Internal Briefing Note  
On Need for Rethinking Vitamin A Policies

To: Regional and Country Offices of Global Alliance for Vitamin A (GAVA) Partners¹  
Fr: Roland Kupka (UNICEF), Alison Greig (MI) and Rolf Klemm (HKI)  
Re: Informal Briefing Note re Mason et al article entitled ‘Vitamin A policies need rethinking’ published online in the International Journal of Epidemiology on October 10, 2014  
Date: 2 November 2014

Executive Summary: Rethinking public health policy when situations change has value, but Mason and colleagues offer no convincing evidence for withdrawing vitamin A supplementation (VAS) in settings where vitamin A deficiency (VAD) remains a public health problem. Indisputable evidence from large and rigorously conducted community trials in Africa and Asia shows that VAS saves children’s lives. Providing semi-annual VAS to children in vitamin A deficient populations is strongly recommended by recent WHO guidelines which carefully weighed the body of evidence for this intervention. The calls for addressing the underlying causes to address VAD are not new and are fully supported by GAVA partners.

Purpose: The purpose of this internal briefing note is to guide country responses and address questions that may arise from the recently published article by Mason et al, entitled ‘Vitamin A policies need rethinking’¹. In this note, we show that the evidence for vitamin A supplementation (VAS) as a child survival intervention is strong and that the intervention is fully supported by World Health Organization guidelines; that VAD remains a global public health problem and that programs addressing its underlying causes need to be scaled up; and that shifts from universal VAS are only indicated in settings where improvements in VA status, child survival, and dietary VA intake are achieved.

Claims made by Mason et al:

Claim 1: There is no longer any evidence that intermittent high-dose VAS has a substantial mortality effect, perhaps due to changing disease patterns

Response:

1. We agree that the epidemiologic landscape has changed since the first VAS trials were published in the early 1990s. Overall, child mortality rates have declined by 49% since 1990², but the rate of decline has been slowest in Oceania, sub-Saharan Africa and Asia. Likewise, the proportionate cause-specific mortality has also changed. In 1990, the three main killers were pneumonia (21% of under-5 mortality; U5MR), diarrhea (20%), and measles (7%)³, while in 2010 the main killers were pneumonia (18%), diarrhea (11%) and malaria (7%)⁴.

2. These mortality declines and changes in causes of death however do NOT rule out a child survival benefit in many contexts. Why?

¹ GAVA is an informal partnership between Helen Keller International, Johns Hopkins University, Micronutrient Initiative, and the United Nations Children’s Fund.
In all, 54 countries globally still have a high U5MR (defined as ≥50 per 1000 live births).\(^5\) A large proportion of these deaths are caused by infections. Furthermore, in these high-mortality countries, VAD is also likely to be high\(^6\), thus reinforcing the need to maintain VAS and other VA interventions.

The argument that VAS will have an insignificant impact on mortality due to lower proportional death rates from measles and diarrhea has several weaknesses and lacks strong evidence.

- Only a fraction of all deaths prevented in the early VA trials were attributed to measles. In fact, in 1990, global measles deaths accounted for only 7% of U5 mortality 1990\(^3\). The measles-specific death rate was even lower in the Nepal VAS mortality trial that was part of the first meta-analysis \(^7\).
- Where U5MR, VAD and infectious disease rates are low, the mortality effect of VAS will likely be reduced. Nevertheless, we must bear in mind that the original VAS studies observed mortality impacts in settings with a wide range of mortality and morbidity rates \(^8\).

3. The disputed and controversial DEVTA\(^9\) program evaluation study is put forth by Mason et al as the evidence needed to refute the mortality benefit of VAS. However:

- The DEVTA study suffered from important methodological limitations related to supplementation adherence and vital event monitoring systems, as acknowledged by other scientists\(^10-12\), but not by Mason et al.;
- It is unwise to base a global policy shift on a single study. Instead findings from the DEVTA study should be viewed in light of the larger body of evidence on VAS and child survival. Recently, the WHO examined evidence from all 17 trials (11 in Asia, 5 in Africa and 1 in Latin America) conducted to date for all-cause mortality. Findings revealed that VAS reduces the overall risk of death by 24% (risk ratio (RR) 0.76; 95% confidence interval (CI) 0.69–0.83). When adding the DEVTA findings to the analysis, the all-cause mortality benefit of VAS remained statistically and clinically significant at 12% (RR 0.88; 95% CI 0.84–0.94)\(^19\).

Claim 2: High-dose VAS programs are ineffective because they do not provide lasting improvements in VA status. On the other hand, frequent intakes of VA in physiological doses (e.g. through food-based approaches, including fortification, and through regular low-dose supplementation) are highly effective at reducing VAD

Response:

1. The success of high-dose VAS programs should be judged by their appropriate targeting to populations with high VAD, equitable coverage, and quality implementation. Currently, about 80 countries promote periodic VAS among preschoolers based on a >20% prevalence of VAD (defined as serum retinol < 0.70 µmol/l) in most recent surveys or high child mortality (U5MR ≥ 50 per 1000 live births). The global coverage of the recommended two VAS dosages per year is 70%, and high-dose VAS has strong links to U5MR reductions in different settings\(^10,11\).

2. VAS should not be expected to improve VAD as the underlying cause is a chronically low dietary intake of VA. In this regard, GAVA partners compiled the required evidence to illustrate that improving VA status of children (as measured by serum retinol) is only transient (usually <2 months) and that the prevalence of VAD remains high even in settings with good VAS coverage \(^12\). Low or marginal serum retinol distributions in areas with high VAS coverage rates do not signify program failure, but rather suggest the need to continue VAS while working to improve dietary VA intakes through other interventions such as regular and adequate consumption of VA-rich foods.
3. There is good evidence to suggest that an adequate amount of VA through the diet is the optimal approach to prevent VAD. As a result, GAVA partners support programs on optimizing breastfeeding practices, improving the quality of complementary foods (including home fortification with micronutrient powders, industrial fortification of staple foods, biofortification), as well as disease-control and nutrition-focused agricultural programs. Even though programs such as home fortification with micronutrient powders and fortification of cooking oil promise to become important sources of VA, further strengthening of VAD control programs is needed.

Claim 3: A policy shift is needed, replacing high-dose VAS programs with programs to increase frequent, regular intake of VA at physiological levels

Response:

1. In the same way they are used to determine if VAS is needed, country-level estimates of VA deficiency, child mortality, and documented shifts in dietary intakes should be used to guide the decision whether high-dose VAS programs should be phased out.

2. Mason et al create a scenario in which either high-dose VAS programs take place OR programs to improve VA intakes. However, we believe that these programs should be implemented in parallel, i.e. that VAS programs are needed while programs to improve VA intakes are scaled up.

3. VAD continues to be a global public health problem that puts children at increased mortality risk. Globally 33% of children under the age of five years are VA deficient based on low serum retinol (<0.70 µmol/L) with the highest prevalence estimates in Africa (42%) and Asia (34%) 15. WHO firmly recognizes the importance of addressing VAD-related mortality in these settings. In its 2011 guidelines, WHO states: ‘High-dose VAS is recommended in infants and children 6–59 months of age in settings where VAD is a public health problem’ 16.

4. GAVA partners support scaling back VAS only when governments can assure and verify that vulnerable populations have a sustained and adequate vitamin A status from dietary and other interventions. An expert group convened by GAVA in 2012 (and attended by Mason) proposed a framework to help governments assess if and when a shift from universal VAS among children 6-59 months is justified 17. This framework, based on earlier published work 12, has been field tested and will be released in 2015. The framework recommends the following:

- Children need a dependable dietary safeguard in place before VAS is withdrawn. Fortification and other dietary interventions need to produce documented, sustained, normal vitamin A levels in risk groups before VAS is scaled back.
- Any scale back of semi-annual universal VAS should be guided by a population’s VA status. Evidence documenting a sustained low prevalence (e.g. <5%) of subclinical VAD may be used to justify scaling back or withdrawing universal VAS. GAVA partners recommend at least two nationally representative cross-sectional surveys documenting <5% of low serum retinol (<0.70 µmol/l) would indicate that universal VAS would probably confer no further benefit.
- Countries that have embarked on VA fortification and other food-based approaches, but whose prevalence of low serum retinol among children exceeds 5% for instance, should continue VAS along with these other interventions until evidence from at least two nationally representative cross-sectional surveys confirm VAD is no longer a public health problem.
- Countries for which there is little or no evidence of adequate VA intake or who have not made large gains in reaching most children with food-based interventions that ensure regular and adequate VA
intake, should be strongly encouraged to achieve regular high (i.e. ≥80%) VAS coverage among preschoolers, while strengthening complementary interventions such as VA fortification, micronutrient powders, dietary diversity, nutrition education and prevention and control of infectious disease. Investing resources in measuring VA status in the population should probably be delayed until there is evidence that the food-based approaches have reached a large enough scale and quality to likely result in improved dietary intake of VA.

Conclusions

Re-examining VA policies and programs is valuable in the context of a changing health and nutrition landscape. But Mason and colleagues offer no new or persuasive evidence to withdraw VAS in settings with high U5MR and VAD. While they restate the known fact that VAS neither reduces VAD nor improves VA status, they wrongly conclude that as a result VAS programs are not effective. The authors’ call for shifts in national VAS programs are not new but were in fact developed during a 2012 GAVA workshop. Scaling back universal VAS is justified only when evidence shows that normal VA levels are sustained through adequate dietary intakes from food-based and other solutions. Because VAS can save children’s lives, there must be strong and compelling evidence to justify scaling back this intervention. Evidence put forth by Mason and colleagues is neither strong nor compelling. Vitamin A deficiency will not be eliminated until populations achieve normal vitamin A status through dietary intake and other interventions that address the underlying causes of deficiency. In the meantime, periodic VAS remains an important child survival intervention.

Recommendations

1. We urge decision makers in national governments and donor agencies to maintain support for VAS programs as an evidence-based child survival intervention in settings with high prevalence of VAD and child mortality.
2. We pledge our support to improve the implementation of twice-yearly VAS programs to reach vulnerable populations with high VAD and U5MR, ensure integration in health systems, improve monitoring systems, and facilitate co-delivery with other high-impact child survival interventions.
3. We support the strengthening of interventions to address the unacceptably high prevalence of VAD worldwide. Such interventions include optimizing breastfeeding practices, improving the quality of complementary foods (including home fortification with micronutrient powders), industrial fortification of staple foods, biofortification, as well as disease-control and nutrition-focused agricultural programs.
4. We promote the generation of high-quality population-based data on VA (and other micronutrient) status, intervention coverage and quality, as well as dietary intake in order to guide program and policy decisions.
5. We encourage the use by national governments of the GAVA decision-making framework (to be released in early 2015) to guide decisions on shifts from universal VA supplementation among children 6-59 months.
Work cited