

WN *Hot stuff*

World Nutrition **Volume 5, Number 11, November 2014**

Journal of the World Public Health Nutrition Association
Published monthly at www.wphna.org/worldnutrition/

Development. Malnutrition. Vitamin A
Let food be our medicine



John Mason
Tulane University, New Orleans, Louisiana, US

Ted Greiner
Hanyang University, Seoul, South Korea

Roger Shrimpton
Tulane University, New Orleans, Louisiana, US

David Sanders
University of the Western Cape, Republic of South Africa

Joshua Yukich
Tulane University, New Orleans, Louisiana, US

Email for correspondence: masonj@tulane.edu

Access 1993 UN ACC-SCN report on Vitamin A here
Access May 2010 Cover here
Access May 2010 Editorial here
Access May 2010 Michael Latham on Vitamin A here
Access June 2010 letters in response to Michael Latham here
Access July 2010 letters in response to Michael Latham here
Access October 2010 Keith West, Rolf Klemm, Alfred Sommer on Vitamin A here
Access September 2012 Independent Science News Ted Greiner on vitamin A here
Access October 2014 IJE John Mason, Ted Greiner et al on Vitamin A here

Editor's note



This picture was first used to promote the universal vitamin A supplementation programme. It was the cover picture of the first issue of WN, introducing Michael Latham's commentary

The WN Editor writes: This month in *WN*, John Mason, Ted Greiner, Roger Shrimpton, David Sanders and Joshua Yukich discuss global policy to prevent and treat vitamin A deficiency. Their views derive from their paper *published elsewhere in October.* This is based on new literature reviews, knowledge of changing patterns of disease, and assessment of primary health care priorities. Current global material and professional commitment to 4-6-monthly very high doses of vitamin A in capsule form to young children (as shown above) remains massive and powerful. John Mason and his colleagues conclude that this policy is no longer justified, and that it should be phased out and replaced by food-based programmes.

The main points

WN has an interest here. In our first issue in May 2010, Michael Latham came to similar conclusions in his *'The great vitamin A fiasco'.* His main points are as follows. One, the case that the vitamin A capsule programme saves children's lives is not proven. Two, supplementation with medicinal levels of vitamin A could harm health. Three, immunisation against measles, and de-worming, or lack of them, confound the vitamin A capsule evidence. Four, externally administered programmes are likely to be unsustainable. Five, the capsule programme blocks food-based programmes. These include exclusive breastfeeding, and support of horticulture including of plant foods rich in carotenoids.

Response to Michael Latham's contentious commentary was dramatic. We published a commentary from the *Johns Hopkins School of Public Health* which opposed his view. We also received many letters which with one exception *supported his view.* These included letters from senior officials at the *UN Food and Agriculture Organization.*

In what follows here, the authors, three of whom have held *senior relevant positions in the UN system,* explain why they support food-based approaches to potential and actual vitamin A deficiency. The evidence and the justification, judged by many contributors to *WN* in 2010 to be compelling, is now stronger still, and even better attested. It is time for a change.

Introduction

John Mason, Ted Greiner, Roger Shrimpton, David Sanders and Joshua Yukich write:
The prevalence of vitamin A deficiency, which affects about one-third of children in middle- and low-income countries, is only falling slowly. This is despite extensive distribution and administration of periodic (4 to 6 monthly) high dose vitamin A capsules over the last 20 years. This programme now covers a reported 80 per cent of children in these countries.

This massive programme was motivated largely by an expectation of reducing child mortality, which stemmed from findings in the 1980s and early 1990s. But efficacy trials since 1994 have in most cases not confirmed a mortality impact of vitamin A capsules. Only one large scale programme evaluation has ever been published. This showed no impact on mortality among 1 to 6 year-old children. (This was the *Deworming and Vitamin A* or DEVTA trial ending in 2003, carried out in Uttar Pradesh, India).

Periodic high dose vitamin A capsules may have less relevance now with changing disease patterns. These notably include reductions in measles and diarrhoea. High dose vitamin A administered 6-monthly does not reduce prevalence of the deficiency itself, as estimated by low serum retinol. We propose as follows.

- There is no longer any evidence that intermittent high dose vitamin A programmes are having any substantial mortality effect, perhaps due to changing disease patterns.

- Frequent intakes of vitamin A in physiological doses, for example by food-based approaches, including fortification, and regular low dose supplementation – are highly effective in increasing serum retinol and reducing vitamin A deficiency.

- Therefore a policy shift is needed, based on consideration of current evidence. A prudent phase-over is needed towards increasing frequent regular intakes of vitamin A at physiological levels, daily or weekly, replacing the high-dose periodic capsule distribution programmes. Moving resources in this direction must happen sooner or later. It should be sooner.

Our full paper was published in October in the *International Journal of Epidemiology*. In the commentary that follows, we respond to four questions and points agreed between us and the *WN* editors. These are

- Why am I an author of this paper?
- Why are the issues raised important?
- Identify a couple of key issues
- What now needs to be done?

Why am I an author of this paper?



John Mason

I started in the right time, in the 1960s, and the right place, the UK Medical Research Council and University of Cambridge Dunn Nutritional Laboratories. Tommy Moore, Dunn deputy director from 1927 to 1965, did much of the early work on vitamin A there, and his 650 page monograph on vitamin A had been published in 1957. When I was there I saw the extensive effects of vitamin A deficiency on the gut function of experimental animals.

Twenty years later, now working at the United Nations as Secretary of the UN Sub-Committee (now Standing) on Nutrition (ACC-SCN), I was enthusiastic to promote broad vitamin A interventions, and see if they worked. But I was puzzled at being told, by one agency bureaucrat, that 'you can't use serum retinol to evaluate vitamin A interventions' (what did that really mean?). I was puzzled even more by failure to suggest a credible biological mechanism for mortality reduction from un-physiological intermittent megadoses, which apparently did not involve normal vitamin A metabolism. And then I was increasingly disappointed with the total – and seemingly deliberate – absence of evaluations.

When it became clear that vitamin A capsules had only a small effect on serum retinol, I mentioned this on several occasions to those who were promoting capsule programmes, and was dismissed. Some results showed that 3-monthly vitamin A capsule administration might shift serum retinol levels, but our own studies in the Philippines on 3-monthly capsule regimes showed that it did not.

In 2009 I was invited by Phil Musgrove to write a paper on vitamin A capsule programmes for the journal *Health Affairs*, of which he was a deputy editor in charge of global health coverage. I warned him that it would not say what he expected. He said fine, and he liked my draft.

Fate intervened, for Phil died in an accident the next year. It wasn't until 2013 that I got back to revising and resubmitting the paper. Outrage unprecedented in my experience ensued from the peer reviewers. Comments were along the lines of 'how dare I suggest that vitamin A capsules were anything else but marvellous life-savers'. The rejection made me determined to persevere. I had long discussions with my colleagues, and together we substantially revised and re-oriented the paper. In 2013

the vast Indian de-worming and vitamin A trial (DEVTA) was finally published, ten years after its completion. We sent a comment to *The Lancet*, which was rejected. *BMJ* accepted a comment. Then we were encouraged to submit to the *International Journal of Epidemiology*, which we did, and here we are.



Ted Greiner

My main concern has been 'donor misbehaviour'. It is beneath us as citizens of a shrinking world to use development assistance as a Trojan horse for political or economic objectives. This not only continues apace, it is getting worse, as new products like ready-to-use foods (Ready to Use Therapeutic Foods or RUTFs, Ready to Use Supplementary Food or RUSF, Lipid-Based Nutrient Supplements or LNS, and so on) gain the attention and funding that ought to go to community-based approaches that have been proved to reduce malnutrition sustainably.

I watched in horror for decades as the vitamin A capsule programmes displaced the already inadequate interest in dietary improvement that existed up until the 1990s. I observed how those promoting the capsule programmes even worked actively against food-based approaches, which they felt would slow full and rapid implementation of what they believed would save many lives right away.

At the International Vitamin A Consultative Group meeting in 1993, IVACG being the forum for policy discussions between those most engaged, I proposed that donors should fund both supplementation and food-based programmes and approaches simultaneously, with simple monitoring to decide when supplementation was no longer necessary,. This could be done perhaps district by district as had been in Tanzania in phasing out iodised oil capsules as iodated salt began to achieve adequate effectiveness. But the attractiveness of the 'magic bullet' solution seems to have a blinding quality about it and initial interest in that idea was quickly suppressed.



Roger Shrimpton

I have long had an interest in vitamin A nutrition. I first saw vitamin A deficiency 'in the flesh' in East Java as a Voluntary Service Overseas worker in 1973, when I did nutrition surveys in schools. I then saw at least one kid in most classrooms with keratomalacia. This is not something I will forget.

In the 1970s while working in Brazil at the Amazon Research Institute (INPA) in Manaus, our team set up the analytical methods and carried out surveys in the local population as well as looking at local foodstuffs for their carotene and vitamin A content.

Then in the late 1990s as chief of nutrition with the UN Children's Fund (UNICEF) in New York, I was heavily involved in mobilising support for vitamin A capsule programmes globally. At that time I was convinced by the conclusions of the 1993 Standing Committee on Nutrition (UN SCN) policy paper 13 by George Beaton, Reynaldo Martorell and others. This had reviewed the effectiveness of vitamin A supplementation programmes, and had concluded that these reduced mortality rates by about 23 per cent.

But more recently collaborating with John Mason in developing the 2010 UN SCN *Sixth Report on the World Nutrition Situation* we showed that despite high vitamin A capsule coverage (more than 80 per cent) in most lower and middle income countries, a third of young children were vitamin A deficient with little sign of improvement. We then flagged the need for new approaches. But little has changed since.



David Sanders

I have long been concerned about the use of 'magic bullets' when more accessible and effective items are available and much more sustainable. This is the case for vitamin A (which a varied diet can supply), packets of oral rehydration salt (ORS) (which gruels with added salt can supply), and ready-to-use therapeutic foods (RUTFs)(which energy-dense legumes and nuts can supply).

Vitamin A capsules, in common with these other products, require expensive and often fragile supply chains.



Joshua Yukich

As an epidemiologist and health economist focusing on infectious diseases mostly in the global South, I have had a longstanding interest in efficient use of resources to prevent child mortality. Thus, much of my work has focused on the use of insecticide-treated bed-nets and indoor residual spraying for malaria, one of the major global causes of mortality in children.

With all public health interventions, contextual factors change over time, and therefore the mix of interventions most efficient to prevent premature mortality also changes. This implies periodic review of the evidence base, with consideration of both time and place. Like many others I was impressed by the null results of the massive DEVTA trial of mega-dose vitamin A intervention, and its implications. I wanted to understand further the reasons for the outcome and the potential implications for policy.

Why are the issues raised important?

John Mason

I teach about nutrition in poor countries. I tell students that when people look back at the late twentieth and early twenty-first centuries, they will discover that there was a bizarre period when the industrialised countries shipped literally billions of cheap capsules for children to eat, all over the world, twice a year.

No-one knew – or tried to find out – if there was any effect. The huge and increasing opportunity cost was not considered. Hundreds of thousands of over-stressed health workers were pulled off their normal routine twice a year to hold child health days. These initially had a key use for supplementary immunisation. But as this succeeded, and was wound down, they basically gave a placebo – which may indeed have been the main effect.

None of this would stand up to a rigorous and objective evidence-based review. The reviews in which I have been involved have been stacked in favour of vitamin A capsule programmes. But that is what we now need.

Ted Greiner

Vitamin A and its impact on human health are important in their own right. If vitamin A capsules actually do reduce young child mortality substantially, then phasing them out needs to be quite slowly and carefully. If (or where) they do not have a substantial effect, then the money, time and commitment being used on them should be used for actions that really do work, and that are preferably of lasting value to entire communities, not just to one small segment (young children).

This segment, the current age group targeted by vitamin A capsule programmes, is not even the one in which most young child mortality is found today in most countries – it is in the first months of life.

If women's nutrition were improved before and during pregnancy, perhaps much of this early mortality would be reduced. Food based approaches could perhaps have achieved that by now if all the attention and resources given to supplementation had gone to more sustainable approaches.

For several decades now I have seen examples at many levels of how implementation of all-or-nothing pushes for supplementation have inhibited and suppressed efforts to achieve solutions for vitamin A deficiency by way of dietary improvement and food fortification (the latter because policy-makers fear that young children will be even more at risk of side effects from overdosing). Supplementation thus may actually have done harm overall, even if it was effective in the early years (which was never proven by means of any published effectiveness trial).

Roger Shrimpton

Mega-dose vitamin A capsule programmes have become an obstruction to the elimination of vitamin A deficiency. They were always considered a 'stop –gap' measure until more sustainable and effective interventions were developed. But they have become 'the solution'. In consequence a half of all the children in Asia and Africa continue to suffer from vitamin A deficiency.

David Sanders

The issues raised apply to vitamin A but are also generic, as indicated above. With vitamin A additional issues are raised. These include involvement of the private pharmaceutical sector (which is always expensive), and the emergence of new 'non-profits' which coordinate such initiatives and consume a significant proportion of donor assistance.

These issues are important in effect as 'markers' of an approach to health that is in conflict with the need for universal primary health care (PHC).

Joshua Yukich

Over the past twenty years, measles vaccination coverage has massively increased, and with this there have been major reductions in child mortality rates, including from measles and diarrhoea. Interventions once relevant for child mortality prevention in some places may need to be replaced.

The null results of the DEVTA trial were a jarring reminder that intervention effects may well not be uniform from place to place, or over time. When evidence begins to suggest that conditions which once made an intervention necessary and efficient may not be uniformly present any longer, there is a need to understand what has changed, and what interventions might be right in different places or at different times.

Identify a couple of key issues

John Mason

The opportunity cost of displacing health care in favour of an intervention which is now based primarily on magical thinking, seems to me a larger ethical issue than concern for 'withdrawing a life-saving intervention'. This is one ground on which the vitamin A capsule programme should be assessed.

The key policy debate of the moment is whether malnutrition can best be prevented through community-based programmes (for which the evidence is reasonably good) or through supply-side interventions (for which most of the funds cycle back to western corporations – 70 per cent of the proposed annual overall requirement of $US 10 billion, as estimated by the World Bank). I think we need another paradigm shift, away from top-down interventions and towards local solutions.

Above all this, nutritionists should, in my view, take professional responsibility for providing objective and evidence-based advice, and always be willing to change this as conditions change and data change.

Even more, nutritionists should be far more careful to distance themselves from commercial interests. It is absolutely essential that their opinions and advice are not tainted by possible competing interests from their association with these interests.

This too is an ethical issue. It is particularly unfortunate when such interests are in positions of responsibility within the international public sector, whose independence (which, when I was a United Nations official, was in our oath of office) is increasingly under attack.

Ted Greiner

Vitamin A has little impact on morbidity for any disease except measles and probably some forms of or causes of diarrhoea. This has been known for a long time. It is not logical that mega-dose supplementation could have an impact on mortality from other diseases when it has no impact on morbidity. Now that mortality linked to measles and diarrhoea is greatly declining, it makes sense that the mortality reducing impact of vitamin A supplementation will also greatly decline. Our evidence shows this to be the case.

Roger Shrimpton

Originally promoted as a blindness prevention strategy in Indonesia in the 1970s, vitamin A capsule programmes were then serendipitously discovered to reduce young child mortality.

Our contention is that these findings are no longer true today. The burden of disease in most lower and middle income countries has changed dramatically since the 1980s when capsule programmes were shown to reduce mortality. Increases in immunisation and breastfeeding rates among young children, as well as oral rehydration therapy in some places, have reduced the importance of measles and diarrhoea as young child killers. The mortality-reducing effect of capsules is no longer evident, most likely because of these changes in disease burden.

Subclinical vitamin A deficiency is important and needs to be addressed, especially in the countries of Africa and Asia where more than half of young children are so affected. Biennial mega-dose capsule campaigns do not reduce subclinical vitamin A deficiency.

David Sanders

One issue is the opportunity costs of such 'vertical' programmes, which undermine 'horizontal' health work by sucking up human and material resources.

Joshua Yukich

If the current policy debate pits community based nutrition interventions against vitamin A capsules, it may be a bit misaligned. These interventions are not globally mutually exclusive. I think the debate should focus on determining where and when vitamin A capsule programmes are effective, and where and when other interventions may be more effective.

The results of DEVTA alone do not refute the efficacy of vitamin A capsules in all times and places. They do show a need better to understand the causes of

heterogeneity in the various trial results, including secular trends and underlying mortality patterns. Where there are alternatives to vitamin A capsules that may do more good with similar or less investment, it is probably not wise to continue to devote resources to less efficient interventions.

What now needs to be done?

John Mason

What is needed now is a clearly objective, independent, disinterested, and evidence-based review of the situation. I believe this will cause the paradigm finally to shift. WHO could do this, but their recent reviews of vitamin A have not moved the field ahead.

Previously, the UN's Advisory Group on Nutrition would have been the place to centre such work. But the group no longer exists. The dire condition of international nutritional science's application to policy is partly reflected in the difficulty of identifying a clearly objective high quality process. Suggestions will be welcome.

Ted Greiner

Like the tobacco industry in the past and the oil and junk food product industries now, when any vested interest feels threatened, it fights back and tries to deflect attention. If pushed too hard, it even takes to denigrating its opponents. This is pretty much what happened with Michael Latham and with *World Nutrition* as a result of publication in *WN* of his May 2010 commentary 'The great vitamin A fiasco'.

We will now be told that our evidence and conclusions are based on research that has weaknesses and limitations. But so does all research. We will be told that phasing out vitamin A supplementation would be an unethical thing to do. This is patently untrue. We must stand firm and do all we can to ensure that the shift in paradigm comes sooner rather than later.

Roger Shrimpton

Our research confirms the need to revisit global vitamin A programmes. It confirms the need urgently to shift the emphasis of these programmes away from biennial mega-dose capsule campaigns, and towards food based approaches, by means of locally produced foods that are rich in vitamin A, and fortification.

Advocacy is needed, to halt the vitamin A capsule 'status quo' and to move policies and programmes in this direction.

David Sanders

What is needed now is dissemination of the insights of our paper, and advocacy for policy change. Further work on the opportunity costs of vitamin A capsule and other products is also needed.

Joshua Yukich

Rigorous, independent programme evaluations that focus on measurable health outcomes, child mortality, and biomarkers of vitamin A deficiency in varied contexts, are needed. These should help to understand the causes and correlates of the outcomes of vitamin A capsule programmes, and other types of nutrition programmes, now that vaccination programmes are improved and diarrhoea mortality is reduced, compared with the times when the vitamin A capsule programme was developed.

Conclusion



Another photograph taken in the field to show how the very high doses of vitamin A contained in capsules are given to young children. The programme involves massive human and material resources

- High-dose vitamin A capsules (200,000 International Units) given 6-monthly, are as reported, being provided to some 80 per cent of 1-5 year-old children in low and middle income countries, amounting to 8 billion capsules to date. The purpose is to reduce 1-5 year-old child mortality.
- However, the efficacy trials which support the programme were conducted over 20 years ago. Only one programme evaluation has been done (DEVTA in India, 1999-2004), and this showed no mortality impact. Capsules affect mortality from

diarrhoea and measles. This has dropped sharply. Thus current impact is likely to be small (say, 3-5 per cent) or non-existent.

- Capsules given 6-monthly do not sustain reduction in vitamin A deficiency itself (measured as low serum retinol), which affects about 30 per cent of children in low and middle-income countries. Deficiency can be reduced by increased regular intakes of vitamin A at physiological levels, by means of improved diets, fortification, and frequent (daily or weekly) supplements. Unlike high-dose capsule, these are also safe for reproductive-age women.
- Therefore it is proposed that a broader approach to reducing vitamin A deficiency, in line with long-standing policy recommendations, should now be adopted. This means shifting judiciously from periodic vitamin A capsules to increasing regular intakes, while monitoring changes in vitamin A deficiency.

There is no longer any good reason for inaction on the issue of vitamin A deficiency and how this should be prevented and treated. The current predominant practice of universal administration of high-dose vitamin A capsules to young children is unsatisfactory. It should be phased out. Instead, economical and sustainable programmes centred on improvement of diets as a whole, preferably with locally sourced foods, should now have foremost priority, in principle and practice.

Status

Readers may make use of the material in this commentary if *WN* is cited. Cite as: Mason J, Greiner T, Shrimpton R, Sanders D, Yukich J. Development, Malnutrition. Vitamin A. Let food be our medicine. *[Hot stuff] World Nutrition* November 2014, **5**, 11, 940-952. All *WN* contributions are obtainable at www.wphna.org/

World Nutrition commentaries are reviewed internally or by invitation. Contributions to *WN* are the responsibility of their authors. They should not be taken as the view or policy of the World Public Health Nutrition Association unless this is explicitly stated.

How to respond

Please address letters for publication to wn.letters@gmail.com. Letters should usually respond to or comment on contributions to *World Nutrition*. More general letters will also be considered. Usual length for main text of letters is between 350 and 1000 words. Letters are edited, may be developed, and once edited are sent to the author for approval.