

a rigorous analysis of available efficacy data from randomised controlled trials from different settings, which informed the delivery of vitamin A in deficient populations.<sup>3,4</sup>

Members of our three agencies attended a 2 day consultation in 2008, in Oxford, UK, which reviewed the DEVTA study, provided constructive comments, and discussed globally relevant lessons on the challenges facing large delivery programmes and their assessment, in terms of design, implementation, and resources needed. Many concerns were raised that, in our opinion, have not been fully addressed, either in the Article<sup>1</sup> or in the Comment.<sup>5</sup> It was agreed that these proceedings would be made publically available and so we call on the authors to share the proceedings in order to have a fully informed and ethical public debate.

We concur with the authors of the Comment<sup>5</sup> that science should inform policy. We therefore call on the appropriate normative bodies to take account of both the DEVTA study and the Oxford proceedings when assessing what, if any, adjustments should be made in the estimation of the expected effect of vitamin A supplementation on child mortality, and to provide any appropriate changes to vitamin A supplementation policy. As representatives of agencies dedicated to saving children's lives, we are gravely concerned by the call in the Comment<sup>5</sup> for new controlled trials of such supplementation. Any further controlled trials would inherently deprive those children assigned to control groups of a proven, life-saving intervention.

We urge decision makers in national governments and donor agencies to continue to provide strong support for vitamin A supplementation as a core, evidence-based child survival intervention that has been used so effectively in the past decade in combination with other proven interventions to address underlying determinants of vitamin A deficiency, including food-based approaches.

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- 1 Awasthi S, Peto R, Read S, Clark S, Pande V, Bundy D, and the DEVTA (Deworming and Enhanced Vitamin A) team. Vitamin A supplementation every 6 months with retinol in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial. *Lancet* 2013; **381**: 1469–77.
- 2 WHO. Guideline: vitamin A supplementation in infants and children 6–59 months of age. 2011. [http://whqlibdoc.who.int/publications/2011/9789241501767\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241501767_eng.pdf) (accessed March 14, 2013).
- 3 Mayo-Wilson E, Imdad A, Herzer K, Yakoob MY, Bhutta ZA. Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. *BMJ* 2011; **343**: d5094.
- 4 Imdad A, Herzer K, Mayo-Wilson E, Yakoob MY, Bhutta ZA. Vitamin A supplementation for preventing morbidity and mortality in children from 6 months to 5 years of age. *Cochrane Database Syst Rev* 2010; **12**: CD008524.
- 5 Garner P, Taylor-Robinson D, Sachdev HS. DEVTA: results from the biggest clinical trial ever. *Lancet* 2013; **381**: 1439–41.

The results of the DEVTA study<sup>1</sup> of vitamin A supplementation delivered through an Indian Government programme show that this particular programme did not reduce mortality. This could be a worthwhile finding if the reasons for the failure were elucidated—eg, were supply chains properly set up and implemented and was the supplement delivered to those who could most benefit? Sommer and colleagues<sup>2</sup> addressed the methodological shortcomings of the trial, but in our view the most important issue is that programme assessments need more complex designs than do biological efficacy trials.

Causal chains in large-scale programmes are long and complex,

and therefore careful documentation of what takes place at all levels in such chains is essential.<sup>3</sup> These questions were only partly addressed in a non-random opportunistic subsample of 2106 of the million children in the study, who were likely to be easily reached and therefore received both the supplement and the validation visits. There is thus no plausible evidence that the intervention was or was not given to those who could most benefit.

Programme assessments must address complex causal pathways, including bottlenecks to delivery and use.<sup>4</sup> By contrast, biological efficacy studies must concentrate on establishing that vitamin A is actually ingested by most, if not all, children. As a consequence, these different types of study should never be included together in meta-analyses, no matter how well they are done.

Both biological efficacy and programme studies are important, so we heartily concur with the recommendation that “funders should invest—and invest heavily—in such studies”.<sup>5</sup>

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- 1 Awasthi S, Peto R, Read S, Clark S, Pande V, Bundy D, and the DEVTA (Deworming and Enhanced Vitamin A) team. Vitamin A supplementation every 6 months with retinol in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial. *Lancet* 2013; **381**: 1469–77.
- 2 Sommer A, West KP, Martorell R. Vitamin A supplementation in Indian children. *Lancet* 2013; **382**: 591.
- 3 Arifeen SE, Hoque DME, Akter T, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. *Lancet* 2009; **374**: 393–403.
- 4 Habicht JP, Peltó GH, Lapp J. Doing impact evaluation 13. Methodologies to evaluate the impact of large scale nutrition programs. Washington DC: World Bank, 2009.
- 5 Garner P, Taylor-Robinson D, Sachdev HS. DEVTA: results from the biggest clinical trial ever. *Lancet* 2013; **381**: 1439–41.