standard at HH level; which means that the average is 30 ppm	Consumption 10g/person/day Fish sauce: 1 producer w/ 4% of market iodizes Noodles: 1 company w/ 60% of market iodizes at a third of RDA	2003: HH coverage w/ adequately iodized salt 51% (per RTK) Trend in HH coverage (>10mg/kg): 74% (2000), 66% (2001), 78% (2002), 63% (2003) per cyclic monitoring data (RTK) Significant regional variation Population: 100% Pregnant women: 78%	Not available	Salt: 300 ug/ person / day = 280%% based on 10g / person / day consumption; Iodized fish sauce, noodles: Negligible based on consumption	Salt: 300 ug/ person / day = 280%% based on 10g / person / day consumption; Plus amounts supplied by other sources.	2000-2003: Median UI in pregnant women (surveillance data) show curve from 153ug/L (2000) to 115 ug/L (2003) Marked variation in UI values for each province (w/ very high maximums)	Not available	1996 to present: <5% TGR Decreased from 19% in 1989, and ~20% in 1984

Table 5.2. Data quality for coverage and impact of iodine fortification of salt programs

Country / Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors / Enabling factors
Cambodia: National	National coverage survey: schoolchildren w/ their HH salt, RTK and titration and UI Estrapolation to regional level (3 clusters/region, non-weighted)	HH coverage with iodized salt consistent between National USI survey and DHS 2005	Data at regional level based on only 3 clusters, thus likely not representative.	No evidence of bias Data quality good (except for limited clusters per region)	Clear relationship between low HH coverage and UI values for most, but not all regions (though based on small # of clusters per region)	Historically moderate to high goiter rates (12% average among schoolchildren, 16% of provinces w/ rates \geq 40%) Possible confounding with fish sauce made with iodized salt—the distribution and use of which is not clear All production from 2 regions—more easily controlled. Fortificant is subsidized
Tibet Autonomous Region	Combination of reported MOH data and surveys. Surveys at month 3, and 1 st , 2 nd , and 3 rd years Specific methods not explained	No evidence available	Mention is made of higher iodized salt coverage in urban/peri urban areas, but methods not included Unclear how capsule coverage is ascertained	Monitoring done by project, no independent observation Data quality not known	Difficult to differentiate between contribution from iodized salt, and iodized oil capsule	Strong central control, strong donor support and financing Rapid socio-economic changes in China concurrent w/ project
Bhutan	HH coverage (based on samples from schoolchildren) from national survey Salt iodine content from both single iodization facility and district reports	Consistent association between UI and HH salt, consistent trend for all indicators (TGR, UI and HH consumption)	Some missing information on salt quality District reports: only 45-80% of districts reporting salt iodine content annually Likely regional variation (no evidence)	Survey method 30x30 PPS, but with some cluster 'selection' Retail shop salt tested from shops encountered during survey (non-random) Sub-samples for titration of salt and UI in children	Excellent trend data on both goiter rates and median UI over time as salt iodization program improved.	No confounding factors Program enabled by single source for iodization, strong government oversight Note some weakening of quality assurance with less government oversight.
Indonesia	National IDD survey 2003, HH based, representative at provincial level	Reasonable correlation between Susenas and National IDD surveys at upper levels of coverage, with more differences at lower levels Improvement in different	No evidence for missing data in survey	Susenas reflects program self assessment; National survey more independent Some concern about same standard at production and HH levels	Statistical review of correlation between UI and HH coverage—showing good consistency	Concurrent iodized oil program confuses results. Degree of contribution to overall UI results not clear

Country / Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors / Enabling factors
		indicators consistent with regard to trends				
Thailand	National survey 2003 (HH coverage) Cyclic surveillance data (HH coverage, UI)	Trend in reduction in goiter rates in children not consistent with trends in HH coverage or UI values in pregnant women	Limited data on UI in other than pregnant women; Limited data on iodized salt production Cannot determine contribution of iodized water, fish sauce or egg (all felt to be minimal) Data on HH salt iodine content based on RTK, not titration	Surveillance data reflects program self-assessment to some degree	Weak correlation between UI and HH coverage Known weakness in goiter grading once interventions in place; smaller goiters more difficult to detect	Other fortification vehicles; variable use of table salt Some food industries may use iodized salt, and this effect not measured or known

Table 5.3. Summary description of the key implementation components of iodine fortification of salt programs

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Quality Assurance Program Monitoring Program Evaluation	Information, Education & Communications
Cambodia: National	<p><u>Strengths:</u> Sub-decree no.69 (Oct 2004): Government has legal mandate to ensure that all salt produced, imported, sold and/or distributed in Cambodia for human or animal consumption is iodised.</p> <p>Ordinances adopted by all 24 Provinces</p> <p>Salt Producers' Community of Kampot and Kep established in 2004, and represents 170 out of 172 local salt producers</p> <p>Strong coordination across different government sectors and w/ private sector</p> <p><u>Limitations:</u> Continued use of non-iodized salt in salt production areas</p>	<p><u>Strengths:</u> Good cooperation w/ major producers</p> <p>Fortificant cost hand-over plan being developed</p> <p><u>Limitations:</u> Fortificant cost covered by UNICEF/Gates 2005-2006</p>	<p><u>Strengths:</u> Producers association fully supportive of iodization</p> <p><u>Limitations:</u> Limited use of titration</p>	<p><u>Strengths:</u> Regulations provide for enforcement actions</p> <p><u>Limitations:</u> No evidence presented on actual enforcement done</p> <p>Continued difficulty w/ leakage of non-iodized salt in producing regions, and across border (w/ Vietnam)</p>	<p><u>Strengths:</u> National Sub-committee for the Control of IDD's and CamControl, the Ministry of Commerce structure responsible for monitoring; computerized database established</p> <p>UNICEF supported revision of monitoring and enforcement plan</p> <p><u>Limitations:</u> Remaining high rate of inadequately iodized salt</p>	<p><u>Strengths:</u> Standard media effort supported by UNICEF</p> <p><u>Limitations:</u> HH coverage remains below 80%</p>
Tibet Autonomous Region	<p><u>Strengths:</u> USI legislation enacted in 1993</p> <p><u>Limitations:</u> National situation in China assessed by 1997 survey showed good results, with Tibet Autonomous Region as a significant outlier.</p>	<p><u>Strengths:</u> Central production from one state factory supplies most salt.</p> <p><u>Limitations:</u> Multiple small scale individual producers (salt often bartered, non-commercial)</p> <p>Fortificant provided by Project</p>	<p><u>Strengths:</u> Capacity building done at multiple levels by Project</p> <p><u>Limitations:</u> No ability to manage multiple small producers</p>	<p><u>Strengths:</u></p> <p><u>Limitations:</u> No evidence of enforcement actions being taken</p>	<p><u>Strengths:</u> Strong factory quality assurance noted, with frequent batch testing.</p> <p><u>Limitations:</u> Exact methods not explained</p>	<p><u>Strengths:</u> Large IEC campaign done using multiple media approaches</p> <p><u>Limitations:</u> No evidence on behavior change related to use of non-iodized salt from small producers</p>

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Quality Assurance Program Monitoring Program Evaluation	Information, Education & Communications
Bhutan	<p><u>Strengths:</u> Strong government policy and commitment</p> <p>Salt iodization done by government enterprise</p> <p>Controlled import of salt</p> <p><u>Limitations:</u> Some leakage from Indian border</p>	<p><u>Strengths:</u> All salt imported from India under control of Bhutan Salt Enterprises—government owned.</p> <p>Imported salt iodized by this company.</p> <p><u>Limitations:</u> Delays in procurement of salt noted in 1996 evaluation</p> <p>1995: only 1947MT sold (40% of annual need) per records</p>	<p><u>Strengths:</u> Initially strong push for capacity building among policy makers and salt importers, and for salt iodization.</p> <p><u>Limitations:</u> Recent problems with sustaining quality assurance at iodization plant, which was outdated in 1996</p>	<p><u>Strengths:</u> Strong regulatory environment</p> <p><u>Limitations:</u> No information available on enforcement actions taken</p>	<p><u>Strengths:</u> Good monitoring system in place with strong government support</p> <p><u>Limitations:</u> Some breakdown in monitoring at production level in 1994; documented high variability in HH sample iodine content in 1996 (<15->69mg/kg)</p>	<p><u>Strengths:</u> 74% of consumers aware of iodized salt,</p> <p><u>Limitations:</u> Only 46% of retailers knew of regulations for sale of non-iodized salt</p> <p>Limited awareness among retailers (50% of sample of retailers didn't know any effects of IDD; 74% had heard of iodized salt; 46% don't know benefits)</p>
Indonesia	<p><u>Strengths:</u> 1994: Legislation mandated iodization of all salt for human consumption</p> <p><u>Limitations:</u> Numerous small producers</p>	<p><u>Strengths:</u> National Association for Iodized Salt Producers includes 271 iodized salt producers, 236 of which meet gov't standards</p> <p><u>Limitations:</u></p>	<p><u>Strengths:</u> (Limited information in report)</p> <p><u>Limitations:</u></p>	<p><u>Strengths:</u> Regulations in place, and supported by government</p> <p><u>Limitations:</u> No information presented on enforcement actions taken</p>	<p><u>Strengths:</u> Survey w/ QA measures; routine data at retail and HH level limited</p> <p><u>Limitations:</u></p>	<p><u>Strengths:</u> (Information not reviewed)</p> <p><u>Limitations:</u></p>
Thailand	<p><u>Strengths:</u> Initial law in 1965 endorsed iodization, but did not make it mandatory. Law changed in 1994: Legislation mandating that table salt be iodized</p> <p>National Coordinating Committee exists</p> <p><u>Limitations:</u> Law did not include salt for food industry</p>	<p><u>Strengths:</u> Salt produced in several places—both rock salt and evaporated sea water contribute</p> <p>Fortificant (KIO₃) provided by government, and comprises 60% of IDD budget</p> <p><u>Limitations:</u></p>	<p><u>Strengths:</u></p> <p><u>Limitations:</u> Very weak monitoring system at production level</p>	<p><u>Strengths:</u> Regulations in place, and supported by government</p> <p><u>Limitations:</u> No information presented on enforcement actions taken</p> <p>Limited ability to limit non-iodized salt available in market</p>	<p><u>Strengths:</u></p> <p><u>Limitations:</u> Weak monitoring at retail level</p>	<p><u>Strengths:</u> 83% aware of importance of IDD (2003 report, HH level)</p> <p>High awareness of need to use iodized salt, but based on prevention of goiter, not intellectual development</p> <p>Strong support by royal family 1997</p> <p>National IDD day declared beginning 2003</p>

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Quality Assurance Program Monitoring Program Evaluation	Information, Education & Communications
	Coordinating Committee does not meet	Lack of clarity about salt produced for human consumption vs. industrial salt				<u>Limitations:</u> Limited awareness of intellectual deficit risk from IDD

References

1. Background information on IDD/USI in Cambodia, UNICEF, personal communication
2. Report Of National Representative Survey Of Iodine Nutrition And Implementation Of Universal Salt Iodization Program In Cambodia, Government of Cambodia and UNICEF, 2008
3. Cambodia DHS 2005.
4. Li, Mu; Eastman, Cresswell; and Cavalli-Sforza, Tomasso. Iodine Deficiency Disorders Elimination Project in Tibet. Final Activity Completion Report, December 2004
5. *Tracking Progress Towards Sustainable Elimination Of Iodine Deficiency Disorders In Bhutan*. Nutrition Section, Directorate Of Health Services, Royal Government Of Bhutan; International Council For Control Of Iodine Deficiency Disorders (ICCIDD), New Delhi (India); Clinical Epidemiology Unit, All India Institute Of Medical Sciences, New Delhi, India; Unicef, Thimpu (Bhutan); WHO, Thimpu (Bhutan) & Who-Searo, New Delhi (India); The Micronutrient Initiative, Ottawa (Canada). August, 1996
6. Bhutan's Story of Controlling IDD, ICCIDD, www.searo.who.int/LinkFiles/Public_Information_&_Events_vol3-2_bhutan.pdf
7. Tracking Progress Toward the Elimination of Iodine Deficiency Disorders in Indonesia, Draft consultant report, Dr. Jonathan Gorstein, UNICEF, 2005
8. Review of Progress Towards Sustainable Elimination of Iodine Deficiency in Thailand, Report of a Network Review Mission, 18-28 April 2004

6. Sugar Fortified with Vitamin A

Key examples of mass-fortification programs (staples and condiments) that have been implemented at the national level were selected for review. Those selected had information available on biological indicators of impact in the target populations, as well as estimations of the additional intake of micronutrients that are being delivered by the programs. Programs were reviewed to assess the strength of the evidence used to show public health impact, and the quality of the program components.

For sugar fortification with vitamin A, three programs were reviewed:

- Guatemala
- Nicaragua
- Zambia

The results varied somewhat for these three programs. In Guatemala and Nicaragua, the prevention of vitamin A deficiency and its consequences is clearly associated with the presence of the sugar fortification program. In both countries, coverage is high (more than 90% in Guatemala, and 75-80% in Nicaragua) and in each case, the program is delivering large proportions (158-233%) of the Estimated Average Requirement (EAR) of this vitamin to the average person. Nevertheless, complete control of this deficiency has required the simultaneous use of vitamin A supplementation (VAS) to children 6 to 36 months of age. Xerophthalmia has almost completely disappeared in Guatemala, and the prevalence of low serum retinol levels ($< 0.7 \mu\text{mol/L}$) in Nicaraguan pre-school age children is lower than 2%, through the combined use of sugar fortification and VAS.

The two countries monitor annually the quality, access and coverage of fortified sugar at the household level. Nicaragua also measures serum retinol levels in 6-59 month old children yearly, using a sampling design that allows making deductions applicable to the main geographical regions of the country every 3 years. However, none of the countries assesses the additional intake of vitamin A that is provided through the consumption of fortified sugar.

These two programs demonstrate that fortified sugar can reach a high proportion of the population, and can demonstrate improvement in measures of vitamin A deficiency, suggesting that the program can reproduce results expected from efficacy trials.

However, unlike the Central American countries, in Zambia despite the combined use of sugar fortification and VAS, the persistent prevalence of low serum retinol levels suggests that vitamin A deficiency is still a public health problem. The estimated additional intake of vitamin A through the consumption of fortified sugar in this country is 3 to 9 times smaller than that in Nicaragua or Guatemala because the vitamin A content in sugar is lower (4.3 against 7.8-11.8 mg/kg), the sugar consumption is smaller (25-52 against 87-100 g/day), and household coverage with fortified sugar is poorer (25% against 75-90%). This explains the inability of fortification to have the expected impact on vitamin A deficiency. The lack of biological impact commonly associated with VAS, which has a good coverage ($> 80\%$), could be explained by the failure of serum retinol as a suitable indicator in a population largely affected by infection and inflammation. Acute-phase proteins were found in 40-67% of children during the national survey of 1998.

The Zambia example suggests that fortification programs must achieve both high coverage and adequate levels to have an impact on serum retinol as a measure of deficiency.

Operational components of sugar fortification are discussed in the section “Operational Components of Mass-Food Fortification Programs,” starting on page 76.

Table 6.1. Coverage and impact of vitamin A fortification of sugar programs

Country Scale Population Year	Provision		Coverage (% homes with <u>fortified</u> product)	Utilization Food Intake (g/d)	Micronutrient Intake (% EAR)			Biological Indicators of Impact		
	Food Supply	At Household (HH) Level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
Guatemala National 13 millions Started in 1976-77. Halted in 1979. Reactivated in 1989.	1976-77: 75% of the national produced sugar was fortified, at 15 mg/kg ¹	10.1 mg/kg ¹	Studied towns receiving fortified sugar: 70% ¹	General: 38 g/day ¹ in almost all homes.	197 µg/d = 46% ¹	381 µg/d = 89% ¹	578 µg/d = 135% ¹	N.A.	1-5 y: low serum retinol level (<0.7 µmol/L) decreased from 21.5% to 5-10%. Low breast milk retinol (<1.05 µmol/L) decreased from 24.1 to 11.1% ¹ .	Conjunctival xerosis decreased from 3.7 to 1.7/1000 children after 6 mo of fortification ¹ .
	Since 1989, all national sugar is fortified at 15 mg/kg. In 2007, 500,000 MT fortified sugar was produced; i.e 100 g/day per person ² .	2005: 9.4 mg/kg; 2006: 8.9 mg/kg; 2007: 11.8 mg/kg ^{7 2}	Country: More than 90% 2003-07 ²	6-12 m: 10 g/day ³ 6-36 m: 24 g/day ⁴ Lactating women: 100-150 g/day ⁵ General: 100 g/day.	6-12 m: 60 µg/d = 15% ^{3,8} 6-36 m: 257 µg/d = 90% ⁴	6-12 m: 112 µg/d = 28% ³ 6-36 m: 80 µg/d=28% ^{9,4} Lactating women: 982-1470 µg/d = 161-241% ⁵ General: 1000 µg/d = 233% ⁶	6-12 m: 172 µg/d = 43% [proportion < AI: 43%] ³ 6-36 m: 337 µg/d = 118% ⁴	N.A.	National low serum retinol level (<0.7 µmol/L) in 12-59 m decreased from 26% (1988) to 16% (1995), but children 12-23 m: 20%, and 48-59 m: 12% ⁶ .	Xerophthalmia in 6m-10y decreased by 30% from the '80s to early '90s associated to sugar fortification. Further declined by 70% occurred coupled with VAS in late 1990's ⁷ . Nowadays, xerophthalmia has disappeared or it is very rare.
Nicaragua National 5.8 millions Started in 2000	15 mg/kg of vit. A are added to sugar. In 2007 150,000 MT fortified sugar was produced; i.e. 70 g/day per person.	7.8 mg/kg as average for 2003-2005 ⁸	Country: 75-80% 2004-5 ⁸	General: 87 g/day ⁸ in almost all homes.	-	General: 678 µg/d = 158% ⁸	-	N.A.	National low serum retinol level (<0.7 µmol/L) in 6-59 m decreased from 31% (1993) to 9% (2000) with VAS, and to 2% (2003-05) with VAS ¹⁰ and fortification ⁸ .	-
Zambia	10 mg/kg of vit. A are added to	4.3 mg/kg estimated from	Country: 25% ¹¹	General: 26-52 g/day ¹²	-	General: 111-222 µg/d =	-	N.A.	National low serum retinol level	-

⁷ These averages were estimated using the content reported in the reference and multiplied by the proportion of samples that were identified as positive, because the procedure only analyzes the samples that were positive. Thus for example, in 2007 91% of samples had an average vit. A content of 13.0; hence the average for all samples was 13.0 x 0.91 = 11.8.

⁸ For this age group, the dietary parameter was Adequate Intake (AI), whose values are more similar to RNI than to EAR.

⁹ At the moment of the study, the vitamin A content in sugar at households was 4.5 mg/kg. Now, the vit. A level is about 12 mg/kg.

¹⁰ VAS started in 1994, and its coverage in 2003-05 was 80-96%. Prevalence of high levels of AGP –indicative of infection or inflammation- was 26%.

¹¹ Although 50% of households had sugar, it was found that only 51.1% of the sugar samples contained vitamin A with levels above 2.5 mg/kg.

¹² The higher value is because only approximately half of the population has access to sugar.

Country Scale Population Year	Provision		Coverage (% homes with <u>fortified</u> product)	Utilization Food Intake (g/d)	Micronutrient Intake (% EAR)			Biological Indicators of Impact		
	Food Supply	At Household (HH) Level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
National 11.7 millions Started in 1998	sugar. Current production is estimated in 110,000 MT of fortified sugar; i.e. 26 g/day per person.	survey data of 2003 ¹¹		Urban: 65.6% ⁹ Rural: 24.7% ⁹		26-52% ¹³			(< 0.7 µmol/L) in 6-59 m decreased from 66% (1997) ¹⁰ to 54% (2003) ¹⁴ ; and from 22% to 12% among women ¹¹ . There is a VAS program since 1992 ¹⁵ .	

¹³ Estimated from the per capita national intake of sugar and the average content of vitamin A found at homes in 2003.

¹⁴ Prevalence of very low serum retinol levels (<0.35 µmol/L) also decreased from 12% in 1996 to 5% in 2003¹¹. Prevalence of high levels of acute phase proteins –indicators of infection or inflammation- was 40% for CRP and 67% for AGP.

¹⁵ Coverage of the VAS for pre-schoolers improved from 28.7% in 1997 to 80% in 2000¹², but then back to 65% in January 2003 to return to 87% in June 2003¹¹. VAS Coverage of postpartum mothers was 21% in 1997 and 39% in 2003¹¹.

Table 6.2. Data quality for coverage and impact of vitamin A fortification of sugar programs

Country Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency Dose-Response Relationship	Potential Confounding Factors
Guatemala National	<ul style="list-style-type: none"> • 1965-67 (Pre-fortification) National Survey • 1975-1977 Survey of 12 randomly selected rural communities (pre-fortification baseline: 1975; post-fortification: 4 surveys every 6 mo in 1976) 	<ul style="list-style-type: none"> • Findings from survey conducted in 1975-77 & 1996-7 were consistent in terms of coverage, dietary intake & biochemical outcomes 	<ul style="list-style-type: none"> • Precise data; Indicator used is a good proxy for coverage & impact • Data on biochemical & functional outcomes were collected from ~70% of the original samples: no difference between the loss-to-follow up vs. those who were measured for biochemical & functional outcomes 	<ul style="list-style-type: none"> • Independent data collection • Forms editing done in the field by the same field workers • Data error rates assumed to be low 	<ul style="list-style-type: none"> • Fully consistent: intake of retinol, change in serum retinol concentration among children (1-5 y), change in breast milk retinol concentration, liver retinol level all showed significant improvement following the fortification program • Magnitude of increase in serum retinol concentration among children (1-5y) was greater among those who had lower baseline serum retinol concentration 	<ul style="list-style-type: none"> • No potential negative confounding factors
	<ul style="list-style-type: none"> • 1989-to date • National Survey in 1996-1997 • Vitamin A content in the fortified sugar at the HH level was assessed every year using samples collected from children in randomly selected rural public schools • Xerophthalmia study used hospital records as the main data source • Specific measurement of sugar intakes done in small research studies 	<ul style="list-style-type: none"> • Reduction in xerophthalmia prevalence coincides with the introduction of sugar fortification and VAS programs • Decreasing trend in the prevalence of low serum retinol level from 1989 to 1996 is clearly associated with the introduction of sugar fortification program 	<ul style="list-style-type: none"> • Acute phase proteins were not used to discard that low serum retinol may be due to infection/inflammation and not to low vit. A intake. • Since 1997 serum retinol level has not been assessed 	<ul style="list-style-type: none"> • Vitamin A fortificant level has been assessed using samples collected from rural public schools, rather than from households • Sugar quality has been assessed every year at the provincial level • Data on micronutrient intake of children 6-36 mo of age & lactating women are obtained from small studies 	<ul style="list-style-type: none"> • In the survey conducted in 1996-7, variations in serum retinol levels according to the age of children may be associated with fortified sugar intake, but other factors also need to be considered, such as reduction of infections, and lower micronutrient requirements at increasing child age 	<ul style="list-style-type: none"> • The inverse association between age and the prevalence of low serum retinol level in young children may be explained by factors other than vitamin A intake • Difficult to isolate the individual effects of sugar fortification & VAS programs for children < 36 mo of age
Nicaragua National	<ul style="list-style-type: none"> • National survey with sugar and serum samples collected monthly during a 3-year period. 	<ul style="list-style-type: none"> • Retinol serum levels associated with the interventions, but it is difficult to isolate the individual effect of VAS & sugar fortification programs 	<ul style="list-style-type: none"> • Sugar intake and the associated vit. A intake level have not been determined • Impact of fortified sugar intake has not been determined for the population older than 5 years of age 	<ul style="list-style-type: none"> • No evidence of bias • Serum & sugar samples were obtained randomly from households 	<ul style="list-style-type: none"> • Despite the presence of infection/inflammation, serum retinol has been a good indicator of vit. A status 	<ul style="list-style-type: none"> • None if both VAS and sugar fortification programs are considered together
Zambia National	<ul style="list-style-type: none"> • National Survey: 1997 (baseline) & 2003 	<ul style="list-style-type: none"> • High prevalence of low serum retinol level observed despite the sugar fortification & VAS program which had a high coverage rate 	<ul style="list-style-type: none"> • Sugar intake and the associated vit. A intake level have not been determined • Sugar sample available only among 43% of HH 	<ul style="list-style-type: none"> • No reporting bias as independent data collection was done • Forms editing by the supervisors 	<ul style="list-style-type: none"> • No information available to assess dose-response relationship • High prevalence of low serum retinol levels observed despite 	<ul style="list-style-type: none"> • High levels of sub-clinical infection (including malaria): likely depressed serum retinol concentration • Child malnutrition was

Country Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency Dose-Response Relationship	Potential Confounding Factors
			<ul style="list-style-type: none"> • Acute phase protein present in 40-67% of respondents • Serum retinol level may not be an adequate indicator of vitamin A status in this population which has high infection (including malaria) rates • Lack of data to determine annual compliance and quality of the sugar fortification program 	<ul style="list-style-type: none"> • Identified errors corrected by verifying answers with respondents • Double data entry; data error check system in place • Data errors assumed to be low 	<p>the recent VAS program which had a high coverage rate</p> <ul style="list-style-type: none"> • Association between serum retinol level and sugar fortification program cannot be established because of low program coverage, sugar intake & fortificant level 	<p>deteriorating possibly due to drought & HIV/AIDS</p>

Table 6.3. Summary description of the key implementation components of vitamin A fortification of sugar programs

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
<p>Guatemala</p> <p>National</p>	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Vitamin A fortification of sugar is mandated by law • Regulations for levels, packaging & labeling are established in standards • Multisectoral food fortification committee (CONAFOR) established and have played active role in program implementation • In Guatemala all sugar mills (around 12) are integrated to one Association of Sugar Producers of Guatemala (ASAZGUA) which has coordinated the fortification program & acted as a liaison with MOH • Sugar producers are exempted from paying import duties on fortification equipment, vitamin A concentrate, and other inputs <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Program planning & implementation started in the 1970's without industry consensus • Conflict between the government & sugar industry concerning sugar price & importation of unfortified sugar 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • In Guatemala: Sugar Producer Association procures fortificant & other necessary inputs for the premix, produces & distributes premix • Cost of fortification is incorporated to the sugar price <p><u>Limitations</u></p> <ul style="list-style-type: none"> • For political reasons, government (2000-04) authorized Importation of unfortified sugar and created a serious conflicts with the local sugar producers, which placed the continuation of the program in jeopardy 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • All sugar mills have the necessary equipment for sugar fortification and for QC/QA • Annual training & continuing education courses are provided to staff members for handling vitamin A premix and for quality control at the refineries • All factories have introduced QC/QA of sugar fortification as part of their internal QC/QA system for the overall sugar production process • Vitamin A content in sugar premix is monitored daily • External laboratories are periodically used to confirm reliability of the sugar mills practices <p><u>Limitations</u></p> <ul style="list-style-type: none"> • QC/QA information related with the sugar fortification process is not readily available/accessible 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Program supervisory manuals were developed & updated by INCAP • In Guatemala: laboratory facilities checking vitamin A content of sugar were upgraded • Government officers visit refineries to observe compliance with the process & obtain samples to assess vitamin A level • Samples are also obtained at the retail levels & analyzed for vitamin A content <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Government did not allocate sufficient human & financial resources for enforcement & inspection • Lack of systematized procedures for the control & supervision of fortified foods at the retail level 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Micronutrient Sentinel Schools system has been developed: 20 sugar samples from students in 420 randomly selected rural public schools are obtained to assess program coverage; the system has been running annually since 1995 • Annual reports of program M&E are published by CONAFOR, UNICEF and INCAP, and usually in a public meeting <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Lack of epidemiological or nutritional surveillance system which assess the dietary quality and population nutritional status on a regular basis, as well as the contribution of fortified sugar to vit A intake of the population • Vitamin A status of the population was assessed more than 10 years ago 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • <u>None currently running</u> At the beginning, it was forbidden to make any remark about sugar fortification. However, after conflict between the industry and the government '00-'04, Information on sugar fortification was disseminated through meetings, TV and radio interviews, papers • Labeling of fortified food to facilitate identification by consumers • In Guatemala: ASAZGUA launched a publicity and distribution initiatives of fortified sugar in rural areas <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Popularity and public acceptance of the program is at risk of being used to advertise special types of sugar fortified with other micronutrients without the required epidemiological design and governmental supervision

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
Nicaragua National	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Vitamin A fortification of sugar is mandated by law • Regulations for levels, packaging & labeling are established in standards • In Nicaragua all sugar mills (around 5) are integrated to one Association of Sugar Producers of Nicaragua which has coordinated the fortification program & acted as a liaison with MOH • Sugar producers are exempted from paying import duties on fortification equipment, vitamin A concentrate, and other inputs • Program planning & implementation started in the 1990's in coordination and in agreement with the industry; a soft loan was obtained for starting the first year of the program 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • In Nicaragua: Sugar Producer Association procures fortificant & other necessary inputs for the premix, produces & distributes premix • Cost of fortification is incorporated to sugar price 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • All sugar mills have the necessary equipment for sugar fortification and QC/QA • Most factories have introduced QC/QA of sugar fortification as part of their internal QC/QA system for the overall sugar production process <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Reliability of the QC/QA system of all the sugar mills has not been confirmed • QC/QA information related with the sugar fortification process is not readily available/accessible 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Program supervisory manuals were developed & updated by INCAP, and they are being used by the Department of Food Control • Government laboratory has the capacity to perform quantitative determination of Vit. A in sugar • Government officers visit refineries to observe compliance with the process & obtain samples to assess vitamin A level <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Government did not allocate sufficient human & financial resources for enforcement & inspection • Lack of systematized procedures for the control & supervision of fortified foods at the retail level 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • An annual comprehensive and integrated monitoring system of the nutrition interventions is in its fourth year of existence; it includes assessment of the vitamin A content in sugar samples from home, as well as serum retinol level in pre-school age children. • Annual reports of program M&E are published, although with some delay; Every three years the information has statistical significance by the main geographical regions of the country. <p><u>Limitation</u></p> <ul style="list-style-type: none"> • The epidemiological or nutritional surveillance system does not include the assessment of intakes of fortified food & micronutrients • Monitoring system highly depends on external financial & technical assistance • There is no information about xerophthalmia prevalence and its evolution in the country 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • <u>None currently running</u>, but in the past Information on sugar fortification was disseminated through meetings, TV and radio interviews, press releases • Labeling of fortified food to facilitate identification by consumers <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Popularity and public acceptance of the food fortification programs have prompted the introduction of many industrially-produced foods that are fortified but whose design and supervision do not follow epidemiological criteria.
Zambia National	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Vit A fortification of sugar is mandated by law • Legal fortificant level is established 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Only two large domestic sugar producers exist • Despite the weakness of the government enforcement, sugar 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Members of the FTF traveled to Guatemala to receive training on food fortification • Training materials for health 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Government laboratory is able to determine the vitamin A content in the fortified sugar product 	<p><u>Limitations</u></p> <ul style="list-style-type: none"> • Other than the 2003-national survey –financed and organized by external cooperation- no initiatives for program M&E 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • At the start of the program, preliminary research on consumer's attitude towards sugar fortification supported

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
	<ul style="list-style-type: none"> • Strong political commitment • Multisectoral Fortification Task Force (FTF) was established & have coordinated program implementation • Decision of the 2-3 sugar industries to comply with the fortification process • Cost-sharing of the initial fortification expenditure among various partners (i.e., USAID, JICA, UNICEF and others) during the first years of the program <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Delay in enacting enforcement regulations • Sugar producers not exempted from paying import duties on vitamin A fortificant • Minimum content is being interpreted as the average content • It is uncertain whether the Fortification Task Force is still operating 	<p>industry has been complying with the fortification process, although adding lower vit. A levels than expected</p> <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Production of unfortified sugar for industrial use is allowed but with no mechanism to prevent it from being leaked to the domestic market • Non-fortified sugar is smuggled from the neighboring countries, where sugar price is lower: this is estimated to cover 10% of the national demand. • In the past, vitamin A producers sold their product without checking first that vitamin A premix adhered to sugar crystals; compliance problems were identified but they have been overcome now • Heterogeneity in the vit. A fortificant level has not been solved 	<p>inspectors & enforcement officers were developed</p> <ul style="list-style-type: none"> • National training workshops for laboratory technicians at the government / industry, health inspectors & enforcement officers were conducted <p><u>Limitations</u></p> <ul style="list-style-type: none"> • QC/QA data are not accessible/available to other stakeholders of the program 	<ul style="list-style-type: none"> • Several manuals and training courses have been offered <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Currently, NO external quality control of fortified sugar exist at the refineries or retail levels due to lack of funds for transport & reagents • Inadequate enforcement standards 	<p>have been established</p> <ul style="list-style-type: none"> • There is no updated information about the extent of use and intake of fortified sugar in the country and among the different segments of population (regions, social strata, age groups) • There is no information about xerophthalmia prevalence • FTF has not played an active role in program monitoring & evaluation 	<p>development of IEC materials & strategies</p> <ul style="list-style-type: none"> • At the beginning the pioneer sugar industry launched an aggressive marketing campaign (e.g., tv & radio spots in English and local languages, leaflet & posters, community information sessions etc) • Campaigns organized by the government emphasize health implications and benefits of consuming fortified sugar <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Sustainability of social marketing & communication campaigns is uncertain

References:

1. Arroyave G, Aguillar JG, Flores M, Guzman MA. Evaluation of sugar fortification with vitamin A at the national level. PAHO Scientific Publication No. 384: Pan American Health Organization, Washington DC. 1979.
2. CONAFOR, INCAP/OPS, UNICEF. Situación de los Programas de Fortificación de Alimentos. Informes Anuales, Guatemala. Annual reports from 2000 to 2007.
3. Palma Escobar AV, and Solomons N. Personal communication. 2008. CESSIAM, Guatemala.
4. Krause VM, Delisle H, Solomons NW. Fortified foods contribute one half of recommended vitamin A intake in poor urban Guatemalan toddlers. *J Nutr* 1998; 128: 860-4.
5. Hernandez J, Solomons N. Bulletin of Research Abstracts of CESSIAM 2005; 16(1):
6. Dary O, Martinez C, Guamuch M. Sugar fortification with vitamin A in Guatemala: the program's successes and pitfalls. In Freire WB (Ed) Nutrition and an Active Life. PAHO: Washington D.C., USA. 2005.
7. Martinez C, Mena I, Boy E, Dary O. Evolution of nutritional blindness in Guatemala and its association with sugar fortification and vitamin A supplementation: Retrospective study of hospital cases from 1980 to 2000. PAHO/Institute of Nutrition of Central America and Panama, Guatemala City. 2005.
8. Ministerio de Salud Pública de Nicaragua. Sistema Integrado de Vigilancia de Intervenciones Nutricionales (SIVIN). Informe de Progreso 2003-2005. 2008.
9. Mwela C et al. Vitamin A Supplementation and Sugar Availability (March 1999). Cited in: Serleimitsos JA, Fusco H. Vitamin A Fortification of Sugar in Zambia 1998 – 2001. The Most Project, Arlington, USA. 2001¹².
10. Luo C, Mwela CM. National Survey on Vitamin A Deficiency in Zambia: A Rando Cluster Study for Children (1-5 years) and Mothers Attending National Immunization Days in August 1007. Cited in: Serleimitsos JA, Fusco H. Vitamin A Fortification of Sugar in Zambia 1998 – 2001. The Most Project, Arlington, USA. 2001¹².
11. MOST / UNICEF / CDC / The National Food and Nutrition Commission of Zambia. Report of the national survey to evaluate the impact of vitamin A interventions in Zambia. 2003.
12. Serleimitsos JA, Fusco H. Vitamin A Fortification of Sugar in Zambia 1998 – 2001. The Most Project, Arlington, USA. 2001.

7. Flours Fortified with Folic Acid

Several country programs for fortification of flour with folic acid were reviewed. These include programs in:

- Chile
- South Africa
- Guatemala

Reduction in the prevalence¹⁶ of newborns affected with neural tube defects (NTDs) in Chile and South Africa has a clear plausible association with the introduction of folic acid fortification of flours; wheat in Chile and wheat and maize in South Africa. The consumption of folic acid fortified flour is confirmed with the rise of serum and RBC folate in the populations of the two countries.

The efficacious folic acid dose varies: it was 427 µg/day (227% of EAR) in Chile and 47-357 µg/day (25-190% of EAR) in South Africa. In South Africa, it seems that the main source of folic acid is maize flour, which is especially consumed by the rural population. However, the results of the NTDs were not reported by geographical location, which would have strengthened the plausibility of this association. Furthermore, the estimation of the additional intake of folic acid nationally in South Africa is uncertain because the results come from studies that measured changes in the nutritional value of foods from only one province.

Like in the case of fortified sugar in Zambia, it is expected that the wheat flour fortification program in Guatemala is going to have a modest, if any, impact in the nutritional status of folate for the poor and very poor segments of the population, because of the low consumption of flour-containing products by these groups.

Monitoring of folic acid levels in flour is rarely done in Chile and South Africa, but recent results suggest that the levels have been raised too much in the Metropolitan area of the Chilean capital, to the point that a large portion of individuals may have intakes larger than the Upper Tolerable Level of intake (UL). The Ministry of Health of Chile has already started to take actions to improve the quality control and enforcement of the fortification standard in order to avoid excessive intakes and the potential adverse effects linked to them.

Operational components of folic acid fortification are discussed in the section “Operational Components of Mass-Food Fortification Programs,” starting on page 76.

¹⁶ This is indeed the incidence, but the term prevalence is used with this meaning in the field of neural tube defects.

Table 7.1. Coverage and impact of folic acid fortification of cereal flour programs

Country Scale Population Year	Provision		Coverage (% homes w/ <u>fortified</u> product)	Utilization Food Intake (g/day)	Micronutrient Intake (% EAR ¹⁷)			Biological Indicators of Impact		
	Food Supply	At Household (HH) Level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
<p>Chile</p> <p>National</p> <p>16.5 millions</p> <p>Folic acid Fortification Started in 2000</p> <p>Original Fortification Program started in 1953: fortification with vitamin B-1, B-2, niacin & iron</p>	<p>2 - 2.4 mg/kg of folic acid added to wheat flour</p> <p>Annual production of 1,200 MT: 200 g/d per person</p>	<p>National: 2.0 mg/kg¹</p> <p>Metropolitan area: 7 mg/kg¹</p> <p>Bread is 77% wheat flour and thus, bread contains ~77% of the folic acid level found in the flour</p>	<p>Country: Almost all homes, but overall compliance of the program has not been measured</p>	<p>Women: 219 g/d (89% consuming more than 140 g/d as bread²)</p> <p>Elderly (≥ 70 y): 186 g/d³</p> <p>General: 200 g/d</p>	<p>Women: 291 µg/d DFE= 91%, but >50% had intakes below EAR¹⁸</p> <p>Elderly: 410 µg/d FA = 218%³.</p> <p>General population (national): 400 µg/d FA= 213%</p> <p>General population (Metropolitan area): 1,400 µg/d FA= 745%</p>	<p>Women: 427 µg/d FA = 227%; < 3% consumed <100 µg/day; and 48% women consumed >400 µg/day of folic acid²</p> <p>Elderly: 410 µg/d FA = 218%³.</p> <p>General population (national): 400 µg/d FA= 213%</p> <p>General population (Metropolitan area): 1,400 µg/d FA= 745%</p>	<p>Women: 1142 µg/d DFE= 357%, and >30% with intakes >1400 µg/d DFE^b.</p>	<p>Women: Change in mean serum folate: 9.7 → 37.2 nmol/L^{19 2}</p> <p>Change in low serum folate (<10.7 nmol/L) prevalence: 65% → 0%²</p> <p>Change in high serum folate (>45 nmol/L) prevalence: 0% → 48%²</p> <p>Elderly: Change in mean serum folate: 16.2 → 32.7 nmol/L³</p> <p>Change in low serum folate (< 10.7 nmol/L) prevalence: 8% → 0%³</p>	<p>Women: Change in mean red blood cell (RBC) folate: 290 → 707 nmol/L²</p> <p>Change in low RBC folate (<365 nmol/L) prevalence: 82% → 1%²</p> <p>Elderly: Change in prevalence of hyperhomocysteinemia (≥ 14 µmol/L): 31% → 17%³.</p>	<p>Change in neural tube defects (NTD) rates: 15.7-17.5 → 7.9/10000 births (i.e. 49-55%)⁴</p> <p>In subsequent years, NTD prevalence has been kept between 7.4 and 8.6/10000⁵ (i.e. 50-57% reduction from the baseline).</p>
<p>South Africa</p> <p>National</p>	<p>2.0 mg/kg of folic acid added to maize flour</p>	<p>Maize porridge: 0.43 mg/kg⁶</p>	<p>Maize porridge: urban: 63%; rural: 95%^{6 20}.</p>	<p>Maize porridge: urban: 771; rural: 906⁶.</p>	<p>Men urban: 323 µg/d DFE= 101%⁶.</p>	<p>Men urban: 55 µg/d FA= 29%^{6 21}.</p>	<p>Men urban: 416 µg DFE= 130%⁶.</p>	<p>Women rural: Change in mean serum folate:</p>	<p>Women rural: Change in mean RBC folate: 505</p>	<p>Change in NTD rates: 14.1 → 9.8/10000 births (i.e. 30%)⁸</p>

¹⁷ It is assumed an EAR of 188 µg/day as folic acid, which is equivalent to 320 µg/day of Dietary Folate Equivalents, because folic acid is 70% more bioavailable than dietary sources of folate.

¹⁸ Estimated from basal serum folate level in reference (2), and using equation of Quinlivan and Gregory (Am J Clin Nutr 2007; 86:1773): Dietary Folate Equivalents (DFE) intake = (serum folate in µg/L -0.132)/0.0145.

¹⁹ In order to transform nmol/L into µg/L, the values should be divided by 2.226.

²⁰ These figures are the users of the food and not necessarily the percent of homes where the foods is indeed fortified. It is estimated that only 70% of maize flour and 90% of wheat flour are fortified in South Africa⁹.

Country Scale Population Year	Provision		Coverage (% homes w/ <u>fortified</u> product)	Utilization Food Intake (g/day)	Micronutrient Intake (% EAR ¹⁷)			Biological Indicators of Impact		
	Food Supply	At Household (HH) Level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
44 millions Folic acid fortification started in 2003	1.4 mg/kg of folic acid added to wheat flour Vit A, B-1, B-2, niacin, B-6, iron & zinc also added to flours	White bread: 0.0 mg/kg ⁶ Brown bread: 0.4 mg/kg ⁶	White bread: urban: 34%; rural: 22% ⁶ . Brown bread: urban: 51%; rural: 60%	White bread: urban: 165; rural: 154 ⁶ . Brown bread: urban: 157; rural: 172 ⁶ .	Men rural: 234 µg/d DFE= 73% ⁶ . Women urban: 218 µg/d DFE = 68% ⁶ . Women rural: 246 µg/d DFE= 77% ⁶ .	Men rural: 440 µg/d FA =234% ⁶ . Women urban: 47 µg/d FA= 25% ⁶ . Women rural: 357 µg/d FA =190% ⁶ .	Men rural: 982 µg/d DFE=307% ⁶ . Women urban: 298 µg/d DFE= 93% ⁶ . Women rural: 854 µg/d DFE= 267% ⁶ .	8.0 → 23.4 nmol/L Prevalence of low serum folate (<6.8 nmol/L): 28% → 0% ^{7,22}	→ 955 nmol/L Prevalence of low RBC folate (<365 nmol/L): 26% → 2% ^{7†}	Mortality of children and mother associated to NTD also declined ⁸
Guatemala National 13 millions Folic acid Fortification Started in 1992	In 1992: 0.35 mg/kg of folic acid added to wheat flour In 2002: minimum was raised to 1.8 mg/kg of folic acid added to wheat flour Vitamin B-1, B- 2, niacina and iron also added to wheat flour	Wheat flour: 1.8 mg/kg in retail samples ¹¹ . White bread (77% flour): 1.3 mg/kg Sweet bread (65% flour): 0.85 mg/kg ¹¹ .	Sweet bread: (54%): 90% ¹² Non-poor (35%): 89% ¹² Poor (11%): 76% ¹² .	Flour equivalent through breads. Non-poor (54%): 124 ^{12, 23} Poor (35%): 48 ¹² Very poor (11%): 14 ¹² .		Women (as 0.677 of adult equiv.) Non-poor: 133 µg/d FA = 71% ¹² Poor: 30 µg/d FA= 16% ¹² Very poor: 21 µg/d FA= 5% ¹² .	Women poor: 364 µg/d FA= 114% ¹³ .	Women rural and poor Mean serum folate: 32 nmol/L ¹³ Prevalence of low serum folate (< 6.8 nmol/L): 3% ¹³	Women rural and poor Mean RBC folate: 437 nmol/L ¹³ Prevalence of low RBC folate (< 317 nmol/L): 22% ¹³ Prevalence of hyper-HCys (≥ 14.4 µmol/L): 4% ¹³	

²¹ These figures were corrected multiplying the additional amount of folic acid for 1.7 because the higher bioavailability of the synthetic forms over the dietary sources; the paper did not make this transformation.

²² This is a small study carried out in the Capricorn district of the Limpopo province.

²³ Estimated per adult equivalent units (reference of adult males) using the proportional daily energy requirement for each age and gender.

Table 7.2. Data quality for coverage and impact of folic acid fortification of cereal flour programs

Country Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency Dose-Response Relationship	Potential Confounding Factors
Chile National	<ul style="list-style-type: none"> • NTD data of 1982 to 2002 from 25 hospitals that belong to the Latin American Collaborative Study of Congenital Malformations. • Folic acid intake from bread & blood folate level from in 1999-2000, as well as data for elderly persons, are from specific studies done in three public outpatient clinics of Santiago. 	<ul style="list-style-type: none"> • Similar trend in serum folate levels found in women of reproductive age & elderly people • Reduction in hyperhomocysteinemia and NTD prevalence associated with increased folic acid intake 	<ul style="list-style-type: none"> • Precise data; Indicators used are a good proxy for coverage & impact. • Recent information of folic acid content of folic acid and NTD prevalence from data obtained mostly in Santiago, Chile. • Evidence mostly applicable to Santiago, Chile, although it may be extrapolated to the rest of the country if the program performs equally well in the provinces. 	<ul style="list-style-type: none"> • Independent data collection was done • Overall data quality assumed to be good 	<ul style="list-style-type: none"> • Coverage, dietary intake, biochemical & functional data all show consistent findings • Association between intake and blood levels is clear • Dose-response relationship between intake & NTD prevalence has still been undetermined: Additional intake level is too high to establish the dose-response relationship 	<ul style="list-style-type: none"> • No potential negative confounding factors
South Africa National	<ul style="list-style-type: none"> • Dietary intake data: Secondary data analysis of small independent surveys • Biochemical data: collected from rural areas of the Limpopo Province • NTD prevalence data: hospital based surveillance data from 12 sentinel sites 	<ul style="list-style-type: none"> • Significant decline in NTD perinatal deaths observed using both hospital-based surveillance data & independent perinatal mortality data source • Increment in the folate content of foods, and rise of the serum folate level are evidence that the program is having impact that has a plausible association with the reduction of NTDs. 	<ul style="list-style-type: none"> • Indicators used are good proxy for coverage & impact • National changes in blood folate levels are only from the Limpopo province; national data is lacking. • Estimations of additional intake of folic are highly approximated because food composition data has not been reviewed along the implementation of the fortification program. 	<ul style="list-style-type: none"> • Prevalence of NTD & NTD perinatal mortality rate calculated using independent data sources • Dietary intake data obtained from secondary data analysis, and there are inconsistencies in the estimates 	<ul style="list-style-type: none"> • No evidence to evaluate dose-response relationship 	<ul style="list-style-type: none"> • Reductions in the prevalence of NTD & NTD perinatal mortality might be due to the improvement in folate status, but assessment of the quality and compliance of the program has not been done yet
Guatemala National	<ul style="list-style-type: none"> • Data obtained from household income & expenditure surveys, which provide rough estimates of individual food intakes¹². • Biochemical data obtained from a study carried out in a rural poor community¹³. 	<ul style="list-style-type: none"> • Discrepancies between indicators of good folate status as high serum folate and low hyper-homocysteinemia, with indicators of low folate status as low levels of RCB folate. • Dietary intake revealed folate inadequacy¹³. 	<ul style="list-style-type: none"> • Serum folate levels have not been determined in a national sample, and lack of response to different dose schemes with folic acid supplementation makes very difficult to interpret the biochemical results. 	<ul style="list-style-type: none"> • Data of the household survey and expressed as adult equivalent units allows predicting the additional folate intake of different members of the family, but they may not coincide with intra-house distribution of foods. 	<ul style="list-style-type: none"> • Difficult to examine the dose-response relationship, because four different supplement (schemes or composition?) had similar outcomes¹³. 	<ul style="list-style-type: none"> • No clinical signs have been evaluated

Table 7.3. Summary description of the key implementation components of folic acid fortification of cereal flour programs

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity Quality Control & Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
Chile National	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Folic-acid fortification of wheat flour mandated by law Legal fortificant level established at 2.0 -2.4 mg/kg Positive impact of fortification program on NTD prevalence has been well documented; research on the potential adverse effects of excessive folic acid (FA) intake is ongoing <p><u>Limitations</u></p> <ul style="list-style-type: none"> Legal range of fortificant level is too narrow, which has caused conflicts between the government and industry regarding compliance issues Strong enforcement on the minimum fortificant level of 2 mg/kg has caused excessive folic acid content in fortified products in the Metropolitan area There is no permanent inter-institutional body to solve public-private partnership issues; Currently, government is the leading force behind the program. 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Flour manufacturers directly purchase the premix from the providers; cost is incorporated to fortified flour price <p><u>Limitations</u></p> <ul style="list-style-type: none"> Premix vary in quality; no standards exist to control the quality of premix 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> All mills have the necessary equipment to carry out the fortification process <p><u>Limitations</u></p> <ul style="list-style-type: none"> QC/QA system is not widely used by the industry for checking compliance with the fortification standards 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Inspection of the fortified flour has been conducted by the department of Food Control (DFC) across the country <p><u>Limitations</u></p> <ul style="list-style-type: none"> Although inspection is conducted by the DFC, the quality & strictness vary widely, according to the availability of resources & motivation of the DFC officers (e.g., very strict inspection is being conducted in the Metropolitan area, but not in the rest of the country) Results and actions originated from the governmental actions are not made public. 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Tremendous efforts have been made to demonstrate the positive impact of folic acid fortification program on the biochemical indicators & NTD prevalence Academic institutions which have the capacity to analyze micronutrient content in the fortified flour & biological samples are involved in the program M & E activities <p><u>Limitations</u></p> <ul style="list-style-type: none"> Program M & E has not been systematically designed & implemented as part of the program; instead it has been conducted as a separate research activity 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Program is compulsory, and hence it does not require of intense IEC activities. Results of research papers and news associated to this program have been widely divulged. <p><u>Limitations</u></p> <ul style="list-style-type: none"> Fear for an excessive intake of folic acid is increasing in the public & some policy makers
South Africa	<u>Strengths</u>	<u>Strengths</u>	<u>Strengths</u>	<u>Strengths</u>	<u>Strengths</u>	<u>Strengths</u>

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity Quality Control & Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
National	<ul style="list-style-type: none"> • Micronutrient fortification of all (including imported) maize meal & wheat flour mandated by law • Legal fortificant level established, as well as regulations for packaging & labeling • Strong political commitment & program support: DoH is leading the initiative • Multisectoral National Fortification Alliance (NFA) established for program implementation • Efforts were made to engage both large & small millers from early stage of the program, with plans to subsidize operations of the latter <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Government bureaucracy & lack of resources have hindered enforcement • Small millers have perceived legislation as a way to force them out of the market • Industry frequently refuse to attend the NFA meetings 	<ul style="list-style-type: none"> • Minimal increase in flour cost due to fortification <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Inadequate handling & storage of fortified products by small retailers: results in nutrient loss • Large variations in stability, quality & cost of the micronutrient fortification mix: some millers choose a fortification mix which is of low quality, less stable, & cheaper • Difficult to engage small maize millers, which produce about 20% of the national demand 	<ul style="list-style-type: none"> • Large industries have the necessary equipment to comply with the fortification process <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Training of the millers relatively ignored • Quality & strictness of the QC/QA system of the industry is uncertain • Currently no standards for fortification mix quality • Limited communication with the premix manufacturers; premix quality has not been controlled • Some of the small mills are located in remote rural areas or have seasonal operations: hard to reach & monitor • Retailers not trained on how to store / handle fortified flour products: results in inadequate handling & storage 	<ul style="list-style-type: none"> • Provide National framework for training all enforcement agents • EHPs take samples from the mill & monitor their compliance with legislation • Efforts are being made to make the South African Bureau of Standards (SABS) responsible for testing fortification mix manufacturers/suppliers <p><u>Limitation</u></p> <ul style="list-style-type: none"> • EHPs overstretched with other responsibilities: excessive demands already placed on EHP's daily duties • EHPs lack resources & proper equipment to take samples adequately • Inability of the national government to control local units • Government laboratories are overstretched & overburdened: delays in sample analysis process 	<ul style="list-style-type: none"> • Comprehensive dietary surveys & biochemical assessments conducted at baseline • Existence of several research institutions that are interested in program M & E <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Performance of the program and its outcomes have not been monitored and evaluated at the national level • Adult food intake was not assessed at baseline • A comprehensive M&E plan has neither been designed nor implemented; most efforts in this matter have only garnered academic interest 	<ul style="list-style-type: none"> • Funds are allocated to social marketing & communication activities • Mass media campaigns were conducted to sensitize consumers about the prevalence & consequences of micronutrient deficiencies & benefits of consuming fortified foods • Mass media campaigns focused on low to middle SES groups <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Sustainability of social-marketing campaigns is uncertain when the external funds are exhausted • Effectiveness & efficiency of the marketing campaigns have not been determined
Guatemala National	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Folic acid fortification of wheat flour mandated by law • Legal minimum fortificant level established • Regulations for packaging & 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Procurement of fortificant & other necessary materials done by the wheat flour millers • Fortification cost is incorporated to the fortified 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • All millers have their own QC/QA system that includes monitoring of the fortification process 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Program supervisory manuals were developed & updated by INCAP, but the extent of use of this supervisory manual is uncertain 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • INCAP's laboratory has the capacity to analyze folic acid content in the fortified products, and has supported M & E activities 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • No IEC activities are necessary because the program is compulsory, and the consumers do not have influence over the quality of the

Country Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity Quality Control & Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
	<p>labeling standards are established</p> <ul style="list-style-type: none"> • Multisectoral food fortification committee (CONAFOR) established and have played active role in program implementation • Wheat flour production is centralized & industry is well developed • Compliance is high despite minimal inspection by the government <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Current high price of wheat has pressed government to reduce costs, and fortification may be considered as an “unnecessary” expense (product price	<p><u>Limitations</u></p> <ul style="list-style-type: none"> • Although QC/QA systems are in place at all millers, QC/QA information is not readily available / accessible • Folic acid level is not regularly monitored 	<p><u>Limitation</u></p> <ul style="list-style-type: none"> • Government has not carried out inspections at the factory level as frequently as desirable • No formal inspection of fortified product at the retail level 	<ul style="list-style-type: none"> • Wheat flour & bread samples have been taken from the market for monitoring purposes • Annual reports of program evaluation are published by CONAFOR, UNICEF and INCAP, usually in a public meeting <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Lack of epidemiological or nutrition surveillance system that would assess the dietary quality and population nutritional status on a regular basis, • Folate status of the population is unknown 	<p>product (they purchase bread and not flour).</p> <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Lack of data showing the benefits of wheat flour fortification, which makes it difficult to convince some government bodies about the importance of the fortification program

References:

1. Ministry of Health of Chile. Personal communication, January, 2008.
2. Hertrampf E, Cortes F, Erickson D, Cayazzo M et al. Consumption of folic acid-fortified bread improves folate status in women of reproductive age. *J Nutr* 2003; 133:3166-9.
3. Hirsch S, Maza P, Barrera G, Gattas V et al. The Chilean flour folic acid fortification program reduces serum homocysteine levels and masks vitamin B-12 deficiency in elderly people. *J Nutr* 2002; 132: 289-91.
4. Lopez-Camelo JS, Orioli IM, Dutra MG, Nazer-Herrera J et al. Reduction of birth prevalence rates of neural tube defects after folic acid fortification in Chile. *Am J Med Genet* 2005; 135A:120-5.
5. Hertrampf E. Personal communication. 2008.
6. Steyn N, Wolmarans P, Nel JH, Bourne LT. National fortification of staple foods can make a significant contribution to micronutrient intake of South African adults. *Public Health Nutr* 2007; 11: 307-13
7. Modjadli SEP, Mamabolo RL. Folate and iron status of South African non-pregnant rural women of childbearing age, before and after fortification of foods. *South Afr J Clin Nutr* 2007; 20: 89-93NTD's
8. Sayed A, Bourne D, Pattinson R, Nixon J, Henderson B. Decline in the prevalence of neural tube defects following folic acid fortification and its cost-benefit in South Africa. *Birth Defects Res. Part A Clin Mol. Terol.* 2008:1-5
9. Ministry of Health of the Republic of South Africa, GAIN, UNICEF. A Reflection of the South African Maize Meal and Wheat Flour Fortification Programme (2004 to 2007). 2008.
10. Dary O. Lessons learned with iron fortification in Central America. *Nutr Rev* 2002;60:S30-S33.
11. CONAFOR, INCAP/OPS, UNICEF. Situación de los Programas de Fortificación de Alimentos. Informes Anuales, Guatemala. Annual reports from 2000 to 2007
12. Imhoff-Kunsch B, Flores R, Dary O, Martorell R. Wheat flour fortification is unlikely to benefit the neediest in Guatemala. *J Nutr* 2007; 137:1017-22.
13. Nguyen P, Grajeda R, Melgar P, Marcinkevage J, Flores R, Martorell R. Weekly may be as efficacious as daily folic acid supplementation in improving folate status and lowering serum homocysteine concentration in Guatemalan women. *J Nutr* 2008;138:1491-98.

8. Foods Fortified with Iron

Iron fortification of many vehicles is common. Reports were assessed from:

- South Africa
- Venezuela
- China

Rigorous evaluations of large-scale iron fortification programs are needed. Reports of program in Venezuela (3-6) have concluded that consumption of maize and wheat flour fortified with ferrous fumarate caused the reduction of anemia prevalence in target groups. These conclusions are weakened by changes in the program at the time of the evaluation and also the absence of a comparison group to allow an assessment of secular trends. The effectiveness trial (7) of NaFeEDTA-fortified soy sauce in China demonstrated reductions in anemia, although the lack of impact on serum ferritins remains puzzling. The monitoring data from sentinel sites presented in the preliminary report of the scaling up phase of the soy sauce fortification program (8) reported impressive reductions in anemia, but without information on secular trends, this impact is difficult to attribute to the program.

Efficacy trials using these foods fortified with the same iron compounds have been found to be efficacious, but some studies have used much larger concentrations of fortificants than would be feasible in programs (equivalent to 60 to 110% EAR), and thus these results need to be interpreted with caution. The additional iron intakes provided in the Venezuelan and Chinese programs were in the range of 25-35% EAR for adult persons) and this is may have limited impacts on the biological indicators associated with iron status.

The absolute lack of impact on iron status in the South African program –which was shown to be efficacious with respect to folic acid- is explained by the very low additional intake of iron (8-11 % EAR for women of reproductive age) of a type that has very low bioavailability (electrolytic iron) in diets rich in iron absorption inhibitors. These factors all contributed to the lack of measurable impact.

Monitoring of the fortification quality of the three programs (Venezuela, China and South Africa) has not been intensive enough to guarantee compliance with the fortification recommendations. Without clear oversight to ensure adequate levels of fortification and study designs that allow at least plausible comparisons to be made, it is difficult to attribute any positive impacts to the fortified foods, rather than, say, secular trends.

Operational components of iron fortification are discussed in the section “Operational Components of Mass-Food Fortification Programs,” starting on page 76.

Table 8. 1. Coverage and impact of iron fortification programs

Country Food Scale Population Year	Provision		Coverage (% HH using <u>fortified</u> product)	Utilization Food Intake (g/d)	Micronutrient Intake (% EAR ²⁴)			Biological Indicators of Impact		
	Food Supply	At Household (HH) level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
South Africa Maize & wheat flour National 44 millions Started in 2003	35 mg/kg electrolytic iron added to maize & wheat flour Vit A, B-1, B-2, niacin, B-6, folic acid, and zinc also added to maize & wheat flour Total amount produced not reported	Maize porridge: 11 mg/kg ¹ White bread: 24 mg/kg ¹ Brown bread: 23 mg/kg ¹	Maize porridge: urban: 63% rural: 95% ^{1 25} White bread: urban: 34% rural: 22% ⁶ Brown bread: urban: 51% rural: 60%	Maize porridge: urban: 771 rural: 906 ¹ White bread: urban: 165 rural: 154 ¹ Brown bread: urban: 157 rural: 172 ¹	Men urban: 15 mg/d = 60% ⁶ Men rural: 12. 5 mg/d = 50% ⁶ Women urban: 8.5 mg/d = 32% ⁶ Women rural: 9.0 mg/d = 34% ⁶	Men urban: 6 mg/d = 15% ¹ Men rural: 16 mg/d = 43% ¹ Women urban: 3 mg/d = 8% ¹ Women rural: 4 mg/d = 11% ¹	Men urban: 75% ¹ Men rural: 93% ¹ Women urban: 40% ¹ Women rural: 55% ¹		Women rural ²⁶ : Change in mean serum ferritin (SF) level: 35 → 30 µg/L ² Change in low SF (< 12.0 µg/L) prevalence: 25% → 25% ²	Women rural : Change in mean Hb level: 13.5 → 14.0 g/dL ² ; Mean hematocrit (HCT): 39.9 → 41.7 % ² . Change in anemia (Hb < 11 g/dL) prevalence: 7.5% → 5.0% ² ; Low HCT (< 35%) prevalence: 7.5% → 8.8% ²
Venezuela Pre-cooked maize flour & wheat flour National 27 millions Started in 1993	From 1994: 30 mg/kg ferrous fumarate + 20 mg/kg electrolytic iron ²⁷ added to maize flour 20 mg/kg ferrous fumarate added to wheat flour ^{3,4} Total amount produced not reported		In 2001: Maize flour: National: 88% ⁶ Wheat flour: National: 77% ⁶	Maize flour: General: 80 g/day Low SES: 110 g/day ⁵ Wheat flour: 44 g/d as bread, and 30 g/d as pasta ³	Children 7-15 y of low SES of Caracas: Poor (38%): 14 mg/d = 65% in 1992 ³ Very poor (42%): 12 mg/d = 56% in 1992 ³	Children 7-15 y of low SES of Caracas: Poor: 5.5 mg/d = 25% in 1994 ³ Very poor: 6.0 mg/d = 28% in 1994 ³	Children 7-15 y of low SES of Caracas: Poor: 19.5 mg/d = 90% in 1994 ³ Very poor: 18.0 mg/d = 84% in 1994 ³	-	Children 7-15 y in Caracas: Change in mean SF: 15 → 22 µg/L (⁹² to ⁹⁴) ³ , and remained constant thereafter. Change in low SF (< 12.0 µg/L) prevalence: 37% → 16% (⁹² → ⁹⁴) ³ and then constant.	Children 7-15 y in Caracas: Change in anemia (Hb < 11-13 g/dL) prevalence ²⁸ : <u>19%</u> → 9% (⁹² to ⁹⁴) ³ , but increased to <u>17%</u> in subsequent years ⁴
China	NaFeEDTA added to soy	230 mg Fe/L ²⁹ as NaFeEDTA ⁶	High coverage in the	Average daily consumption of	Children 3-6 y <u>15.5 mg/d</u> =	Children 3-6 y ³⁰	Children 3-6 y 381%		After 1 year:	After 1 year:

²⁴ Using EAR values for a diet low for iron absorption, 5%: children 1-6 y = 5.1; 7-9 y = 7.3; females 10-18 y = 34.2; females 19-50 y = 26.5; males 10-18 y = 25.0; males 19-59 = 20.6 mg/day. EAR values for electrolytic iron and reduced iron are 1.5 and 2.0 times higher. EAR values for NaFeEDTA are 2 times smaller.

²⁵ These percents are the users of the food only. It is estimated that only 70% of maize flour and 90% of wheat flour are fortified in South Africa⁹.

²⁶ This is a small study carried out in the Capricorn district of the Limpopo province.

²⁷ Maize flour also contains vitamin A, B-1, B-2 and niacin; wheat flour is enriched with the same micronutrients, except for vitamin A. Before 1994, the only iron source for fortification was ferrous fumarate.

²⁸ 11.5 g/dL for 7 y, 12 g/dL for 11 and 15 y old females, 12.5 g/dL for 11 y males, and 13.0 g/dL for 15 y males.

²⁹ The paper report this iron content based on the actual analysis of the soy sauce, although for the abstract and the discussion the theoretical amount of 296 mg/L is used.

Country Food Scale Population Year	Provision		Coverage (% HH using <u>fortified</u> product)	Utilization Food Intake (g/d)	Micronutrient Intake (% EAR ²⁴)			Biological Indicators of Impact		
	Food Supply	At Household (HH) level			Baseline	Additional	Total	Primary (Linked to intake)	Secondary (Metabolic biomarker)	Tertiary (Clinical or Functional)
<p>Soy sauce</p> <p>2000-2003 Effectiveness trial⁷</p> <p>2003-2007: First attempt to implement a large-scale program in 7 Provinces. Monitoring data⁸</p> <p>Plan is to cover 50 million people out of a total of 425 million (12%) in 8-12 provinces.</p>	<p>sauce⁷</p> <p>The plan is to produce 48,000 MT of soy sauce in 2008⁸; assuming that each person consumes 10 mL/d, this amount will cover 13.2 million persons</p>	<p>effectiveness study.</p> <p>Potential for the nation: 80% of the population consume soy sauce⁸</p>	<p>fortified soy sauce in study: 16.4 mL⁷</p> <p>Estimated for country: Urban: 10.6 mL./day⁸ Rural: 8.9 mL./day⁸</p>	<p><u>304%</u>⁷</p> <p>Adult Women 30.0 mg/d = 89%⁷</p> <p>Adult Men 25.5 mg/d = 124%⁷</p>	<p>1.9 mg/d = 77%</p> <p>Adult Women 2.9 mg/d = 22%</p> <p>Adult Men 3.8 mg/d = 37%</p>	<p>Adult Women 111%</p> <p>Adult Men 161%</p>		<p>Women Change in mean SF: 3 → 5 µg/L⁷</p> <p>Men Change in mean SF: 6 → 13 µg/L⁷</p>	<p>Children 3- 6 y Change in mean Hb: 11.1 → 12.1 g/dL Change in anemia prevalence: <11 g/dL 50.8% → 8.6%⁷</p> <p>Women: Change in mean Hb: 11.7 → 12.4 g/dL Change in anemia prevalence: <12g/dL 61.5% → 13.3%⁷</p> <p>Men: Change in mean Hb: 13.3 → 14.5 g/dL Change in anemia prevalence: <13 g/dL 36.8% → 7.7%⁷</p>	

³⁰ The population mean of the additional iron intake from fortified soy sauce was considered as the median of adult males. That value was multiplied by **0.53** to estimate the additional intake of children 3-6 y, and by **0.79** to estimate the additional intake of adult women, based on the proportional daily energy requirements, and using adult males as the reference unit.

Table 8.2. Data quality for coverage and impact of iron fortification of food

Country Food Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors
<p>South Africa</p> <p>Maize flour & wheat flour</p> <p>National</p>	<ul style="list-style-type: none"> • Dietary intake data: Secondary data analysis of small independent surveys • Biochemical data: collected from rural areas of the Limpopo Province 	<ul style="list-style-type: none"> • Lack of biological impact in women may be explained by the low additional intake of iron (in terms of %EAR) & the low prevalence of anemia 	<ul style="list-style-type: none"> • National changes in hematological parameters associated to iron status, as well as the additional intake of iron, both at the national level have not been determined. 	<ul style="list-style-type: none"> • No bias in the biological study, but extrapolation of the results to the rest of the country is not justified. • Dietary data and food composition information deserves additional studies 	<ul style="list-style-type: none"> • No evidence to evaluate dose-response relationship • Increment in iron intake was too low for women 	<ul style="list-style-type: none"> • Many other factors have likely influenced the hematological indicators of iron status
<p>Venezuela</p> <p>Pre-cooked maize flour & wheat flour</p> <p>National</p>	<ul style="list-style-type: none"> • Survey done in children 7, 11, and 15 y of low socioeconomic strata of Caracas 	<ul style="list-style-type: none"> • Impact results are controversial: It is difficult to understand why SF and Hb increased only one year after introduction of fortification (1993-94), but baseline levels returned in the subsequent years. 	<ul style="list-style-type: none"> • Information at the national level is lacking or not available. 	<ul style="list-style-type: none"> • Interpretation of the results seems to be biased to show that the intervention has a positive impact. • No information about real content of micronutrients in the foods consumed by the population. • Studied population (7 to 15 y) very heterogeneous regarding the iron requirements, and data was not presented for the different age groups. 	<ul style="list-style-type: none"> • Inconsistencies in anemia prevalence & serum ferritin level after 1994: anemia prevalence increased while serum ferritin level remained adequate (However, it is important to note that the change of 40% of the iron source from ferrous fumarate to electrolytic iron took place in 1994) • No evidence to evaluate dose-response relationship 	<ul style="list-style-type: none"> • Maize flour also contains vitamin A which could affect Hb levels; Vit A status has not been measured • Increase in anemia prevalence after 1994 despite the adequate serum ferritin levels indicate that other nutritional deficiencies or factors which have not been identified were causing anemia • Many other factors have likely influenced the hematological indicators of iron status
<p>China</p> <p>Soy sauce</p>	<ul style="list-style-type: none"> • NaFeEDTA provided in soy sauce in a large effectiveness 	<ul style="list-style-type: none"> • Small increase in iron intake from a good bioavailable source 	<ul style="list-style-type: none"> • Data of the effectiveness study is acceptable, but results 	<ul style="list-style-type: none"> • Results of the study should be confirmed in other places and 	<ul style="list-style-type: none"> • Data show a positive impact of NaFeEDTA fortified soy 	<p>Surprising that serum ferritin levels remained very low in all</p>

Country Food Scale	Type of Data	Results and Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias / Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors
<p>Effectiveness trial⁷</p> <p>Scale up in 7 provinces</p>	<p>study conducted in 14,000 persons</p>	<p>(NaFeEDTA) might explain reduction of anemia prevalence because the studied population had hemoglobin levels very near to normal; serum ferritin levels remained very low.</p>	<p>for the implementing program are lacking.</p> <ul style="list-style-type: none"> • Formal independent evaluation is required 	<p>populations, especially because the additional intake of iron would be different in the real program.</p>	<p>sausage in anemia prevalence, but not in the reduction of iron deficiency, which seems to be large.</p> <ul style="list-style-type: none"> • No evidence to evaluate dose-response relationship 	<p>gender and age groups, while anemia was largely corrected through the iron fortification program</p> <ul style="list-style-type: none"> • Consumption of soy sauce is 65% and 50% in urban and rural areas, respectively, of the amounts used in the effectiveness study. It means that the supply of additional iron for the population at large, if fortified at the same level as in the study, would be half than the amount supplied in the study.

Table 8.3. Summary description of the key implementation components of iron fortification programs

Country Food Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
<p>South Africa</p> <p>Maize & wheat flour</p> <p>National</p>	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Micronutrient fortification of all (including imported) maize meal & wheat flour mandated by law • Legal fortificant level established, as well as regulations for packaging & labeling • Strong political commitment & program support: DoH is leading the initiative • Multisectoral National Fortification Alliance (NFA) established for program implementation • Efforts were made to engage both large & small millers from early stage of the program, with plans to subsidize operations of the latter <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Government bureaucracy & lack of resources have hindered enforcement • Small millers have perceived legislation as a way to force them out of the market • Industry frequently refuse to attend the NFA meetings 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Minimal increase in flour cost due to fortification <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Inadequate handling & storage of fortified products by small retailers: results in nutrient loss • Large variations in stability, quality & cost of the micronutrient fortification mix: some millers choose a fortification mix which is of low quality, less stable, & cheaper • Difficult to engage small maize millers, which produce about 20% of the national demand 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Large industries have the necessary equipment to comply with the fortification process <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Training of the millers relatively ignored • Quality & strictness of the QC/QA system of the industry is uncertain • Limited communication with the premix manufacturers; Premix quality has not been strictly controlled • Some of the small mills are located in remote rural areas or have seasonal operations: hard to reach & monitor • Currently no standards for fortification mix quality • Retailers not trained on how to store / handle fortified flour products: results in inadequate handling & storage 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Provide National framework for training all enforcement agents • EHPs take samples from the mill & monitor their compliance with legislation • Efforts are being made to make the South African Bureau of Standards (SABS) responsible for testing fortification mix manufacturers/suppliers <p><u>Limitation</u></p> <ul style="list-style-type: none"> • EHPs overstretched with other responsibilities: excessive demands already placed on EHP's daily duties • EHPs lack resources & proper equipment to take samples adequately • Inability of the national government to control local units • Government laboratories are overstretched & overburdened: delays in sample analysis process 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Comprehensive dietary surveys & biochemical assessments conducted at baseline • Existence of several research institutions that are interested in program M & E <p><u>Limitation</u></p> <ul style="list-style-type: none"> • Performance of the program and its outcomes have not been monitored and evaluated at the national level • Adult food intake was not assessed at baseline • A comprehensive M&E plan has neither been designed nor implemented; most efforts in this matter have only garnered academic interest 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Funds are allocated to social marketing & communication activities • Mass media campaigns were conducted to sensitize consumers about the prevalence & consequences of micronutrient deficiencies & benefits of consuming fortified foods • Mass media campaigns focused on low to middle SES groups <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Sustainability of social-marketing campaigns is uncertain when the external funds are exhausted • Effectiveness & efficiency of the marketing campaigns have not been determined
<p>Venezuela</p> <p>Pre-cooked maize flour and wheat flour</p>	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Fortification of all wheat and precooked maize flour mandated by law 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Centralized industry: 13 maize mills, and 12 wheat flour mills • Minimal increase in price due 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Flour industry is well developed and centralized 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • At the industry level, surveillance and quality control of premix is being conducted 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Interest of researchers to lead in the design, implementation and evaluation of the program 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • At the beginning, open & continuous debate & publicity in the mass media generated

Country Food Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
National	<ul style="list-style-type: none"> • Legal fortificant level established • Started with strong political support due to an enthusiastic initiative among the local nutrition researchers • Strong support & participation of the industry • Multisectoral Commission for the Nutritional Enrichment of Foods (CENA) , under the President's office, was established as leading advocate for fortification⁴ <p><u>Limitations</u></p> <ul style="list-style-type: none"> • No information on regulations for packaging or labeling standards • Recently there have been discrepancies between the central government and the nutrition research community regarding information on nutritional status 	<p>to fortification (an increase of <1% over the actual price)</p> <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Technical problems: darkening of arepas (corn-based bread) in certain regions, which led to a reduction in fortificant level from 50 to 30 mg/kg of ferrous fumarate • At the beginning it was difficult to obtain homogeneity of the fortificants in the premix & final product 	<p><u>Limitations</u></p> <ul style="list-style-type: none"> • No information on capacity building of producers & enforcement agents • Quality and strictness of the QC/QA procedures of the flour industry is uncertain 	<ul style="list-style-type: none"> • Department of Food Hygiene is responsible for enforcement; Iron content is checked by the National Nutrition Institute (NIN) for compliance • The NIH & NIN collects random samples of commercial flour packages every 2 months from food stores and analyze for iron levels: results are presented as public information <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Difficulty in obtaining funds for strengthening enforcement of the regulations • Type of iron fortificant in the premix or fortified foods is not checked and the content/quality of vitamins that are added to flours are not being assessed 	<p><u>Limitations</u></p> <ul style="list-style-type: none"> • Limited resources for program evaluation: explains why analysis was done only for children 7, 11, 15 y in Caracas • Lack of formal M & E plans • Type and quality of fortificants not confirmed 	<p>support for the program & helped to dissipate opposition</p> <p><u>Limitations</u></p> <ul style="list-style-type: none"> • No campaigns or programs to inform the public of the risk of micronutrient deficiencies and that the flours were fortified
<p>China</p> <p>Soy sauce</p> <p>Plan is to cover 50 million persons out of a total of 425 million (12%) in 8-12 provinces⁸</p>	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Chinese MOH approved NaFeEDTA as a fortificant & has provided strong program support • MOH urged provincial health authorities to support the iron-fortified (IF) soy sauce project • Food Fortification Office 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Advocates of the program claim that factories of soy sauce are increasingly being consolidated in a few large industries because competition in the market does not favor permanence of small producers. This new situation would 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • FFO, CCLIA, & the Health supervision department (HSD) of the MOH are sponsoring training programs for the designated soy sauce producers on fortification technology & fortificant level testing capacity • Designated producers are 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Soy sauce producers have to be certified by the China CDC to participate in the program • “IF soy sauce” logo was developed by FFO & CCLIA: can only be used by the certified producers • Authorization to use the logo 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Surveillance on local nutrition condition has been operating at 21 sites from the start of the program <p><u>Limitations:</u></p> <ul style="list-style-type: none"> • Additional iron intake level 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Intensive mass media campaigns on IDA & benefits of IF soy sauce were conducted • Community based education on the benefits of IF soy sauce was conducted by village doctors • Educational programs

Country Food Scale	Policy & Legislation Political Support Public-Private Partnership	Production Importation Supply of Fortificant	Industry Capacity & Quality Control and Assurance	Governmental Food Enforcement Actions	Program M&E	Information, Education & Communications
	<p>(FFO) was established by the China CDC to coordinate & collaborate with multiple public sectors</p> <ul style="list-style-type: none"> • Close collaboration with Chinese Condiment Industrial Association (CCIA) <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Resistance of some large soy sauce producers to participate in the program due to low business profit; some still think that fortification is not a good idea 	<p>facilitate introduction of the fortification process as well as its control.</p> <p><u>Limitations</u></p> <ul style="list-style-type: none"> • Currently, more than 2000 producers across the country produce 5 million MT of soy sauce to meet the national demand⁸ • Program goal for the next three years is to cover 50 million persons. Thus, 182,500 MT/y of soy sauce needs to be produced, assuming a per capita intake of 10 mL/d. However, the current plan is to produce 48,000 MT/y, which is only 26% of this objective 	<p>trained on the health benefits of IF soy sauce</p> <ul style="list-style-type: none"> • All designated producers are requested to have HACCP & other quality assurance systems in place • By April 2007, 20 enterprises out of 73 applicants had been authorized to produce IF soy sauce <p><u>Limitations:</u></p> <ul style="list-style-type: none"> • Covering the whole country may be slow, because there are too many producers (~2000) • Project may remain as a voluntary-based fortification driven by manufacturers that are trying to attract consumers with an enhanced nutritional value of their product 	<p>have to be renewed every year</p> <ul style="list-style-type: none"> • FFO will monitor fortificant level by having certified producers send soy sauce samples every 6 mo • Government agencies take soy sauce samples from producers periodically to monitor fortificant level; test results are announced publicly <p><u>Limitations:</u></p> <ul style="list-style-type: none"> • Permanent enforcement is challenging, especially because popular products are easily faked⁸ • Rural communities usually buy unbranded products because they are cheaper 	<p>provided by the program would be lower than that found to be efficacious in the effectiveness study. This is because the usual soy sauce intake is lower than the level reported in the effectiveness study (9-11 vs. 16.4 ml/d)</p>	<p>promoting IF soy sauce were integrated into various cultural festivals & events</p> <ul style="list-style-type: none"> • IEC materials were developed by local CDCs to help effective nutrition education • Social marketing & Community mobilization strategies were developed/implemented in program areas • FFO has worked with retailers to promote IF soy sauce in 400 stores • Village doctors & workers who conduct community-based education are trained by the local CDC <p><u>Limitations:</u></p> <ul style="list-style-type: none"> • Costly to keep as a governmental function • Urban consumers mistrust health claims of many products⁸

References:

1. Steyn N, Wolmarans P, Nel JH, Bourne LT. National fortification of staple foods can make a significant contribution to micronutrient intake of South African adults. *Public Health Nutr* 2007; 11: 307-13.
2. Modjadli SEP, Mamabolo RL. Folate and iron status of South African non-pregnant rural women of childbearing age, before and after fortification of foods. *South Afr J Clin Nutr* 2007; 20: 89-93.
3. Layrisse M, Chavez JF, Mendez-Castellano H, Bosch V et al. Early response to the effect of iron fortification in the Venezuelan population. *Am J Clin Nutr* 1996; 64: 903-7.
4. Layrisse M, Garcia-Casal MN, Mendez-Castellano H, Jimenez M et al. Impact of fortification of flours with iron to reduce the prevalence of anemia and iron deficiency among schoolchildren in Caracas, Venezuela: A follow-up. *Food Nutr Bull* 2002; 23: 384-9
5. Garcia-Casal MN, Layrisse M. Iron fortification of flours in Venezuela. *Nutr Rev* 2002; 60: S26-9.
6. Scrimshaw N, Guzman M, Layrisse M, Mendez-Castellano H, Chavez JF, Garcia-Casal MT. *Success of the Micronutrient Fortification of Cereal Flours in Venezuela*. Report of the Micronutrient Initiative, 2001.
7. Chen J, Zhao X, Zhang X et al. Studies on the effectiveness of NaFeEDTA-fortified soy sauce in controlling iron deficiency: A population-based intervention trial. *Food Nutr Bull* 2005; 26:177 – 89.
8. Two Wheels Turning (A): Partnership in China's soy sauce fortification program. Part of the World Bank Institute/GAIN business innovation to combat malnutrition series. Unpublished
9. Two Wheels Turning (B): Partnership in China's soy sauce fortification program. Part of the World Bank Institute/GAIN business innovation to combat malnutrition series. Unpublished
10. Sadighi J, Sheikholeslam R, Mohammad K, Pouraram H et al. Flour fortification with iron: a mid-term evaluation. *Public Health* 2008; 122:313-21.

9. Operational Components of Mass-Food Fortification Programs

All fortification programs have specific operational components that contribute to their success, or which present difficulties for implementation. The operational components that were examined for the country fortification programs were:

- Policy and legislation; political support; and public-private partnerships
- Production, importation and supply of fortificant
- Industry capacity and quality control and assurance
- Government food enforcement actions
- Program monitoring and evaluation
- Information, education and communication

A common feature of all the reviewed mass-fortification programs is the expressed strong political support at the moment of their introduction. However, it is interesting to note that following introduction, governments do not necessarily sustain the same level of enthusiasm for these programs. A Guatemalan government tried to abolish the requirement of fortification for sugar in order to allow importation of unfortified products, and the Venezuelan government has placed in doubt that the nutritional situation has been deteriorating in recent years. During these periods, attention to and enforcement of fortification programs has declined.

Legislation, regulations and standards are all critical components of fortification programs. Invariable, these legal instruments were enacted due to the advocacy efforts of research institutions and scientists in public health nutrition. In some cases, these policy tools have been introduced without the participation of the food industry (sugar in Guatemala in 1974, wheat flour in Chile in 1953 and modified in 2000). More recently, the coordination between the public and private sectors is being recognized as necessary for the good performance of the programs.

Except for some salt iodization programs, the fortification programs reviewed had industry purchase the fortificant directly and have transferred the cost of the fortification process to the price of the product. Elimination of import tariffs and taxes has helped to reduce the cost, but this has not been essential to start all programs. When fortification is done by large centralized formal factories, the fortification process is easily implemented, and the fortified products can reach the market in a short period of time. When smaller producers are involved, success is limited, difficult and slower. In South Africa, where small flour (maize) producers supply 20% of the market, the situation remains unclear even after 5 years of initiation, and recently the government has offered to subsidize some of the costs of the program in order to motivate the small producers.

Even for large and formal industries, the introduction of quality control and assurance practices has been difficult. The food industries are adding the fortificants, but the care in the process may still be unsatisfactory. Improvements in these processes have taken place when governments have implemented enforcement actions, as happened in the sugar fortification program in Guatemala, and the wheat flour fortification program in metropolitan area of Chile. In summary, although fortification is taken place in all the cited countries, the quality of the process and the products may still be suboptimal.

In addition to the usually weak government enforcement, the other limiting factor that affects most programs is monitoring and evaluation. M&E have been done by the special interest of researchers in public health nutrition, but in general there are not official and permanent systems of M&E. There are some exceptions. Salt iodization programs may have established quality assurance and household monitoring. Guatemala has maintained (independently from the central government, and sponsored by UNICEF and INCAP/PAHO) a surveillance system that assesses the penetration and quality of the fortified foods at the community level (through rural public schools) since 1995, but this system has not been accompanied by determination of biomarkers or assessment of the additional intake. Similarly, in Nicaragua, there is an integrated surveillance system (supported by international partners) for nutrition interventions (SIVIN), which takes food and human samples to test for quality and biological impact, respectively. In this case also, the additional micronutrient intake from the fortified product is not assessed.

Finally, the component of information, education and communication is seen as useful but not essential in mass-food fortification programs, mainly because most of these are compulsory and the consumer thus has little choice. Nevertheless, IEC activities have increased the awareness and appreciation for these programs, and they remain despite loss of attention by temporal central governments. In any case, IEC should be carefully designed and follow clear objectives, because often the need is to avoid opposition rather than promote consumption of certain foods (for example salt and sugar, for which intake should be kept low). It looks like the IEC activities should be regulated too with the purpose of avoiding excessive and misleading messages.

Conclusions

1. Efficacious food fortification programs are those that replicate the successful conditions of efficacy trials; i.e. a) providing sufficient additional intake of a specific micronutrient; b) filling the nutritional gap; and c) addressing the need of the population. Examples of these programs are salt iodization in many countries, sugar fortified with vitamin A in Guatemala and Nicaragua, and flour fortified with folic acid in Chile and South Africa.
2. Unlike salt iodization, the other mass-fortification programs are not simultaneously efficacious and safe for all individuals of the population, and thus they should be carefully monitored and complemented with other nutritional programs.
3. Though mass-fortification programs may be partial solutions for a proportion of the target population, they still make an important contribution to the prevention and reduction of micronutrient deficiencies. The magnitude of their biological impact varies and depends on the particular nutritional needs and the food habits of each country and social group. Unlike salt iodization, there are not universal specifications that can be applied to the other mass-fortification programs.
4. In the absence of information about the overall diet, it is practical to assume that biological biomarkers and functional or clinical signs associated with micronutrient status may experience positive changes if more than 60% EAR or 90% EAR, respectively, are supplied through the fortified foods to 50% or more of the vulnerable population.
5. Thus far, the evidence for successful iron-fortification programs is not convincing. This is an area that deserves serious attention and critical discussion.

6. The key factors for establishing mass-fortification programs have been: (a) triggered and defended by the enthusiasm of institutions and researchers in public health nutrition; (b) supported by legislative instruments (standards, regulations or laws); and (c) implemented by a few centralized and formal factories.
7. Improvements of the industry QC/QA and governmental enforcement are necessary for optimizing the performance of the mass-fortification programs. If these two components are weak, program M&E may provide evidence about progress, and hence M&E contributes to the appreciation and permanence of the programs.
8. M&E has commonly been done through local research institutions or international institutions providing technical assistance. However, it is necessary that this component be adopted as an important responsibility of the national government, and M&E should include assessment of the additional micronutrient intakes.
9. Public-private partnerships and IEC, although not strictly essential for mass-fortification, facilitate program implementation and acceptance, and they are useful for preventing and solving conflicts.
10. The weakest operational components of the current mass-fortification programs are factory QC/QA, governmental enforcement, and especially program M&E. Development of these components should take priority.

10. Complementary Feeding Interventions

The period of complementary feeding, from 6 to 24 months of age, is widely accepted as a “critical window” for the prevention of undernutrition and attainment of optimal growth, health and development (1-3). Stunted growth and delayed mental and motor development in the first two years of life due to poor complementary feeding practices, coupled with frequent infections are often irreversible (4, 5). In many developing countries, complementary foods are usually of inadequate nutrient density as they are extremely diluted and predominantly cereal-based, and are often fed in insufficient quantities. Consequently, growth faltering peaks during this time period and micronutrient deficiencies are common in infants and young children (2).

Several types of interventions aiming to improve the quality and quantity of complementary foods have been tested for efficacies and implemented in large-scale in developing countries. A recent systematic review undertaken by Dewey and Adu-Afarwauh examined the effects of complementary feeding interventions on the growth, morbidity, motor development and micronutrient status of infants and young children (2). Interventions conducted in developing countries were largely categorized into nutrition education, complementary foods providing additional energy, micronutrient fortification of complementary foods, and improving the energy density of complementary foods (2). The evidence from both efficacy and effectiveness trials and large-scale programs was reviewed (2).

Only a few intervention studies reported information on micronutrient intakes, including those of iron, zinc, and vitamin A. The positive impacts on micronutrient intakes were mainly reported from efficacy trials. Overall, nutrition education for mothers increased iron and zinc intakes from complementary foods by 24% and 26%, respectively (2). Provision of centrally processed complementary foods such as fortified cereal/legume blends and milk increased iron, zinc and vitamin A intakes (2). On the other hand, no increase in micronutrient intake was reported from a large-scale milk supplement program in Brazil, primarily due to the intrahousehold sharing of milk, frequent interruptions in milk distribution, and poor maternal compliance (2, 6).

Data on iron, zinc, and vitamin A status were reported from intervention studies providing education for mothers and supplying complementary foods fortified with micronutrients either commercially or through home fortification (2). Most studies reported little improvement in serum zinc concentration due to the low bioavailability of zinc when ingested with cereal-based foods (2). In contrast, serum vitamin A concentration significantly increased and the incidence of vitamin A deficiency decreased on average by 13% in both efficacy studies and large-scale programs providing fortified complementary foods (2).

Maternal educational interventions produced mixed results regarding iron status and anemia prevalence, primarily because of the inconsistencies in key educational messages promoting iron intake (2). Still, educational interventions had an overall impact of 4g/L increase in hemoglobin level and 5% reduction in anemia prevalence (2). Both efficacy studies and large-scale programs providing iron-fortified complementary foods, also reported a positive impact on iron status. There was an overall increase of 4-6g/L in mean hemoglobin and 13-17% reduction in anemia prevalence (2).

Home-based fortification strategies include micronutrient powders, ‘Sprinkles’, crushable tablets called ‘foodlet’ and lipid-based products such as ‘Nutributter’ (2). Dewey and Adu-Afarwauh

reported that home-fortification interventions, as an aggregate, increased mean hemoglobin concentration by 8g/L and reduced anemia prevalence to 21% (2). To date, a few effectiveness trials and large-scale programs of micronutrient Sprinkles have been carried out along with a series of efficacy studies in various locations.

Micronutrient Powders (Sprinkles)

Traditional iron supplementation programs such as the provision of ferrous sulfate syrups to infants and young children have faced challenges with compliance and supply, leading many to consider them ineffective as a long-term strategy to control iron deficiency anemia (IDA). A new strategy for addressing IDA in infants and young children using micronutrient Sprinkles was developed by the research team at the Hospital for Sick Children and the University of Toronto in Canada (7). Sprinkles are encapsulated micronutrients in powder form that are packaged in single-dose sachets and can be added directly to any semi-solid complementary foods prepared in the household (7). Iron and other essential micronutrients such as zinc, iodine, vitamins A, C, and D may be added to Sprinkles sachets (7). A number of efficacy studies conducted in different parts of the world have consistently demonstrated that Sprinkles are as efficacious as iron drops in treating and preventing anemia when added to complementary foods (7-12). It was noted that 12.5 mg of iron provided as Sprinkles for 2 months was adequate for anemia control (7).

The effectiveness of providing 2-months of Sprinkles in reducing anemia among children 6-24 months of age was evaluated in rural Haiti (Table 1) (13). Sprinkles were distributed free of charge in the maternal and child health and nutrition program (MCHN) distributing monthly take-home rations of a fortified wheat soy blend (WSB). Education for mothers on the benefits and appropriate use of Sprinkles was provided (Table 1). Anemia prevalence decreased from 52% to 28% among infants receiving Sprinkles along with WSB, while increased from 37% to 45% among those receiving WSB only (Table 2). When children were revisited after 9 months, anemia prevalence was further reduced to 16% in the Sprinkles group (14). Compliance was high such that 96% of the sachets distributed were consumed and Sprinkles were well accepted by the children (Table 2). Overall, it was concluded that Sprinkles provided for 2 months were effective in reducing anemia in populations with high anemia prevalence and that it was feasible to distribute Sprinkles along with WSB through the MCHN program (7, 13, 14).

Effectiveness trials conducted in Bangladesh, Benin and Vietnam also documented a positive impact of Sprinkles on anemia control (7). In Benin, the prevalence of anemia and IDA decreased by 38% and 28%, respectively, after distributing Sprinkles for 6-months (7). In Vietnam, the cure rate of anemia was 96% after providing Sprinkles for 6 months (7).

The first large-scale implementation and evaluation of Sprinkles was done through the Integrated Nutrition Program (INP) in Mongolia carried out by the World Vision and Mongolian Ministry of Health (MOH) (Table 1) (15). The INP aimed to prevent and treat anemia and rickets among children <5 years of age by improving maternal and child iron and vitamin D status. Sprinkles containing iron, vitamin D and other micronutrients were distributed free of charge to more than 15,000 children 6-35 months of age, along with a maternal iron-folic acid and vitamin D supplementation (Table 1) (15). The Sprinkles distribution achieved a high coverage rate of 89%. The average duration of children taking Sprinkles was 13 months and 88% of households reported using Sprinkles on a daily basis (Table 2) (15). Anemia prevalence in children aged 6-59 months of age fell from 46% to 25% after 26 months of Sprinkles intervention. The prevalence of stunting also

significantly decreased from 23% to 18%. Moreover, 87% of mothers who gave Sprinkles to their children were willing to continue using the product (Table 2) (15).

The high coverage and compliance is attributable to the effective distribution system of Sprinkles and intensive social marketing activities (Table 1) (15). Sprinkles were distributed each month to beneficiaries in their home by the community nutrition workers who were highly efficient in reaching the widely dispersed target population. Social marketing campaigns and community-based education improved the compliance and acceptability of Sprinkles by increasing public awareness and knowledge on nutrition. In addition, there was strong political support for the Sprinkles intervention, which likely facilitated the program implementation (Table 1) (15).

On the other hand, the prevalence of rickets in children 6-59 months of age did not change after 26 months of Sprinkles intervention (Table 2) (15). This was mainly attributed to the low vitamin D content (400 IU) of Sprinkles relative to the high demands for vitamin D among Mongolian infants and young children who have limited sun exposure (15). Poor maternal vitamin D status due to the low coverage of maternal vitamin D supplementation in conjunction with the cultural practice of swaddling infants may also explain the lack of positive impact on rickets (15). There was no true comparison group in the program evaluation, as those who were initially selected as a control group received energy bars containing iron which were distributed in response to a natural disaster (15). Given that anemia prevalence also declined in the comparison group and in pregnant and lactating women, a secular trend of anemia prevalence reduction can not be ruled out.

Sprinkles have also been successfully used in an emergency setting in Indonesia (16). More than 28 million sachets were distributed to caregivers of 200,000 infants and children aged 6 months to 12 years who were affected by the tsunami and earthquake. A high coverage rate of 90% was achieved in almost all program districts within 5 months of the program (16). Anemia prevalence was 25% less among the Sprinkles recipients.

Taken as an aggregate, both efficacy and effectiveness trials have suggested that Sprinkles can be a promising strategy for the prevention and treatment of anemia among infants and young children in developing countries where anemia prevalence is high. It has been shown that the use of Sprinkles is cost-effective, reduces anemia rates, and does not affect the taste and color of the complementary food to which it is added and has a high acceptability among caregivers. To date, however, few large-scale programs distributing Sprinkles at a countrywide level have been carried out. Efforts need to be made to strengthen the scale-up process which involves advocacy, acquirement of necessary funding, development of an effective social marketing strategy and the identification of sustainable distribution systems which allow the provision of Sprinkles to the most vulnerable populations (7). Strong advocacy is also needed to promote the adoption of Sprinkles in nutrition policies in underdeveloped countries (7).

Table 10.1. Summary description of the key implementation components of Sprinkles Programs

Country	Program Description	Policy Political Support	Logistics	Health Worker Training	BCC & Mother's Awareness
Mongolia (15)	<ul style="list-style-type: none"> The first large-scale implementation & evaluation of Sprinkles in the context of an integrated nutrition program Integrated Nutrition Program (NP) <ul style="list-style-type: none"> designed & implemented by World Vision (WV) & Mongolian Ministry of Health (MOH) to prevent and treat anemia & rickets among children <5 y of age by improving maternal & child iron & vitamin D status included home-based fortification “Sprinkles”, supplementation, social marketing, and community nutrition education targeted 14,780 children aged 6-59 mo, 1,250 pregnant & 4,370 lactating women (7% of Mongolia’s total population) carried out in 9 of the 28 Area Development Programs (ADP) covering 4 provinces Sprinkles <ul style="list-style-type: none"> distributed free of charge by community nutrition workers (NW) to children aged 6-35 mo from 2001-2003 carried out in parallel with other activities: iron & vitamin D supplementation to anemic & vitamin D deficient children (3-5 y) & all pregnant / lactating women; promoting exclusive breastfeeding for 6 mo & intake of iron-rich foods; increased sun exposure, etc 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Good political support: <ul style="list-style-type: none"> Government partners (MOH, Public Health Institute, Nutrition Research Center (NRC)) were involved from the inception of the NP 1997 nutrition survey of iron & vitamin D deficiency prompted the development of NP: survey was implemented by NRC with WV’s support WV engaged in an extensive process to satisfy the Government of the Sprinkle’s safety MOH approved its import and enthusiastically supported its use Strong MOH champions No political opposition <p><u>Limitations</u></p> <ul style="list-style-type: none"> Lack of nutrition policy; Nutrition (particularly micronutrients) had low priority in Mongolian MOH 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Supply was well coordinated: procurement done by WV national office staff Effective distribution system established (i.e., WV national office → health facilitators → NW) The NWs distributed Sprinkles to beneficiaries in their homes on a monthly basis: showed flexibility and resourcefulness in delivering Sprinkles to widely dispersed target population <p><u>Limitations</u></p> <ul style="list-style-type: none"> Sprinkles had to be imported from Hospital for Sick Children in Toronto, Canada 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Doctors, nurses, and pharmacists were trained on symptoms, prevention, and treatment of anemia & rickets quarterly Quarterly training of Health Facilitators (HF) by WV national office staff & health professionals Quarterly training of NWs by HFs: each training was attended by WV national office staff for supervision & quality control purposes <p><u>Limitations</u></p> <ul style="list-style-type: none"> High WV staff turnover 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Social marketing campaigns to increase public awareness & knowledge on nutritional issues (e.g., using moving billboards, posters in buses, health clinics, pharmacies etc) 12 nutrition education videos were developed & broadcasted nationwide on TV; Shorter radio spots were developed & aired Focus groups with mothers & doctors prior to the start of the NP: to identify ways to optimize the acceptability of Sprinkles A local artist designed the artwork on the package: instructions & ingredients printed in Mongolian; expiration date stamped NWs held monthly community nutrition workshops to pass on health & nutrition message; Periodically supervised by HFs Nutrition & health messages were passed on during home visits for those who did not attend the workshops Education materials were developed & distributed (e.g., eat right booklet)
Haiti (13)	<ul style="list-style-type: none"> Operational research assessing the effectiveness of providing 2-mo of micronutrient Sprinkles in reducing anemia among children 6-24 mo of age in rural Haiti Sprinkles distributed as part of a maternal & child health & nutrition program (MCHN) distributing fortified wheat soy blend (WSB) to children 6-24 mo of age MCHN Program <ul style="list-style-type: none"> implemented by WV Haiti 		<p><u>Strengths</u></p> <ul style="list-style-type: none"> Re-packaging into re-sealable bags that each contained 15 individual sachets: helped efficient & accurate delivery Health & commodities staff responsibilities in the Sprinkles distribution process clearly defined Efficient Sprinkles distribution 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Commodities and health staff trained on the benefits & use of Sprinkles Training materials developed by the research team 	<p><u>Strengths</u></p> <ul style="list-style-type: none"> Educational strategy for the Sprinkles intervention <ul style="list-style-type: none"> mothers trained on the benefits & appropriate use of Sprinkles at the MC before Sprinkles were distributed: group discussion & demonstration reminder session at the FDP

<p>- services provided at 5 contact points: 1) rally posts: health education, growth monitoring, preventive health care; 2) mother's clubs (MC): small group education on health, hygiene, & nutrition; 3) pre- & postnatal consultations; 4) food distribution points (FDP): monthly food rations; 5) home visits</p> <p>- direct food ration included 8 kg of fortified WSB & 2.5 kg of vitamin A fortified oil</p> <ul style="list-style-type: none"> • Sprinkles <p>- distributed free of charge at the FDPs along with food rations to mothers of children aged 6-24 mo</p> <p>- 6 FDPs were randomly assigned to receive Sprinkles & WSB; 4 FDPs only received WSB</p> <p>- Sprinkles intervention included a 2-mo supply of Sprinkles & BCC strategy on the appropriate use of Sprinkles</p>			<p>tracking system at the storage, transport & distribution stages</p>		<p>on the appropriate use of Sprinkles</p> <ul style="list-style-type: none"> - Pictorial instruction card on the appropriate use & dosage distributed along with Sprinkles
--	--	--	--	--	--

Table 10.2. Coverage, compliance, and impact of Sprinkles programs

Country	Sprinkles Nutrient Composition	Coverage	Compliance	Impact	Knowledge Attitude
Mongolia (15)	<ul style="list-style-type: none"> • Vitamins <ul style="list-style-type: none"> Vitamin D – 400 IU Vitamin A – 180 µg† Vitamin C – 50 mg Folic Acid – 150 µg • Minerals <ul style="list-style-type: none"> Iron – 40 mg Zinc – 10 mg 	<ul style="list-style-type: none"> • 89% of all children <5y had tried Sprinkles by the end of the program • One year into distribution, Sprinkles coverage was 84%, but dropped to 44% by the end of the program 	<ul style="list-style-type: none"> • Average duration of children taking the Sprinkles was 13 mo • 88% of children aged 6-35 mo took Sprinkles for four months or longer • 88% of households reported using Sprinkles on a daily basis • However, most children did not start receiving Sprinkles until 13 mo of age 	<ul style="list-style-type: none"> • Prevalence of anemia (Hb<11.5 g/dl) among children aged 6-59 mo decreased from 46% to 25% after 26 mo of intervention • Prevalence of anemia decreased from 55% to 33% among children aged 6-35 mo & from 29% to 13% among children aged 36-59 mo • Prevalence of anemia among children aged 6-18 mo remained >40% after 26 mo of intervention • No change in the prevalence of rickets (from 31% to 30%) in children aged 6-59 mo • Prevalence of stunting decreased significantly from 23% to 18% after 26 mo of intervention; No change in prevalence of underweight & wasting 	<ul style="list-style-type: none"> • Families attributed positive changes such as increased appetite, more activity & alert to Sprinkles • 87% of mothers who gave Sprinkles to their children showed willingness to continue using the product: of these, 97% expressed willingness to go to a distribution center to receive Sprinkles

Haiti (13, 14)	<ul style="list-style-type: none"> • Vitamins Vitamin A – 400 µg Vitamin C – 30 mg Folic Acid – 160 µg • Minerals Iron – 12.5 mg Zinc – 5 mg 	<ul style="list-style-type: none"> • 90% & 95% of children in the Sprinkles (S)-wheat soy blend (WSB) group received Sprinkles in the 1st & 2nd month, respectively 	<ul style="list-style-type: none"> • Of the 60 sachets distributed, a mean of 58 sachets were estimated to be consumed: 96% compliance rate • 62% of mothers reported feeding Sprinkles to their child 7-days a week; 25% reported feeding Sprinkles to their child 4-6 days a week • 95% of mothers reported using an entire sachet of Sprinkles 	<ul style="list-style-type: none"> • Mean Hb level significantly increased from 10.0 to 10.5 g/dl among the S-WSB group after 2-mo, while decreased from 10.2 to 10.0 among the WSB only group • Anemia (Hb<10.0g/dl) prevalence decreased from 52% to 28% among the S-WSB group after 2-mo, while increased from 37% to 45% among the WSB only group • Anemia prevalence further decreased to 16% among the S-WSB group 9 mo after the start of the intervention • Benefits of Sprinkles greater among children <20 mo of age and those who were anemic at baseline • Side-effects including constipation (16% vs. 10%), black stools (64% vs. 20%) and discolored teeth (19% vs. 12%) more common among the S-WSB compared to WSB-only group 	<ul style="list-style-type: none"> • 99.5% of mothers mentioned at least one benefit of using Sprinkles; ~95% mothers correctly reported the appropriate use of Sprinkles • Sprinkles very well accepted by the children
----------------	--	--	--	---	--

† Vitamin A 600 IU: 1 IU = 0.3µg

Table 10.3. Quality of available data on coverage, compliance, and impact of Sprinkles programs

Country	Source of Data	Consistency of Findings Across Studies	Imprecise or Sparse Data	Reporting Bias Overall Data Quality	Internal Consistency / Dose-Response Relationship	Potential Confounding Factors	Other Determinants of Data Quality
Mongolia (15)	<ul style="list-style-type: none"> • Pre & post-intervention household surveys & assessments (e.g., anthropometric, biochemical, clinical) using cross-sectional design 	<ul style="list-style-type: none"> • Baseline prevalence of anemia & rickets similar to that reported in UNICEF/MOH National Child Nutrition Survey • Not enough evidence to evaluate consistency of findings regarding the impact of Sprinkles 	<ul style="list-style-type: none"> • Precise data; Indicator used is a good proxy for coverage, compliance and impact; 	<ul style="list-style-type: none"> • Non-independent data collection: survey team included the Nutrition Research Center (NRC) & family physicians • Data double-entered & cleaned; • Evaluation data from three surveys had to be excluded due to over-diagnosis: significantly 	<ul style="list-style-type: none"> • High coverage, compliance and significant reduction in anemia prevalence among children <5 y of age; However, no change in rickets prevalence • Prevalence of anemia was significantly lower among children aged 6- 	<ul style="list-style-type: none"> • Frequent consumption of iron-rich foods due to nutrition education as part of the NP: 97% of children aged 6-59 mo ate meat at least 4 times a week • Improved maternal iron status partly due to supplementation as part of the NP: prevalence of 	<ul style="list-style-type: none"> • No true comparison group: BP-5 energy bars containing micronutrients (including 40 mg of iron but no vitamin D) were distributed in response to a natural disaster • Samples representative of program beneficiaries but not nationally

				higher diagnosis than others & significantly higher prevalence than at baseline	35 mo who took Sprinkles for ≥ 4 vs. < 4 mo (31% vs. 48%) <ul style="list-style-type: none"> Prevalence of anemia was significantly lower among children aged 6-35 mo who took Sprinkles ≥ 3 vs. < 3 times weekly (31% vs. 52%) 	anemia decreased from 33% to 22% among pregnant women & 11% to 7% among lactating women <ul style="list-style-type: none"> Exclusive breastfeeding to 6 mo doubled from 17% to 43% during the program period Potential secular trend: prevalence of anemia decreased by 44% in comparison area were BP-5 energy bars were distributed Wheat flour fortified with micronutrients including B-vitamins, iron, zinc, folic acid (coverage 48% in the NP area & 61% in comparison area) It is possible that there were other contributing factors to rickets (e.g., insufficient calcium) 	representative <ul style="list-style-type: none"> No baseline data for meat consumption: increase in meat consumption not verifiable As evaluation data from three surveys were excluded, the adjusted sample size for the rickets data was lower than the minimum required
Haiti (13, 14)	<ul style="list-style-type: none"> Pre & post-intervention surveys & assessments (i.e., anthropometric & hemoglobin) 	<ul style="list-style-type: none"> Not enough evidence to evaluate consistency of findings 	<ul style="list-style-type: none"> Precise data; Indicator used is a good proxy for coverage, compliance and impact Low level of missing data (~4%) 	<ul style="list-style-type: none"> Independent data collection Data error rates assumed to be minimal 	<ul style="list-style-type: none"> High coverage, compliance and significant reduction in anemia prevalence among children 6-21 mo of age Little indication of dose-response relationship; likely to be due to the high compliance with Sprinkles 	<ul style="list-style-type: none"> Impact of Sprinkles on anemia prevalence reduction remained consistent in multivariate analyses controlling for potential confounding factors 	<ul style="list-style-type: none"> Comparison group which received only Wheat Soy Blend exist Sample size (SS) for Sprinkles group small (n=254), but larger than the estimated requirement (n=250); SS for comparison group only 161: due to logistical & funding constrains Program evaluation team, field team and study participants were not blinded to the treatment assignments

References

1. World Bank (2005) Repositioning nutrition as central to development: A strategy for large scale action. The World Bank: Washington, DC.
2. Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Matern Child Nutr* 2008; 4: 24-85.
3. PAHO/WHO (2003) Guiding principles for complementary feeding of the breastfed child. Pan American Health Organization/World Health Organization: Washington, DC.
4. Martorell R, Khan LK, Schroeder DG. Reversibility of stunting: epidemiological findings in children from developing countries. *Eur J Clin Nutr* 1994; 48: S45-57.
5. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. *Nutr Rev* 2006; 64: S34-43.
6. Santos IS, Gigante DP, Coitinho DC, Haisma H, Valle NC, Valente G. Evaluation of the impact of a nutritional program for undernourished children in Brazil. *Cad Saude Publica* 2005; 21: 776-85.
7. Zlotkin SH, Tondeur M. Successful approaches: Sprinkles. In Nutritional Anemia. Sight and Life Press, Switzerland, 2007: 270-83.
8. Zlotkin S, Arthur P, Antwi KY, Yeung G. Treatment of anemia with microencapsulated ferrous fumarate plus ascorbic acid supplied as sprinkles to complementary (weaning) foods. *Am J Clin Nutr* 2001; 74: 791-5.
9. Zlotkin S, Antwi KY, Schauer C, Yeung G. Use of microencapsulated iron (II) fumarate sprinkles to prevent recurrence of anaemia in infants and young children at high risk. *Bull World Health Organ* 2003; 81: 108-15.
10. Zlotkin S, Arthur P, Schauer C, Antwi KY, Yeung G, Piekarz A. Home fortification with iron and zinc sprinkles or iron sprinkles along successfully treats anemia in infants and young children. *J Nutr* 2003; 133: 1075-8.
11. Giovannini M, Sala D, Usuelli M, Livio L, Francesacato G, Braga M, Radaelli G, Riva E. Double-blind, placebo-controlled trial comparing effects of supplementation with two different combinations of micronutrients delivered as sprinkles on growth, anemia, and iron deficiency in Cambodian infants. *J Pediatr Gastroenterol Nutr* 2006; 42: 306-12.
12. Hirve S, Bhav S, Bavdekar A, Naik S, Pandit A, Schauer C, Christofides A, Hyder Z, Zlotkin S. Low dose 'Sprinkles' – an innovative approach to treat iron deficiency anemia in infants and young children. *Indian Pediatr* 2007; 44: 91-100.
13. Menon P, Ruel M, Loechl CU, Arimond M, Habicht JP, Pelto G, Michaud L. 2006. The effectiveness and feasibility of using micronutrient sprinkles to reduce anemia among children 6-24 months old in a programmatic context: evidence from Haiti. Report submitted to The Micronutrient Initiative.
14. Menon P, Ruel MT, Loechl CU, Arimond M, Habicht JP, Pelto G, Michaud L. Micronutrient Sprinkles reduce anemia among 9- to 24-mo-old children when delivered through an integrated health and nutrition program in rural Haiti. *J Nutr* 2007; 137: 1023-30.
15. World Vision Mongolia. Effectiveness of home-based fortification of complementary foods with Sprinkles in an integrated nutrition program to address rickets and anemia. 2005.
16. de Pee S, Moench-Pfanner R, Martini E, Zlotkin SH, Darnton-Hill I, Bloem MW. Home fortification in emergency response and transition programming: experiences in Aceh and Nias, Indonesia. *Food Nutr Bull* 2007; 28: 189-97.

11. Breastfeeding

Exclusive breastfeeding through the first six months and continued breastfeeding with appropriate complementary feeding through the first two years of life is critical to child survival, overall health, and development. Both the 2008 Lancet Series and the technical meeting of the Ten Year Strategy group identify interventions promoting breastfeeding among the highest priorities. The importance of strengthening the coverage and impact these programs is highlighted by WHO and UNICEF estimates that only 39% of infants are exclusively breastfed for less than 4 months.

No review of breastfeeding programs was undertaken for the Innocenti Meeting. Breastfeeding is an indirect MN program rather than a direct one, but is acknowledged in this review of direct programs because of its central role in the integrated package of child health programs.

Bhandari et al. (2008)¹ presented a comprehensive review of 15 studies and programs designed to scale up exclusive breastfeeding. They described two key processes required for scaling up exclusive breastfeeding – first, evidenced-based policy and science-driven technical guidelines, and second, an implementation strategy and plan for achieving high and sustainable exclusive breastfeeding rates in all strata of society. Bhandari et al. then summarized overarching and specific lessons drawn from these experiences.

Overarching factors included: political will, strong advocacy, enabling policies, well defined program strategies for both short and long term, adequate financing, clearly defined roles for all stakeholders, and an emphasis on delivery at the community level.

Specific success factors included: effective use of antenatal, birth, and post-natal contacts; ensuring strong intervention design and delivery through formative research, particularly in areas of high HIV prevalence; promoting effective communication materials; quality trainers and training; monitoring and evaluation systems; and legal frameworks that create environments enabling women to exclusively breastfeed.

Reference

1. Bhandari N, Kabir AKMI, Salam, MA. Mainstreaming nutrition into child health programmes: scaling up of exclusive breastfeeding. *Maternal and Child Nutrition* 2008; 4:5-23