Part 3

How can vitamin and mineral deficiencies be reduced?

Implementing proven interventions at scale

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Summary of findings

- The main options for addressing VMDs are food fortification and supplementation. Support of optimal breastfeeding and appropriate complementary feeding are key food-based approaches that support good micronutrient status during the high-risk period of infancy. Broader dietary diversification has not produced significant results at scale, and plant breeding is relatively new. Public health interventions—especially malaria control, control of intestinal parasites, and measles immunization—have helped reduce deficiency diseases.
- Databases on national coverage of programs are inadequate to assess the relative success of interventions in reaching coverage and reducing deficiencies. The notable exceptions are iodized salt and vitamin A supplementation for which evidence of coverage and impact is available. There is some evidence of the success of folic acid supplementation and fortification but no global databases so far. In countries with a high burden of VMDs, there is strong evidence that fortification and supplementation have been effective. Dramatic reductions in national indicators of childhood mortality and the virtual elimination of clinical deficiencies of iodine and vitamin A have proved the effectiveness of these interventions on a large scale in countries as diverse as Nepal, Nicaragua, and Tanzania.
- The number of countries with iodine deficiency as a public health problem declined substantially from 1993 to 2003, although these countries may still have pockets of iodine deficiency requiring targeted attention. Most countries with scaled-up, high-coverage vitamin A supplementation have linked supplementation with routine immunization or immunization campaigns, or both, at least initially. However, several large, high-burden countries have reached coverage of only 50% or less, a level that will probably not produce the expected declines in mortality.
- In high-burden countries, prenatal IFA supplementation is being attempted, but there is little evidence of impacts. Problems include irregular supplies and noncompliance. Folic acid fortification is likely to have been more cost-effective than supplementation in the few countries where it has been implemented and this needs to be evaluated. Iron and the B vitamins fortification of cereal flours and condiments has been implemented in several countries, but the coverage of fortified products is not well documented. Vitamin A–fortified sugar has been successful in Central America; fortified vegetable oil is widely used in food distribution programs and is expanding commercially in Asia, Africa, and Latin America. Zinc supplementation is being launched as part of the control of diarrheal disease (CDD) efforts; in several countries, the supplement is added to premixes for cereal fortification. Supplements and fortified foods have successfully prevented the emergence of VMDs common in emergencies according to the World Food Programme (WFP).
- The available data on the progress of programs do not provide a complete picture. Many more countries than reflected in current databases have achieved good vitamin A supplementation and iodized salt coverage. It is necessary to define the various kinds of programs currently being implemented and to track their progress systematically, beginning with the high-burden regions of South Asia and sub-Saharan Africa.
- Mandatory public-sector-led food fortification and voluntary industry-led fortification have both demonstrated results. The success factors for fortification programs are availability of suitable food vehicles (i.e., centralized processing and widespread regular consumption); adequate food regulations and labeling; public awareness and demand; quality assurance and monitoring to ensure shelf life and adequate levels of micronutrients; compliance; and advocacy based on evidence of positive impact. Building strong public–private partnerships is a critical first step.
- The majority of supplementation efforts targeting high-risk groups are public health programs linked to antenatal care or immunizations. Success factors for supplementation programs are assured supplies,

trained frontline providers, proactive outreach combined with social mobilization, consumer/target group awareness and compliance, listing/registration of eligible women and children, and regular monitoring of coverage.

» Iodized salt and vitamin A supplementation have both achieved scale. The common factors that appear to have helped in scaling up were strong evidence of impact; low-cost, affordable, and streamlined interventions that could be easily adapted to existing delivery channels; advocacy; documented progress in coverage; leadership in support of the intervention programs at the global and country levels; social mobilization and public awareness; and well-coordinated donor support sustained over several years.

Review of evidence

The principal options for delivering micronutrients are food fortification and supplementation*

The feasibility and effectiveness of the available options vary in different settings, even within countries. Countries are combining and adapting various approaches to suit their local contexts. A growing proportion of the population in many countries fulfills its vitamin and mineral needs through diet, including various kinds of fortified foods complemented with supplements. Strategy development to accelerate progress should be based on a good understanding of age and income disaggregated data on deficiencies and dietary deficits as well as patterns of food consumption and supplement use.

Fortification of foods can provide a substantial proportion of the required nutrients without changing food habits

Table 3.1 provides an example of the range of products being fortified in countries of the Africa region. Proper choices of fortificant and processing methods are necessary to ensure the stability and bioavailability of nutrients. The level of fortification should take into account variations in food consumption to ensure safety for those at the higher end of the scale and impact for those at the lower end. Fortification must be supported by adequate food regulations and labeling, quality assurance and monitoring to ensure shelf life and adequate levels of micronutrients, public education, compliance, and desired impact. In industrialized countries, food fortification has played a major role in the substantial reduction and elimination of a number of micronutrient deficiencies.

Starting in the early part of the 20th century, fortification was used to target specific health conditions: goiter with iodized salt; rickets with vitamin D–fortified milk; beriberi, pellagra, and anemia with B vitamins and iron-enriched cereals; and NTDs with folic acid–fortified flour [64]. It has taken more than five decades to expand fortification within developing countries. Constraints have included the lack of appropriate centrally processed food vehicles, less-developed commercial markets and technology, and relatively low consumer awareness and demand. The long-term sustainability of fortification programs is ensured when consumers are willing and able to bear the additional cost of fortified foods.

Lutter identified the importance of specially formulated fortified foods for infants and young children [65]. She suggests that macro- and micronutrient composition and the cost of products marketed to urban populations will determine the success of this approach. In the high-burden countries of South Asia and sub-Saharan Africa, changes in complementary feeding practices will need to be encouraged, where delayed introduction of complementary feeding and the use of liquids/low-density products are common barriers.

Vitamin and mineral mixes in powder form or "sprinkles" provide a well-tested vehicle to improve micronutrient status in children ages 6 to 24 months [66] that could be expanded quickly. Pastes containing micronutrients in combination with protein and fats are likely to improve growth and micronutrient status, but they are more expensive and thus may not reach those in need through commercial channels [67].**

According to Mannar and Sankar, "[A]lthough a growing number of large-scale fortification programs in different parts of the world are beginning to demon-

* The following are the primary references for this section: Proceedings of the 20th International Vitamin A Consultative Group (IVACG) Meeting, 2002; (b) Pinstrup-Andersen P, Pandya-Lorch R. 2001. The Unfinished Agenda; UNICEF/ UNU/WHO/ Micronutrient Initiative (MI), Preventing Iron Deficiency in Women and Children, 1998; Aguayo et al., 2005; Dary O et al., 2005; Lutter C., 2006; Sanghvi T, Harvey P. 2006. USAID Micronutrient and Blindness Project (A2Z) reports; Mannar MG, Sankar R. 2004. Micronutrient fortification of foods—rationale, application and impact. Indian J Pediatr. 2004 Nov;71(11):997–1002; MI/UNICEF 21 Country Assessment, 2005 Draft Report; Houston/USAID Micronutrient Project (MOST), 2004; World Bank, 2006; Thapa S et al. 2005; Mora JO, Bonilla J. 2002; Zlotkin SH et al. 2005; Galloway R. 2003. Anemia Prevention and Control: What Works?; Deitchler M et al. 2004; Darnton-Hill I and Nalubola R. 2002; Fortification strategies to meet micronutrient needs: successes and failures. Proc Nutr Soc. 2002 May;61(2):231–41; Gibson R. 2004.

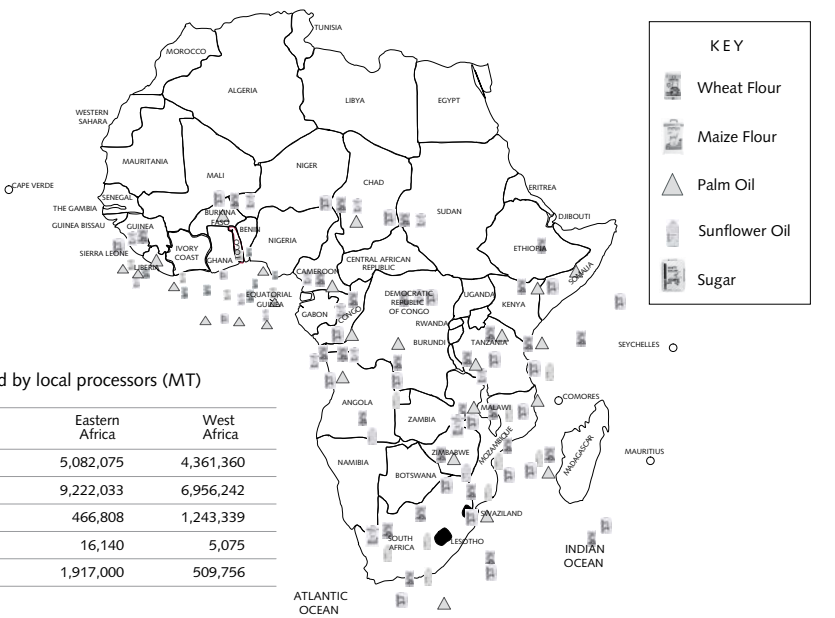
** There are also other presentation options, such as dispersible tablets (see IRIS study, UNICEF). These new approaches are promising and are being documented for effectiveness. Spreads are currently used for the treatment of malnutrition. On-going studies are looking at their preventive uses. However the cost may be a limitation. Research is still needed to explore all possibilities of increasing micronutrient intake, especially during the complementary feeding period (personal communication, B. de Benoist, 2006).

TABLE 3.1. Overview of fortified products in the Africa region, 2005 [63]

Country/region	Wheat flour	Maize flour	Vegetable oil	Sugar	Palm oil
Eastern, Central and Southern Africa (ECSA)	++	+	+	+	
Burkina Faso					+
Eritrea	+				
Ghana	+		+		
Kenya	+	+ (maize porridge)	+ (margarine)		
Malawi			+		
Morocco	+		+		
Namibia		+			
Nigeria	+	+	+ (margarine)	+	
South Africa	+	+	+ (margarine)		
Uganda		+	+	+	
Zambia	+	+		+	
Zimbabwe		+	+ (margarine)		

strate impact at the biochemical level and are leading to the elimination of several nutrient deficiencies, food fortification remains an underutilized opportunity in many developing countries" [68]. But this is changing. The Micronutrient Initiative (MI) has systematically mapped the producer and importer countries and trade flows of key food vehicles in the Africa region [69]. See **map 3.1**.

There is growing support in Asia for public–private partnerships (e.g., the Philippines, India, and others through the Global Alliance for Improved Nutrition (GAIN), MI, International Life Sciences Institute (ILSI), and USAID Micronutrient Project (MOST), and regional organizations such as NEPAD and Eastern, Central, and Southern Africa (ECSA). MI and others have supported the expansion of new products for



Volumes produced by local processors (MT)

	Southern Africa	Eastern Africa	West Africa
Wheat flour	4,315,263	5,082,075	4,361,360
Maize flour	12,336,690	9,222,033	6,956,242
Palm oil	327,387	466,808	1,243,339
Sunflower oil	931,453	16,140	5,075
Refined sugar	4,647,308	1,917,000	509,756

MAP 3.1. Potential food vehicles for fortification in Africa
Source: Micronutrient Initiative (MI) Africa, 2006

TABLE 3.2. Examples of key issues in fortification in Africa [70]

Issues	Recommended actions
Need for advocacy for resources and supportive policies for food fortification	Develop food-fortification policy and action plans at the African and Regional Economic Community (REC) levels. Document impact and cost-effectiveness of food fortification in the elimination of VMDs.
Engagement of the private sector to play a significant role in food fortification	Support harmonization of food-fortification standards and develop enforcement capacity at REC level through strategic relationships with RECs. Develop region-wide markets for fortified-food products by creating an investment climate. Actions would include supplying loans, removing tariff and non-tariff barriers, and building consumer demand, including regional logos and certification systems.
Need for building human resource capacity to advance the food-fortification agenda	Identify key capacity areas and competencies required for specific operations and positions. Develop an Africa-wide training program that includes both short-term and long-term training as well as mentoring. Lobby and support governments, development agencies, and the private sector in providing incentives for retention of specialized personnel.

large, public-sector social programs, such as ICDS in India, as well as commercial marketing of staples and targeted foods at a reasonable cost. Specific issues are beginning to be identified at the regional and country levels, and a number of workshops and meetings have been held in Latin America, Asia, and Africa. **Table 3.2** describes key fortification issues identified for Africa.

The recent developments bode well for the achievement of scale and impact, especially if adequate monitoring and evaluation guide the expansion and targeting of the operational elements of strategies. Joint monitoring and evaluation plans should be developed and baselines established during the initial phases of launching a coordinated global strategy.

Oral supplements can be provided through health services to prevent or treat specific deficiencies. Biannual vitamin A supplementation has been successfully scaled-up through outreach activities of peripheral health centers, in combination with catch-up rounds for immunization with intensified community mobilization. **Map 3.2** shows the global coverage of vitamin A supplementation linked to immunization.

According to the WHO database, of 196 countries with data, about 40% provided vitamin A supplements linked to routine immunization or immunization campaigns, or both [49] (and personal communication, T Goodman, WHO, 2006). More than 60 countries did not link vitamin A to immunization. Prenatal iron supplementation is a universal part of antenatal care policies, but only about 40 countries report data on consumption of prenatal iron supplements (see: www.gainhealth.org) using DHS and other surveys, and most have very low coverage. More than 22 countries have adopted public health policies for iron supplementation for infants and preschool-aged children, but few implement such programs [71]. Programs for improving folate nutrition have been introduced in about 40 countries; these are estimated to account for less than 10% of NTDs caused by folate deficiency [72].

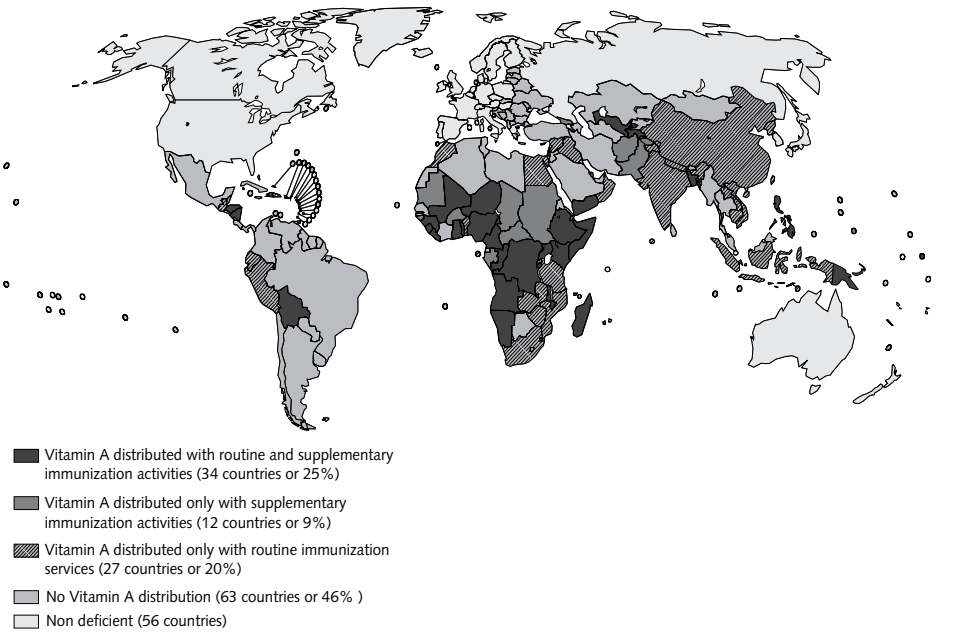
Immunization campaigns are a major delivery channel for vitamin A. As seen in **table 3.3** and **map 3.2**, immunization campaigns are likely to be phased out or redirected to new disease control initiatives. They are not a stable platform on which to build an ongoing strategy.

In theory, activities to enhance dietary diversification are an attractive option for improving micronutrient status, but these have proved difficult to evaluate. Data on the extent and forms of micronutrients in plant-based diets show that it is virtually impossible to correct VMDs through dietary changes. Young children in particular, who have enhanced physiological needs and limited capacity, find it difficult to consume the required amounts of plant foods [70, 74]. However, improving diets to raise micronutrient intake and increasing the use of foods that enhance absorption for the purpose of improving the efficacy of fortified

TABLE 3.3. Proportion of vitamin A doses delivered via national and subnational immunization days

Region	2004 (%)	2005 (%)	2006 (%)
Africa: Eastern, Central, and Southern	14	18	14
Africa: West	86	88	91
Asia: East and Southeast	0	0	0
Asia: South	47	33	33
Latin America and Caribbean	0	0	0
Total	39	38	37
Exclusive of India	49	48	47

Source: UNICEF 2005, as presented by the Micronutrient Initiative, (MI) 2005 [73]



MAP 3.2. Regional patterns of vitamin A supplementation linked to immunization
Source: WHO/IVB database, 2005 192 WHO Member States. Data as of September 2005

products and supplements are valid objectives of public education and dietary counseling programs. People will be able to obtain sufficient micronutrients from a combination of food sources, fortified products, and supplements.

Recently, consumer demand for micronutrient-rich foods of animal origin has accelerated. The livestock and dairy industries have expanded in response to burgeoning demand from consumers in developed and developing countries. Annual production of fruits, vegetables, meat, and fish has accelerated in developing countries (**fig. 3.1**) There is some evidence that fruit and vegetable consumption is higher in upper-income households in sub-Saharan Africa (**fig. 3.2**), and the gap in micronutrient intakes between rich and poor households may have increased. It appears unlikely

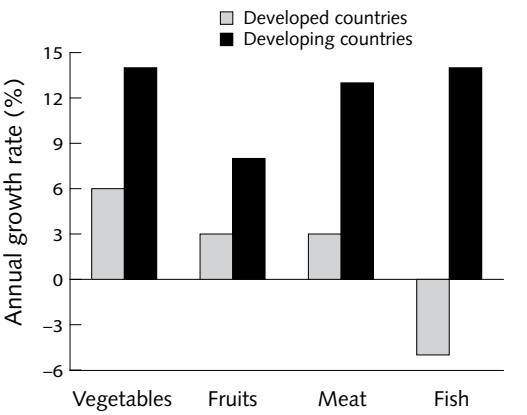


FIG. 3.1. Increased production of micronutrient rich foods
Source: FAO Statistical Databases (FAOSTAT) 2005 [75]

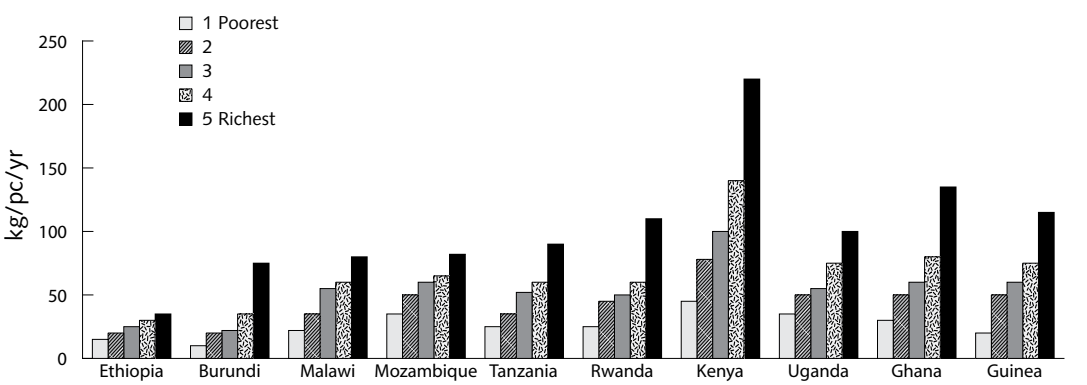


FIG. 3.2. Differential intakes of fruits and vegetables by household income in Africa
Source: Ruel et al. [76]

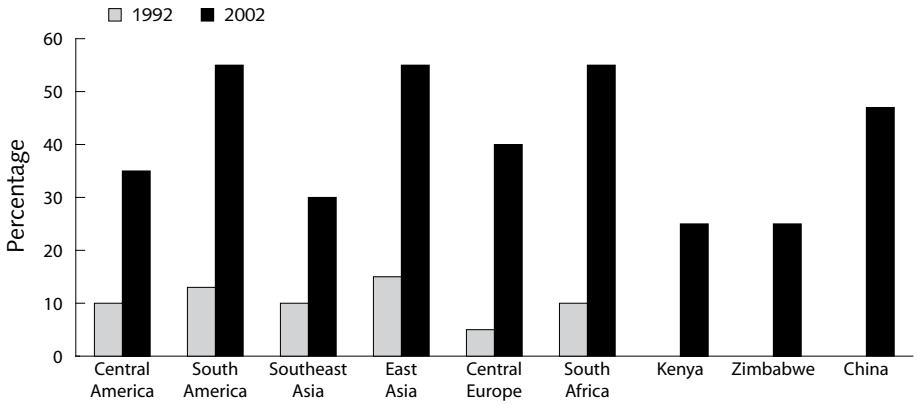


FIG. 3.3. Growth of retail food sales through supermarkets in developing countries and regions
Source: Reardon and Timmer et al [77]

that increased consumption is a result of attempts to improve dietary diversity through traditional nutrition education efforts, as there is little evidence that these programs have achieved sufficient scale. Analysts believe that the increased consumption is the result of low costs of production and marketing, affordable prices, and the image of these foods as prestige foods. The recent trend toward centrally managed purchasing in the food retailing sector (namely, through large supermarket chains in developing countries) offers a new opportunity for market-based improvements in micronutrient intake (see **fig. 3.3**).

The composition of foods can be modified through selective plant breeding and genetic modifications, or biofortification (the development of food crops rich in bioavailable micronutrients, through either conventional breeding and selection or transgenic techniques).* While traditional staples tend to be low in micronutrients, biofortification is showing promise. Although the levels of micronutrients are unlikely to reach those that can be achieved through commercial fortification, once they are developed and integrated into agricultural systems, biofortified cultivars can be incorporated rapidly into the diets of vulnerable groups with important health benefits.

Some health interventions have been important adjuncts for reducing VMDs. Health interventions—such as measles immunization for VAD, deworming for anemia and VAD and malaria treatment for severe anemia—have documented impacts on deficiency diseases such as anemia and VAD. In addition, there is strong evidence that infant feeding practices, especially optimal breastfeeding and appropriate complementary feeding, are closely related to micronutrient status. Epidemiological evidence of causality and program results suggest that country strategies for reducing VMDs should explicitly link with these maternal and child health (MCH) and nutrition services, or vitamin and mineral deficiencies are likely to persist.

Strategies for delivering vitamins and minerals have adapted to new opportunities and evidence. Delivery strategies for interventions that address VMDs have evolved considerably over the past 30 years (see **table 3.4**). Research in the 1970s and 1980s suggested that even where clinical forms of VMDs were not widespread, they could cause functional damage in humans. This finding changed the perception of the problem. It suggested that a much larger proportion of the population needed to be reached, and transformed the way intervention programs were designed and implemented. The emphasis shifted from simply detecting xerophthalmia and treating it with vitamin A, for example, to providing universal biannual doses of vitamin A. A similar shift occurred with goiter and anemia, as intervention strategies sought to provide universal coverage of iodine and iron to prevent the deficiencies.

Food fortification emerged as one of the most cost-effective interventions and one that could achieve scale rapidly if foods commonly consumed by a large proportion of the population were fortified. This led to a new appreciation for the role of the private sector in reducing VMDs. There is growing emphasis on community mobilization and raising public awareness, not only to promote fortified products and motivate uptake and compliance with supplementation protocols, but also to generate ownership and commitment at the community, district, and national levels.

New products, market channels, and health delivery approaches have opened up more options to meet country-specific needs. For example, a broader array of fortified staple foods and specially formulated foods and supplements is now available through a larger number of producers. Processes and frameworks for successful industry-led and government-supported

* The obvious advantages and recognized potential of this approach to address VMDs (Welch and Graham, 2004) have recently attracted many advocates, donors, and commercial interests; it is considered a promising approach for the long term.

strategies are delivering micronutrients in various country settings. Better coverage has recently been documented among high-risk groups, even in remote areas, using intensified outreach from health facilities to deliver micronutrients. Several large countries in South Asia offer government-supported program platforms—such as ICDS in India, Lady Health Visitors (LHVs) in Pakistan, and FCHVs in Nepal—that are capable of reaching a substantial segment of the vulnerable population.

Safety concerns for micronutrients have surfaced periodically, and WHO has addressed them appropriately. Two recent studies have highlighted the importance of supporting the responsible use of supplements where infection rates are high [28, 79]. WHO has been at the forefront of interpreting safety concerns arising from research findings. However, there is currently no central authority or mechanism to help countries manage these issues programmatically. Recognized safety issues are summarized in **table 3.5**.

What is the evidence of effectiveness in large-scale programs?

Fortification has reduced vitamin and VMDs in all geographic regions. Developed countries have benefited from fortification for more than 80 years, and food fortification has been in place in selected countries of Latin America for more than 30 years. In the early 20th century in Switzerland, school children had a high prevalence of goiter, and 0.5% of the population had cretinism. When salt iodization was introduced in 1922, the prevalence of goiter and deaf mutism in children dropped dramatically. Since then, salt iodization has been sustained and the population of Switzerland has achieved adequate iodine status. Recently, several countries have documented a reduction in NTDs following folic acid fortification of cereal flour (**fig. 3.4**).

The addition of vitamin D to milk in Canada and the United States started in the 1930s and virtually eliminated childhood rickets, although rickets is re-emerging as a public health problem. In the 1930s, beriberi, riboflavin deficiency, pellagra, and anemia were public health problems in the United States, leading to the decision to add thiamin, riboflavin, niacin, and iron to wheat flour. In the United States and Europe, a diverse diet containing animal foods plays a role in ensuring healthy micronutrient status, but fortified cereal products still make an important contribution.

Supplementation programs for vitamin A have been followed by mortality declines. The predicted reductions in under-five mortality from vitamin A supplementation [5] have been validated through recent DHS surveys that document shifts in child mortality trends paralleling the scaling up of vitamin A supplementation in several countries. **Figure 3.5** provides data from Nicaragua. Thapa and others [83] showed a stepwise relationship between vitamin A coverage and mortality levels in Nepal based on data from DHS surveys.

A substantial proportion of all vitamin A supplementation is carried out with immunization activities twice a year. Since 1987, WHO has advocated the routine administration of vitamin A with measles vaccine in

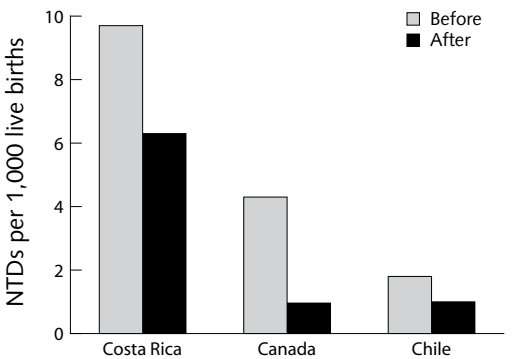


FIG. 3.4. Annual rates of neural tube defects (NTDs) before and after folic acid fortification
Source: PAHO, CDC, MOD, UNICEF, INTA, 2003 [81]

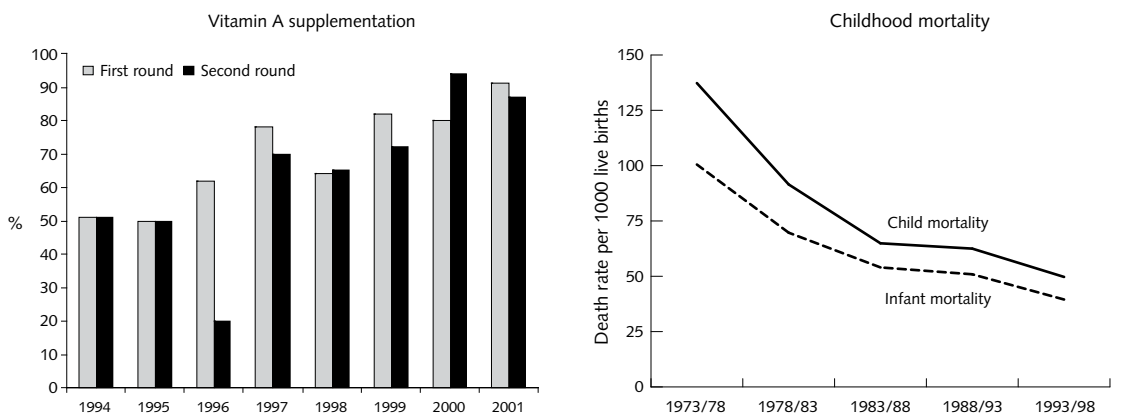


FIG. 3.5. Rising vitamin A coverage and childhood mortality decline in Nicaragua
Source: Ministry of Health (MOH), Nicaragua [82]

TABLE 3.4. Milestones in evolving micronutrient strategies

I. Micronutrients gain a discrete place on national public health agendas	II. Importance of subclinical forms of deficiencies and need for universalization	III. Alternative delivery strategies tailored for local contexts; USI; vitamin A and iron integrated within IMCI	IV. Successful mass distribution of vitamin A; sustainability issues arise; no breakthroughs yet in iron interventions	V. Lancet series reestablishes importance of new "super-nutrients," zinc and folic acid; need for coordinated global strategy for acceleration [78]
Supplementation Recognition of life-saving and functional importance of micronutrients. Vitamins and minerals provided to individuals diagnosed with deficiency diseases.	Establishment of mortality impacts of vitamin A even where clinical signs in the population are not highly significant. Need established for mass supplementation as preventive measure for mortality reduction. Low measles immunization coverage and analysis on vitamin A supplementation during measles puts disease-linked vitamin A supplementation high on priorities for pediatric care. Connection of iodine deficiency to brain development receives attention.	Policies in many countries call for expanded vitamin A supplementation and universal iron/folic acid supplementation in prenatal care. Iodized oil supplements used where iodized salt is not produced or used. Clinical detection and treatment of severe anemia integrated within the IMCI; also, vitamin A for measles and the severely underweight.	Nepal demonstrates the use of community-based volunteers to administer vitamin A at almost national scale. Vitamin A supplements are linked to national immunization days (NIDs) for polio and reach unprecedented numbers of children in large numbers of countries. Iron coverage still lagging behind. Iodine supplements found to be not cost-effective and use severely limited.	Phasing out of NIDs, although a number of countries in Africa still depend on NIDs for vitamin A delivery. Donor-dependent vitamin A supplies raise concerns. Alternatives such as child health weeks (CHW) are found to be feasible and cost-effective when services are combined. The six-month outreach strategy becomes accepted as a public health tool for delivery of basic services. Malaria and deworming are recognized as key adjuncts for anemia reduction. Supplies, formulations for young children, and compliance are identified as key constraints for iron supplementation. Zinc to lead the revitalization of control of diarrheal disease (CDD) and oral rehydration therapy programs.

TABLE 3.4. Milestones in evolving micronutrient strategies *(continued)*

Food fortification Enrichment to replace nutrients lost during processing. Fortified margarine and dairy products.	Need for universal strategies is emphasized as subclinical indicators are found to be associated with important outcomes (e.g., vitamin A, iron, and iodine deficiencies). Potential of fortification gains momentum.	Salt iodization universalized. Sugar fortification in Guatemala and other Central American countries demonstrates feasibility for reaching scale; introduced in Africa (Zambia). Emergence of previously eliminated deficiency diseases in refugee camps raises concerns for providing fortified products and supplements. Fortified foods come under scrutiny in food aid programs.	Intensified efforts in USI, but issues of sustainability, quality, and surveillance arise. Fortification of cereal flours with iron and B vitamins begins to take off, but public health impact is yet to be established at scale. A wide array of products emerge as fortification vehicles, including powders for home fortification for children. Lack of government capacity in enabling industry and enforcement are identified as key barriers.	Capacity building in fortification intensified; recognition of regional nature of production and trade flows in Africa; greater efforts to build public–private partnerships as a bridge. Growing understanding of regulatory frameworks, laboratory needs, creation of public demand, and other hitherto underemphasized elements. Need for more realistic cost projections and time lags. Need to define how to target for better public health impacts (e.g., trends in consumption patterns of high-risk groups).
Dietary diversification Food composition studies help identify good food sources, and these are promoted through nutrition education.	Studies on iron inhibitors, vitamin A absorption, and conversion of beta carotene define the limitations of dietary approaches. Studies on food behavior modification find positive results, but intensity of interventions raises concerns about feasibility.	Cost-effectiveness studies put fortification at the top of intervention priorities. Severe lack of "problem nutrients" in complementary foods identified, reemphasizing the need for fortified special foods and supplements.	Lack of evidence that large-scale reductions in deficiencies can be accomplished through dietary diversification strategies minimizes the role of this approach. Rise of biofortification through plant breeding. Orange sweet potato successfully introduced in East Africa. Biofortification gains momentum with other crops.	Reemergence of dietary diversification as a key component of micronutrient strategies, especially with regard to time lags in take-off of programs at scale, and interactions among micronutrients and between micronutrients and infectious agents (e.g., malaria and HIV/AIDs). Role of phytochemicals (quasi-micronutrients) in disease prevention highlights need for continued work to expand public education and investment in the horticulture/nutri-crops sector.

USI, universal salt iodization; IMCI, integrated management of childhood illnesses

TABLE 3.5. Safety issues

Micronutrient	Issue	Evidence
Vitamin A	Toxicity from excessive intake from high-dose capsules that can cause fetal abnormalities or bone fragility. Acceleration of HIV/AIDS infection in neonates of supplemented mothers.	No confirmed evidence of toxicity in currently implemented programs. New US survey data [80] show dietary excess in young children above recommended levels. The ZVITAMBO study [28] in Zimbabwe indicates adverse events in a small proportion of infants of HIV-positive mothers.
Iron	Iron toxicity in young children from accidental excessive intake of tablets or syrup. Increased morbidity in iron-replete young children where malaria is endemic.	The United States has few cases of overdosing; emergency medical services use simple methods to remove the excess iron to prevent serious effects. The Pemba study [19] in Tanzania shows deleterious effects on malaria progression in children.
Iodine	Excessive iodine that causes hyperthyroidism, tremors, and nodules, especially in the elderly and where low iodine intake has been endemic for a long time.	Iodine-induced hyperthyroidism (IIH) is the most common complication of iodine prophylaxis; it has been reported in some iodine supplementation programs in their early phases. Excess iodine in salt can result from not adjusting added levels to account for greater stability of iodine in processed, refined salt.
Folic acid	Excess can interfere with vitamin B_{12} metabolism and neurologic functions. The US Food and Drug Administration (FDA) has set a safe upper limit of consumption at 1 mg/d of folic acid.	Cases of pernicious anemia incorrectly treated with folic acid instead of B_{12} demonstrated adverse effects; needs further study.
Zinc	Interactions with iron. Effects of excess zinc intakes on the immune system as indicated in the literature.	None; there are no large-scale programs in operation.

Source: WHO website and published documents

countries where VAD is a problem. The first dose of vitamin A is given with measles vaccination at about 9 months of age; children 1 to 5 years old receive vitamin A doses through intensified outreach every 6 months [84].

Lessons learned about scaling up

Public education and social mobilization are critical but often neglected components of supplementation and fortification activities. Mobilizing the community for vitamin A supplementation and creating demand for fortified products are key components of effective strategies. National and district budgets seldom provide adequate resources for these activities (**box 3.1**).

Monitoring and evaluation are important program components that can facilitate scaling up but require ongoing attention. Emphasis on surveillance in USI programs helped maintain a focus on problem-solving as large-scale programs for iodized salt were rolled out. Where salt iodization has been in place for more than five years, improvement in iodine status has been clear cut. Over the past decade, the number of countries with salt iodization programs has doubled, rising from 46 to 93. As a result, 68% of the five billion people living in countries with IDDs have access to iodized salt, and the global rates of goiter, mental retardation, and cretinism have fallen.

Vitamin A supplementation was scaled up at the global level following the meta-analysis of Beaton and others [5]. In early implementation countries, evaluation data were used to initiate action. For example, nationwide vitamin A supplementation was initiated as a result of two key studies on child mortality in Nepal. A unique characteristic of this program was the use of monitoring data for program advocacy; use of data in this way helped obtain resources and motivated staff to maintain high levels of coverage [85].

Progress has been substantial in identifying and improving the use of common indicators among stakeholders. However, technical issues related to methods, interpretation, and comparability must be addressed on an ongoing basis. For example, the complex etiology of anemia requires the use of locally appropriate indicators and methods, and these may not be comparable across programs and countries. The precision of iodized salt testing kits and standard approaches to using different-colored vitamin A capsules to help recall vitamin A supplementation in DHS and similar surveys have created problems of consistency in the field. Greater

BOX 3.1. Mobilizing communities: the vitamin A project in Nepal

» The ongoing success of vitamin A supplementation at the national level over several years is partly due to an innovative communication approach.
» The management body developed a unique and respectful relationship with the primary outreach workers, the Female Community Health Volunteers (FCHVs). The program staff were treated as they were expected to treat mothers.
» Training for field workers was highly participatory, involving extensive role-plays designed to build confidence, support, and a sense of ownership of the program. The approach was entertaining and empowering. These attitudes and approaches led to high levels of motivation among the FCHVs, who then motivated and organized others.
» The program featured creative media and communication approaches combined with carefully field-tested materials and messages to popularize desired behaviors.
» At the community level, special outreach efforts were held in hard-to-reach communities often neglected by local programs. The program achieved and maintained high levels of coverage and produced epidemiologically significant outcomes.
» The periodic reporting of evidence-based results formed the underpinnings of advocacy at the district and national levels.

Source: USAID Basic Support for Institutionalizing Child Survival (BASICS II)/USAID Micronutrient Project (MOST), 2004 [85]

BOX 3.2. Evaluating Vitamin A supplementation programs in the Philippines

The prevalence of vitamin A deficiency (VAD) as measured by serum retinol in children ages one to five years in the Philippines rose from 35.8% to 38% between 1993 and 1998, despite a twice-yearly universal vitamin A capsule distribution program. In-depth analysis showed that there was a detectable impact in groups with the highest prevalence of VAD and that it lasted up to four months after the dose was given. In highly urban cities in Visayas, where very high prevalences were found, the prevalence was reduced from 27% to 9% 1 to 2 months after distribution of vitamin A capsules, and to 16% at 3 to 4 months. Two concerns have been raised following this analysis: (1) the uneven level of magnitude of the effect of high-dose vitamin A capsules; and (2) the fact that the effect did not persist for 6 months, which is the interval between doses. The authors note that with more frequent dosing, especially for those most deficient, a progressive reduction in VAD may occur. The policy implication arising from these results is that a shift in resources is warranted. In areas of low prevalence of VAD, distribution of vitamin A capsules should be targeted to deficient children only. In areas of high prevalence, vitamin A capsules should be distributed to children ages 1 to 5 years at least three times a year.

Source: Pedro et al., 2004 [86]

attention needs to be given to the quality of data.

An issue that has concerned public health leaders in countries such as the Philippines and Zambia is related to the evaluation of vitamin A supplementation using serum retinol as the indicator of VAD. Technical discussion at the global level is needed to clarify how best to capture the success of vitamin A supplementation in reducing VAD at a time when clinical signs are no longer common. **Box 3.2** summarizes an example from the Philippines that reflects current thinking.

Vitamin A supplementation was accelerated with the help of free or subsidized capsules. Global expansion took off when donors pledged free supplies of vitamin A if countries linked polio national immunization days (NIDs) and routine immunization with vitamin A supplementation. Within a 2- to 3-year period, a large number of countries reached millions of children through polio campaigns. However, the trends documented by WHO* reflect instability and frequent transitions between any supplementation, routine immunization-linked supplementation, and supplementation with biannual events or immunization campaigns. Immunization campaigns have been unpredictable and the addition of vitamin A to these campaigns is idiosyncratic.

Partnerships have been crucial to success. In both salt iodization and vitamin A supplementation, progress has been dramatic since global partnerships were formed. To control IDDs, USI was adopted in 1993. Alliances among UN agencies (WHO, UNICEF) and the World Bank, the Network for Sustained Elimination of IDD, the International Council for Control of Iodine Deficiency Disorders (ICCIDD), international institutions, bilateral agencies (e.g., United States Agency for International Development [USAID] and the US Congress), and the salt industry have helped countries put permanent national salt iodization programs firmly in place. Global standards, guidelines, tools, and resources have been provided by international agencies. These agencies have helped public health authorities in various countries successfully partner with the salt industry and have provided critical technology and technical inputs.

Clear evidence of the mental and physical damage done by IDDs, along with mandatory fortification, fueled the momentum for scaling up iodized salt programs worldwide. Salt iodization has proved to be highly cost-effective and feasible for producers, consumers, and governments. Led by a strong global partnership (USI)

*Vitamin A and immunization tables (personal communication, T. Goodman, 2006).

and with the support of WHO, UNICEF, bilaterals, and private donors (e.g., Kiwanis International and the Bill and Melinda Gates Foundation), countries began to mandate iodization of salt. Coverage with iodized salt increased substantially after 1990. Forty-three of 126 countries with national data documented adequate levels of intake [49]. Iodized salt coverage exceeded 75% in 26 countries in 2004. The number of countries with iodine as a public health problem decreased from 110 to 54 during 1993 to 2003, although these countries may still have pockets of iodine deficiency that require targeted support. Constraints to reaching all target groups with iodized salt include the difficulty of equipping, staffing, and monitoring small-scale production; the lack of consumer awareness and demand; weak or no legislation or legislation that is not implemented; and inadequate technical support and accountability.

Sustainable programs are important; micronutrient interventions must be maintained in perpetuity or the deficiencies will reappear. These interventions are unlike disease eradication strategies, such as the eradication of smallpox and polio. The human body cannot manufacture these vitamins and minerals to meet critical life functions; they must be consumed through food or by supplementation. Because of the need to build permanence in this sector and the vulnerabilities of public-sector delivery systems, interest is increasing in strengthening both public- and private-sector delivery systems.

Once fortification programs are put in place, continued advocacy on behalf of fortification is important. In India, salt iodization was once mandatory; later, the ban on un-iodized salt was lifted and this led to increases in iodine deficiency.

To facilitate sustainability, policies must be continuously monitored. Public education and the awareness, motivation, and capacity of healthcare providers play important roles. Data and results from monitoring systems can be effectively used in advocacy for ongoing support.

In programs of iron supplementation for women, ensuring supplies, providing appropriate counseling on compliance, and mobilizing communities are key to impact. Iron supplementation programs for pregnant women are among the oldest micronutrient interventions still being implemented worldwide. In recent years, countries have embarked on iron supplementation programs for adolescents and young children as well, and there is evidence of impact. Experience has provided useful lessons. For decades, prenatal iron supplementation was a neglected program; it was embedded in routine antenatal care but was poorly implemented. Supplies of iron supplements were unreliable and of poor quality, and the program was not considered a high priority. This may be changing now.

For example, in Nicaragua during 2000–2003, several indicators related to IDA improved nationwide. Coverage with prenatal iron rose from 70 to 88%, and the prevalence of anemia in pregnant women fell by one-third [82]. Coverage of children ages 6 to 59 months with iron supplements improved from 37% to 62%, and anemia fell from 29% to 23%. During this period, breastfeeding duration and vitamin A coverage through fortified sugar and supplements also increased, which may explain some of the reduction in anemia.

In India, UNICEF assisted national efforts to intensify programs for adolescent girls ages 10 to 19 years in seven states. All programs provided weekly IFA supplements, and one state provided daily IFA tablets, as well as albendazole to treat worm infestation [87]. All assessments showed a decrease in the prevalence of anemia. The decrease varied from 5% in Jharkhand state to 40% in Andhra Pradesh state after one year. Andhra Pradesh also conducted an assessment 2 years later and reported a total reduction of about 70% in anemia. Programs conducted through schools showed greater impact than non–school-based programs, achieving a more than 20% decrease in the prevalence of anemia. Moderate and severe anemia decreased in all but one program.

Thailand has addressed nutrition in national development policies and plans since the mid-1970s. Anemia is still widespread and observed in almost all vulnerable groups, but there is an improving trend in all regions of the country. Data from national nutrition surveys and routine Ministry of Health (MOH) data show a consistent decline in anemia prevalence among pregnant Thai women during 1986–1996 [88]. The program initially consisted of surveillance and iron supplementation; fortification has been added.

The effectiveness of weekly iron supplementation in women of reproductive age in three Asian countries has recently been documented by Cavalli-Sforza and others [89]. Social marketing and community mobilization were strong elements of the programs.

For preventive vitamin A supplements for children, community mobilization and well-planned outreach sessions at least twice yearly are important. Once polio campaigns began to be phased out, countries developed plans to continue high coverage strategies for vitamin A supplementation. Child health days/weeks/months were seen as a twice-yearly outreach session during which immunization, vitamin A, deworming, and other services and information could be provided, especially to hard-to-reach communities.

The Nepal vitamin A supplementation program was introduced in the poorest districts in 1993 (even before polio NIDs) and was phased in to reach almost national coverage by 2001. Coverage has remained high, attributed to a system of resident FCHVs trained to administer vitamin A with supervision from health authorities on two fixed days each year. The volunteers know the eligible children in their communities and monitor their need for supplementation. Analysis of child mor-

tality trends based on consecutive DHS surveys shows a reduction in child mortality of 50% among children who receive two doses each year of vitamin A in the period from ages 6 to 59 months [83].

In Vietnam, biannual vitamin A supplementation rounds were implemented through NIDs and micronutrient distribution days from 1993 to 1997 [90]. National protein-energy malnutrition (PEM) and VAD surveys carried out in 1985, 1988, and after vitamin A supplementation in 1993–94, found that night blindness, Bitot spots, and corneal scars had declined by 87% to 90% following supplementation.

In Nicaragua, strong partnerships helped achieve and maintain high coverage of the vitamin A supplementation program.

Lessons learned from a large number of countries that followed this model of twice-yearly supplementation have found the following components to be key aspects of success: bringing services closer to communities through a variety of extended outreach mechanisms at fixed times during the year; monitoring and frequent review of coverage; communication and community mobilization; logistics and financing; and training and supervision [91]. Leadership and partnerships across sectors have helped several countries sustain these programs over several years.

How have micronutrients been delivered during emergencies?

Fortification of donated food resources is key to preventing deficiencies. For many years, donated commodities did not contain vitamin and mineral premix. As evidence was reported of deficiencies in vitamins A, B, and C, international donors and NGOs took steps to ensure fortification or supplementation as integral elements of relief efforts. The WFP has implemented local processing and fortification in Angola, Bangladesh, India, Nepal, and Zambia, and in the southern Africa regional drought emergency.* The experience shows that local fortification is possible but challenging. Specifically, the challenges involve technical and managerial capacity constraints, lack of compliance with procurement specifications and quality control, unclear policies on micronutrient content labeling, and inadequate cash resources to support many aspects of local processing and fortification activities. Blended and fortified foods typically given during an emergency now contain added vitamin A, thiamine, riboflavin, niacin, vitamin C, folic acid, iron, iodine and zinc.

Blended foods may not fully meet the needs of pregnant and lactating women or young children in emergencies. This is primarily because the micronutrients may not be absorbed very well and because other critical micronutrients, such as vitamin B_6, vitamin B_{12}, and zinc, are lacking in emergency situations where food and health systems are dysfunctional. UNICEF, WHO, and WFP recommend daily multiple micronutrient supplements that can meet the recommended nutrient intake for these vulnerable groups during a humanitarian crisis. Helen Keller International (HKI), UNICEF, and WFP are also providing "sprinkles" (a mix of vitamins and minerals that can be added to individual portions or a group feeding) for use in tsunami rehabilitation and through the commercial markets in Asia (Saskia de Pee, personal communication, 2006).

Data sources, limitations, and issues

A lack of objective reviews and evaluations of program implementation and coverage seriously limited this stock-taking exercise. The data used in this review, from web searches and available global datasets, have significant gaps. Taking IDD as an example, among 185 countries, only 123 report UI. Of the 123 countries that report a UI value, only 20% have data more recent than 1999. Among the 24 countries that have more recent UI data, only 54% of the data are from a national survey and only 6 countries report low UI. The WHO database does not include household iodized salt coverage, but salt coverage is reported in the 2004 UNICEF database. Of the 188 countries in that dataset, 117 reported salt coverage. Among the 116 countries with a date associated with the salt coverage data, only 86 (74%) had data more recent than 1999. Among the countries with recent data, 62% had coverage of 50% or more.

Household iodized salt coverage is presented in global datasets as using "adequately" iodized salt. Adequacy is almost always based on the subjective interpretation of the salt test kit, which may underestimate the use of salt with some iodine—perhaps enough to reduce deficiency. Thus, the assumptions made using these global data may be outdated or limited by the accuracy of the data and may not reflect the true situation in the country.

The situation is similar for vitamin A. For many countries, there is a lag between prevalence data and supplement coverage data, so the prevalence data may be misleading if supplement coverage has increased dramatically. Data on prevalence should be used with caution, as improved coverage is likely to have changed the prevalence.

Improved data is essential to building a more comprehensive planning and monitoring framework for a global strategy. Various groups maintain valuable databases that can be further built upon: WHO MDIS, Iron Deficiency Project Advisory Service (IDPAS), and MI/

* Partly adapted from WFP WFP/EB.A/2004/5-A/2 Micronutrient fortification: WFP experiences and ways forward. April 2004. Also see WHO/UNICEF/WFP Joint statement on multiple vitamin and mineral supplements for pregnant and lactating women, and for children aged 6 to 59 months, 2005.

UNICEF/Canadian International Development Agency (CIDA) (vitamin A documents); WHO/Expanded Program of Immunization (EPI) (vitamin A and immunization spreadsheets and maps); Flour Fortification Initiative (FFI); Iodine Network; and others.

Data on food intake and the use of supplements by high-risk age and income groups would be valuable for comprehensive planning. Key information is also missing on types of programs, community platforms, and innovative ways of generating ongoing community demand for micronutrient products and services.

Next steps for strategic action and research

» There is an overriding need to develop different types of intervention mixes and program strategies to meet the diverse and changing needs of countries as demographics and disease patterns change; no single intervention, such as food fortification, can address the needs of all target groups (e.g., even iodine supplements are essential in some situations).
» Support for optimal breastfeeding should be a part of micronutrient programs. Operational models for improving micronutrient intake for children ages 6 to 24 months are needed to complement strategies intended for the general population; in South Asia and sub-Saharan Africa, the problem of macronutrients in young children should be addressed at the same time. Solutions for low birth weight are urgently needed in South Asia.
» Programs should aim to reach at least 80% of the target population with adequate levels of each micronutrient. Coverage data on programs for the five main micronutrients should be updated frequently using surveys, tally sheets, or routine health services data.
» Ongoing global monitoring of country progress is critical. Systematic program reviews such as the analytic review conducted under the Integrated Management of Childhood Illness (IMCI) are useful every 2 to 3 years to respond to changing needs and adapt new research findings. More frequent (e.g., annual) reviews of country operations and policy issues should be conducted in each region to maintain momentum and target technical assistance as needs arise. An example of such a mechanism is the regional EPI managers meetings organized by WHO.
» Agreement on program coverage and process indicators and ongoing support for data collection, analysis, and use would help countries target hard-to-reach groups and refocus program efforts.
» Operational programs are needed to expand the use of zinc in diarrheal disease control programs in different contexts; food-based options are needed to enhance coverage with preventive zinc and folic acid.
» A summary of evaluations and studies of programs to reduce adolescent anemia reduction would help spearhead this approach to successful anemia reduction in this target group.
» A review is needed of evidence of effectiveness from large-scale programs of iron fortification of cereal flours.
» Fortification and supplementation approaches must be developed for addressing multiple VMDs while promoting consumption of micronutrient-rich foods.

Conclusions and recommendations

» Food fortification and supplementation are effective strategies for reducing VMDs on a large scale in many different settings, but coverage and scale remain limited. Both are highly cost-effective, especially fortification, as compared with other health interventions. But fortification alone cannot solve the problem of VMDs in any country. Supplementation is an essential component of successful strategies to address the needs to critical targets groups. The intake of foods naturally rich in micronutrients can reinforce the benefits of fortification and supplementation; breastfeeding for infants is particularly critical, as are the use of animal foods and fruits and vegetables.
» Current data limitations and planning mechanisms need to be improved to encourage the development of combined strategies and best intervention mixes for different populations and contexts.
» A global effort should focus on a group of jointly selected high-need and "potential for high-impact" countries. It is important not to overlook small countries where progress has been made and countries that have good programs that could achieve high universal coverage with limited additional input. Focusing only on high-population countries with large micronutrient problems may result in a loss of momentum in countries that are moving quickly in the right direction.
» Public–private partnerships are key for effective national strategies; fortification efforts led by private industry have worked well in several countries. Public education and consumer groups are key. The track record on mandatory fortification is impressive where enforcement capacity exists. Both mandatory and voluntary food fortification are greatly helped by adequate monitoring and quality control by industry and government.
» Micronutrient supplementation can be effectively integrated with routine services and special outreach efforts; supplementation has been successfully combined with other primary health care interventions

such as antenatal care and immunizations. These efforts should be institutionalized through routine monitoring, planning, training, and supervision within district health services.

» Both food and health systems should be strengthened to deliver micronutrients to critical target groups in a sustainable manner; lack of leadership is a major constraint and ongoing advocacy is key. Substantially more must be done to clarify, develop, and implement follow-up, monitoring, and evaluation efforts and the use of data.

» Much more can be accomplished even with current levels of external support. Global and regional coordination mechanisms have served other health initiatives well and should be adapted. Additional resources are needed for implementation and global coordination.