Let food be our medicine

Editor’s note

Current dominant practice to prevent vitamin A deficiency is universal supplementation of entire populations of young children in countries identified as being at risk (picture above, from Vietnam). The contrary view is that dominant policy and practice should be food-based. In May 2010 WN published Michael Latham’s ‘The great vitamin A fiasco’. This strongly criticises current practice. WN then published many letters from scholars, policy-makers, field workers, and others, almost all supporting Michael Latham and contesting universal supplementation as a distraction from rational sustainable food-based policies and actions, and also a commentary from scholars from Johns Hopkins School of Public Health upholding current practice. In November last year WN published ‘Let food be our medicine’ by John Mason and colleagues, following their October paper in the International Journal of Epidemiology. This supports the food-based approach. WN has then published many more letters in Feedback. See above for links. Further letters are below.
Christine Stabell Benn, Peter Aaby and Ane Fisker write:
The debate about high-dose periodic vitamin A supplementation and vitamin A deficiency is two-dimensional. It is based on the idea that vitamin A supplementation works by preventing vitamin A deficiency, and nothing else.

Within this frame, there are two schools of thought. Some, like John Mason and his colleagues, emphasise that the policy of providing supplementation is built on older studies, notice that the recent DEVTA trial of vitamin A supplementation in India found no beneficial effect, and conclude that supplementation may no longer be the best tool for combating deficiency, and that it should be replaced by frequent regular intakes of vitamin A at physiological levels (1,2).

Others, like the Global Alliance for Vitamin A (GAVA), argue that there is still substantial evidence that vitamin A supplementation reduces mortality, that the DEVTA trial was of a poor quality, and that supplementation programmes should be maintained until less than 5 per cent of children have serum retinol <0.70 μmol/l (3).

Vaccination is protective

But vitamin A in high doses is an immunomodulator. This is being overlooked. Apart from combating deficiency, it may also influence the immune system and how this handles other challenges (4,5). This may be very beneficial, but also at times harmful, depending on what else is going on in the immune system. For instance, the original trials of supplementation to older children showed remarkable mortality reductions of around 23 per cent (6). Already at that time it was noted, however, that the effect of supplementation was not associated with the degree of underlying deficiency (6). Thus, supplementation seemed to have other functions than merely prevention of deficiency.

These original trials were carried out before the roll-out of the Expanded Programme on Immunizations. In a reanalysis of one of the trials, from Ghana (7), we showed that the beneficial effect of supplementation was limited to children who had no vaccines. In these children, supplementation was associated with a 36 per cent (12 to 53 per cent) reduction in mortality. In contrast the reduction was only 5 per cent (-26 to 28 per cent) in children who had received vaccines. This was because supplementation was associated with a 160 per cent (41 to 380 per cent) increased mortality in females, who had received some, but not all diphtheria-tetanus-pertussis (DTP) vaccines before entering the trial, and therefore were likely to receive them during follow-up (8). The potential negative interaction between supplementation and DTP vaccines in females has been observed in several other studies (9-13).
Recently we published the first individually randomised placebo-controlled trial of vitamin A supplementation given with vaccines to children above 6 months of age, as recommended by the World Health Organization. This trial, which does not suffer from the same weaknesses as the DEVTA trial, enrolled more than 7,500 children in urban and rural Guinea-Bissau. Mortality was high, the rate during 6 months of follow-up being 21/1000 person-years-at-risk. There was no overall benefit of supplementation, the mortality reduction being 9 per cent (-41 to 41 per cent), very similar to the result of the DEVTA trial.

**Gender differences**

However, the effect differed significantly between males, with a 92 per cent (2 to 275 per cent) increase in mortality, and females, with a 55 per cent (13 to 76 per cent) reduction in mortality (P = 0.003 for interaction between supplementation and gender)(14). The gender-differential effect was particularly pronounced in females who had already received supplementation previously (14), corroborating findings from other studies (15,16). Vitamin A status was assessed in a subgroup of 1,100 participants; the prevalence of deficiency was above 60 per cent, and did not differ between males and females (17). Hence the lack of overall effect was apparently not due to low prevalence of deficiency, and the gender-differential effect on mortality was not explained by underlying gender-differences in deficiency. Most children received supplementation with measles vaccine, or they received measles vaccine shortly after, and hence the combination of supplementation and measles vaccine may be particularly beneficial for females, but may be harmful for males.

Recent trials of neonatal vitamin A supplementation have also been disappointing in terms of their overall effect (18-20), potentially due to interactions between vaccines and gender. Trials and meta-analyses have mainly focused on follow-up to 6 months of age (18-21). It is therefore noteworthy that all studies that present data by gender up to 12 months of age (13, 18-20, 22, 23) find a negative effect of in the second half of infancy, the combined estimate being a 20 per cent (2 to 42 per cent increased female mortality from 6-12 months of age, significantly different from the effect in males (p=0.009 for same effect in males and females) (data not shown).

Thus all evidence supports that vitamin A supplementation has other effects than merely preventing vitamin A deficiency. The existing data can simply not be explained from the prevention-of-vitamin-A-deficiency perspective. There are more dimensions. The effect of supplementation to older children may be most beneficial in the context of no vaccines, or when measles vaccine is the predominant vaccine, in which case it is most beneficial for females. The effect of neonate supplementation may be negative for females once they start receiving DTP vaccines, but this may be reversed if they subsequently receive supplementation with measles vaccine (14).

Taken together, the net effect of giving vitamin A supplementation is the sum of benefit or harm from first, prevention of deficiency, which is probably always beneficial, and second, immunomodulation, which can be both beneficial and
harmful, depending on other factors such as the gender of the child, and which vaccines it receives.

With decreasing prevalence of vitamin A deficiency, the risk of harm after supplementation will inevitably increase. Thus, maintaining supplementation for all children until the prevalence of low serum retinol is <5 per cent, is potentially harmful for some children. With the two recent trials of supplementation to children above 6 months of age showing no beneficial effect (14, 24), we agree with John Mason and his colleagues (1,2) that it is time to reconsider supplementation.

However, we believe there still may be a role for supplementation. Some children may benefit from supplementation due to its immunomodulatory effect, for instance females who receive supplementation with measles vaccine. Hence, we think the time has come to conduct large-scale multi-centre placebo-controlled supplementation trials designed to test the overall effect on mortality of supplementation, as well as the potential interactions with gender and immune-modulating interventions including routine and campaign vaccinations and other micronutrients. These trials should also include a third arm, with provision of low-dose regular vitamin A supplements. Only in this way can we be sure that the children receive the evidence-based interventions they deserve.

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Example of Vietnamese family agriculture in which cultivation of rice and raising of fish and domestic animals is integrated in a local ecologically sensitive and indefinitely sustainable system

Pattanee Winichagoon and Emorn Udomkesmalee write:

The periodic high dose vitamin A distribution for infants and young children between 6 months and 5 years recommended by the World Health Organization and the UN Children’s Fund, together with the International Vitamin A Consultative Group, and put into practice for decades (1) is being questioned, in this journal by Michael Latham (2) and including in this journal by John Mason and colleagues (3-4).

Vitamin A supplementation for all children in the age range above in countries identified as at risk from vitamin A deficiency has been the recommended intervention in low and middle income countries (5). In the last few decades programme carried out all over the world have resulted in a significant improvement of the overall nutritional status, and a marked decline of the severity of nutrient deficiencies including that of vitamin A. Recent report indicate that prevalence of clinical vitamin A deficiency is now of mild public health importance on a global scale (6,7). Evaluation of the extensive vitamin A capsule programme has been limited (3), and a very large trial in India has shown no impact on childhood mortality (8). This is likely to be due to the changing patterns of diseases (measles and diarrhoea), so that vitamin A supplementation no longer reduces mortality. Therefore Michael Latham, and now John Mason and his colleagues, call for a policy shift in global strategy for alleviating vitamin A deficiency, towards food-based approaches (2-4).
We suggest that the public health issue now and in future is not so much whether or not large scale vitamin A supplementation is effective, as rather, what and how interventions, perhaps especially those that are food-based, will be implemented sustainably, in countries where vitamin A deficiency remains a public health issue.

The impact of national vitamin A supplementation on serum retinol in areas in the Philippines with highest prevalence of vitamin A deficiency has been shown to last up to four months post-dose. No effect was observed in other areas with subclinical deficiency (9). This may suggest more frequent dosing is needed, but to do so, programme feasibility and coverage would need to be considered, especially where health infrastructure is weak or non-existent.

Several food-based interventions, included fortification of staples, cooking oil and sugar with vitamin A have been shown to be effective (10-12), as have biofortified staples, such as sweet potato and maize (13,14). But scaling up such interventions would be a challenge. Dietary diversification by promoting local or indigenous food sources has been suggested and tested. But feasibility was shown only on a small scale. The impact on vitamin A status was either not assessed, or the studies only aimed at increasing food security or behavioural changes.

**Integrated programmes needed**

There is now good information from low and middle-income countries showing that the severity of vitamin A deficiency both in children and women is of only mild or moderate significance (6, 15-18). Also, vitamin A supplementation not recommended for women, especially during pregnancy when night blindness has often been reported (19,20).

Food-based strategies therefore seem more appropriate. New policies that direct resources towards integrated approaches should be encouraged. Vitamin A supplementation may continue to be appropriate in situations of endemic deficiency and high childhood mortality, but food-based programmes should be planned and implemented as well. The challenge is how to make such intervention effective and feasible for scaling up at country level.

The community-based nutrition programmes in Thailand and in Vietnam are examples of an integrated food, health and development interventions implemented on a large scale (21-24).

In Thailand, the community-based nutrition programme focusing on underfive children has been implemented through primary health care. The effective integration with agriculture and other aspects of community development has evolved with strong community mobilisation and participation over time (21). Vitamin A deficiency has been addressed as one of the priority programme goals (22).

In Vietnam, universal vitamin A supplementation for under 5s, together with the gardening-fish culture-animal husbandry local food systems have been implemented
nationwide (23-24). The integration with primary health care, successful mobilisation and community involvement, effective monitoring and supervision network have been a great success of the overall vitamin A programme in Vietnam.

In any complex real life situation it is difficult to isolate the contribution of specific initiatives and interventions. The important lesson to be learned is how to integrate combined interventions into any country’s context, situation and resources, including capacity for primary health care and development in general, in a realistic time-frame.

A strategic plan

To move forward, we would like to propose that the following issues be considered by all those concerned with programmes and initiatives to improve and sustain vitamin A status and prevent vitamin A deficiency, and in general to protect the nutritional health and well-being especially of children and women in underresourced countries and settings.

1 Review. We recommend a policy and programmatic review of when and where vitamin A supplementation is still needed and how best to deliver it, convened by relevant UN agencies. Periodic supplementation for child survival may still be needed in specific contexts and considered to ‘do no harm’. Countries look up to United Nations technical agencies including the World Health Organization, the UN Food and Agriculture Organization and the UN Children’s Fund for guidance. A systematic critical review conducted by an independent expert committee should be considered. This could be carried out in collaboration with other relevant organisations such as the Micronutrient Forum, and Biomarkers on Nutrition for Development

2 Discrimination. There is a need for discrimination, to separate vitamin A supplementation as a strategy designed for the survival of children, from broader initiatives, such as combined supplementation, fortification and dietary diversification, designed to improve vitamin A status in a whole population.

3 Biomarkers. The limitation of serum retinol as the biomarker of vitamin A status is well-known and needs review. Currently it is the recommended indicator to determine subclinical vitamin A deficiency of public health significance in population but its validity is questioned. It is essential to understand the complexity of vitamin A biology within different conditions, especially infection environment, the magnitude, scale and severity of undernutrition, and among other micronutrient deficiencies, to be able to select appropriate indicators and to interpret the response of the interventions accordingly.

4 Integration. Programmes to address vitamin A deficiency need to be part of larger nutrition initiative and interventions designed to improve the health especially of mothers and children. The global nutrition policy and reality landscapes have changed, and continue to change, for example now with the call to countries to focus on the ‘1,000 days window of opportunity’. Also, the Scaling-Up Nutrition
(SUN) initiative has rapidly gained momentum, with opportunity to gain new substantial support for countries to implement proven specific interventions. Also such interventions need to be integrated with broader policies and programmes that impact on nutrition, such as those concerning agriculture, education, water and sanitation, environment, social protection.

The outcome documents of the UN International Conference on Nutrition held last November in Rome advocate better linking of nutrition with food systems as a whole. We agree. It is a high time for integrated food-based strategies to be central in nutrition improvement programmes and in relevant public policies and actions. The call to promote regular intakes of vitamin A from habitual diets is, we propose, part of a strategy sustainably to improve and maintain vitamin A status throughout low and middle income countries and any other settings at risk of deficiency.

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References


Vitamin A
The MOON also rises

The impact of climate change on the low-lying farmlands of Bangladesh. To be genuinely sustainable, policies and actions must address fundamental and elemental causes of food and nutrition insecurity

Shamim HayderTalukder writes:

Human development, as in the UN 2000-2015 Millennium Development Goals, is now being defined as sustainable development, as in the UN 2016-2030 Sustainable Development Goals. These take into account social, economic and environmental factors.

The November WN commentary on international vitamin A policy by John Mason and his colleagues (1), following their paper in the International Journal of Epidemiology (2), did not discuss the sustainability of the vitamin A industry. Like manufacturing cigarettes or building weapons, making food is big business. Between 2003 and 2012 according to the marketing organisation Euromonitor, sales of packaged foods throughout the world nearly doubled (increased by 92 per cent) to $US 2.2 trillion (4). Industry-led nutrition solutions always face dispute, but this never affects their production and sales, and debate may even cause an increase in prices, affecting mainly low-income customers.

The main products being pushed by food manufacturers for use in ‘solving’ the problems of food insecurity and under-nutrition are imported packaged ready-to-use therapeutic food (RUTF) and ready-to-use supplementary food (RUSF). RUTF is unnecessarily expensive to use for anything else besides treatment of severe acute malnutrition (at $US 70-200 per child cured, about half of which is for the product itself). Therefore so-called ‘community-based management of malnutrition’ using such products costs several times more than the costs of preventing malnutrition through genuinely community-based approaches. The companies may be able to
sustain their production and profits. But the economics of funding for overpriced interventions using their products certainly is not sustainable.

**Realities in Bangladesh**

Now for vitamin A supplementation. Debate on the effect of high-dose vitamin A capsules on young child mortality has been going on for a long time (1-3). All nutrition-specific and sensitive interventions need to adopt sustainable approaches for ensuring good nutrition throughout the life cycle of a human being. In the UNICEF nutrition framework (5) and The Lancet series nutrition-sensitive nutrition framework (6), young children’s nutritional status is determined by their dietary intake, which is to say, breastfeeding and complementary feeding, supported by mother and child good practice with water, sanitation and hygiene, and other healthful behaviour and habits. Breastfeeding and home based complementary feeding are or should be sustainable interventions. Fortification of rice with appropriate vitamins and minerals may also be a low investment solution to micronutrient deficiency.

But in my country of Bangladesh, where drowning is a major cause of death of children over the age of 2, where a quarter even of children of higher income families are underweight, where more than half of all adolescent females are anemic, and the mean age of marriage for girls is 15, requiring the government to invest in the distribution of vitamin A capsules over the whole of the country is a travesty.

**‘Magic’ can be tragic**

Patterns of disease have changed rapidly all over the world. Now, efforts to deal with under-nutrition in many if not most lower-income countries are a context in which over-nutrition is rapidly increasing. Thus in Bangladesh, iodine deficiency has been successfully reduced, while at the same time the rates of hypertension have soared.

Studies of hypertension from the 1970s to the late 1990s in Bangladesh, show that prevalence is increasing significantly in both the urban and the rural population. Three adults out of 10 of the population in Bangladesh are now hypertensive (7). A 2014 study in the Global Burden of Disease series, of overweight and obesity in children and adults from 1980-2013 has found that worldwide prevalence of overweight and obesity increased substantially in children and adolescents in countries of all income levels (8). Obesity and related chronic conditions and diseases now threaten communities, health systems, economies and the structure and integrity of societies throughout the world. This requires a radical rethink of interventions that were first put in place before chronic diseases became international public health crises.

For example, in countries like Bangladesh, the impact of calorie-dense interventions, supplements and diets for children, especially those of low birthweight, in later life, needs urgent examination. 'Magic' solutions for childhood undernutrition prevention
and treatment may have long term tragic consequences. And while giant food and
drink corporations are enjoying sustained growth and profits, what is the impact of
their activities and their products on human health?

What actually works

So what works? The Scaling Up Nutrition (SUN) initiative states (9)

Nutrition-sensitive development seeks to promote adequate nutrition as the goal of
national development policies in agriculture, food security, social protection, health, and
education programs.

The recent paper in The Lancet cited above (6) defines nutrition-sensitive
interventions as:

Interventions or programs that address the underlying determinants of fetal and child
nutrition and development — food security; adequate caregiving resources at the maternal,
household and community levels; and access to health services and a safe and hygienic
environment — and incorporate specific nutrition goals and actions.

And according to the World Bank (9) the most important enabling factors for the
effects of food price rises to feed through into higher incomes for farmers, are for
them to produce and sell the ‘right’ produce.

Technology becomes more important relative to the household’s resource endowment,
and the selection of crops to be grown is based principally on their tradeability and the
price they are expected to command in local markets. The same technologies that enable
export also enable import, and the variety of food sources available to consumers is likely
to expand, making possible more complex and higher quality diets. Intensification of
staple food production, and opportunities for livestock, fish and fruit and vegetable
production, can also generate employment for landless or land-poor individuals.

But what about actual realities in actual countries and communities, identified by
professionals who know the environment, guided by the wisdom and knowledge of
the people who are most experienced? Our recent experiences in rural areas of
Bangladesh, working with the people of local communities, suggest that sources of
energy — mainly electricity at a reasonable price — is the number one priority for
sustainability of development. Also, without the fundamental fulfillment of women’s
empowerment and economic independence, adequate nutrition will not be
sustainable at household or community level. Additionally, much farmland in
Bangladesh is low-lying. The country cannot make tangible lasting achievements
without addressing the elemental impact of climate change. Again, the realities we
face in my country, and those faced in other countries, are different and often more
basic than those of a couple of generations ago. We live in a different world now.

Women's empowerment, access to appropriate technology, secure supplies of energy,
and development of relevant physical infrastructure such as roads and bridges, are
key nutrition-sensitive initiatives that need to be integrated into all serious policies
and programmes designed to reduce food insecurity, deficiencies, and all sorts of malnutrition. Governments of less-resourced countries, strongly supported by public interest organisations, social movements, and scientists and other experts, need to give top priority to specific nutrition programmes that are cost-effective and environmentally friendly, in this context.

A place in the SUN

Now back to vitamin A policies and programmes (1,2,4). In Bangladesh infant mortality has decreased from 47.8 per 1,000 live births in 2006 (11) to 33.1 in 2013 (12). Most of that improvement took place in children under 6 months of age, though children get their first vitamin A capsule only at 6 months of age. This also implies an urgent national radical policy rethink guided by independent scientists, led by Bangladeshi officials who are not committed to current policies and programmes.

The UN Scaling Up Nutrition initiative has a part to play in this, as do other UN programmes. SUN states that it is an inclusive and country-led movement. So it should have potential to reduce malnutrition. After all, it has top-level backing, committed political leadership, apparently vibrant civil society support, and partnerships with donors and groups linked with big business such as the Global Alliance for Improved Nutrition;

But realism is again needed. Taking the vitamin A programmes as one important example, the history of nutrition and associated interventions in countries such as my own is not good, and some of these interventions may be or are outdated as we prepare now for 2016-2030. Overall and ongoing governance can be weak. Nutrition programmes may include as partners, people and entities whose business is junk food. Priority is often given to commercial products whose cost is unsustainable and which ignore the impact on chronic diseases and impede sustainable locally grown policies and produce.

To be sustainable, development goals must focus on human development, not just business development, and must consider environmental, social and economic issues. Quantified obesity and chronic disease prevention and reduction goals must be included in the national programmes of low-income countries, along with women’s empowerment, education, green energy, and technology transfer.

The MOON also rises

So from Bangladesh, I call for a much needed and timely movement that is beyond the SUN. I call this MOON – the Movement for Open Opportunity for Nutrition (MOON). It will include and recognise nutrition-sensitive interventions, ensure appropriate distribution of resources on the basis of evidence and priority of the local community, seek to make them indisputably sustainable, and give co-equal priority to obesity, hypertension, diabetes and other chronic diseases. It will include initiatives that may be overlooked or neglected by SUN, such as the replacement of
vitamin A supplementation with food-based approaches. It will fight degradation of food supplies with junk and especially sugar-laden products.

All civil society organisations now linked with SUN also need to act for the MOON, which will not revolve round the SUN as a top-down imposed system but revolve independently and effectively around our Earth, maintaining a down-to-top approach. We appreciate SUN for its positive initiatives. These include breastfeeding promotion and involving the public sector in nutrition issues. MOON will recognise the need to overcome industry-led nutrition interventions and to take on the nutrition sensitive works neglected by SUN, given the power and influence of its corporate partners.

Here in Bangladesh, though solutions were introduced by our first prime minister Bangabandhu Sheikh Mujibur Rahman in 1972, and were supposed to have been reinforced in 1997 in our national plan of action for nutrition, effective actions and desirable achievements have often been stalled by environmental disasters and man-made calamities. So let MOON go into orbit!

Thus this is a call to have a MOON for sustainable improvement of global nutrition. Let MOON inspire us all towards a world with nutrition equity, not a world of nutrition traders. Let's move with MOON for the global uplifting nutrition and sustainable human development.

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**How to respond**

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