Vitamin A distribution in danger: should we worry?

In an editorial (May 12, p1866),[1] *The Lancet* supported UNICEF's call for action to prevent a drop in high-dose vitamin A supplementation coverage as the important delivery vehicles, the national oral polio vaccine (OPV) campaigns, are coming to an end. This is reasonable if vitamin A supplementation is an important intervention—but is it?

The policy to provide vitamin A supplementation twice per year to children aged 6–59 months was based on eight trials from the late 1980s and early 1990s.[2] However, results of two recent trials[3,4] published in 2013 and 2014 showed no effect of vitamin A supplementation on overall survival, and there are other reasons to question the continuation of vitamin A supplementation.[5]

Few studies have assessed the effect of vitamin A supplementation campaigns on survival. In Guinea-Bissau, the effect of these campaigns depended on vaccination status (table). Vitamin A supplementation was associated with survival benefits when given with or after measles vaccine, but not with or after diphtheria-tetanus-pertussis vaccine.[6,7] In an assessment of national campaigns, OPV campaigns were associated with survival benefits (mortality rate ratio 0·81, 95% CI 0·68–0·95), but campaigns with OPV plus vitamin A supplementation or vitamin A supplementation alone had no effect, with a mortality rate ratio of 1·10 (0·82–1·48) for OPV plus vitamin A supplementation, and 1·04 (0·80–1·35) for vitamin A supplementation alone.[8]

To our knowledge, no other recent study has assessed the effect of vitamin A supplementation campaigns on survival. Therefore, the available data suggest that vitamin A supplemen-tation campaigns nowadays have no overall effect, the effect can vary by vaccination status, and vitamin A supplementation might be harmful in certain subgroups. Perhaps we should deplore that OPV campaigns are being stopped if they are associated with improved survival,[8] but there seems to be no reason to fear that reducing vitamin A supplementation coverage will decrease overall survival. Is it not time to spend sparse resources more wisely?

	Adjusted mortality rate ratio (95% CI) comparing VAS campaign participants with non-participants
2003[5]	
All	1·11 (0·59–2·08)
VAS co-administered with MV	No deaths for VAS plus MV
VAS co-administered with DTP	3·04 (1·31–7·07)
p value for test of same effect for VAS co-administered with MV and VAS co-administered with DTP	0·0005
2007–08[6]	
All	0·78 (0·46–1·34)
VAS after MV as most recent vaccine	0·34 (0·14–0·85)
VAS after DTP as most recent vaccine	1·29 (0·52–3·22)
p value for test of same effect for VAS after MV as most recent vaccine and VAS after DTP as most recent vaccine	0·04

MV=measles vaccine. DTP=diphtheria-tetanus-pertussis vaccine.

Table: **Mortality effects of vitamin A supplementation (VAS) campaigns by vaccination status in Guinea-Bissau**

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1 The Lancet. Vitamin A distribution in danger. *Lancet* 2018; **391:** 1866.
2 Beaton GH, Martorell R, Aronson KJ, et al. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. Nutrition policy discussion paper no. 13. Geneva: United Nations, Administrative Committee on Coordination, Subcommittee on Nutrition, 1993.
3 Awasthi S, Peto R, Read S, Clark S, Pande V, Bundy D. 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.
4 Fisker AB, Bale C, Rodrigues A, et al. High-dose vitamin A with vaccination after 6 months of age: a randomized trial. *Pediatrics* 2014; **134:** e739–48.
5 Mason JB, Benn CS, Sachdev H, West KP Jr, Palmer AC, Sommer A. Should universal distribution of high dose vitamin A to children cease? *BMJ* 2018; **360:** k927.
6 Benn CS, Martins C, Rodrigues A, et al. The effect of vitamin A supplementation administered with missing vaccines during national immunization days in Guinea-Bissau. *Int J Epidemiol* 2009; **38:** 304–11.
7 Fisker AB, Aaby P, Bale C, et al. Does the effect of vitamin A supplements depend on vaccination status? An observational study from Guinea-Bissau. *BMJ Open* 2012; **2:** e000448.
8 Andersen A, Fisker AB, Rodrigues A, et al. National immunization campaigns with oral polio vaccine reduce all-cause mortality: a natural experiment within seven randomized trials. *Front Public Health* 2018; **6:** 13.

In an editorial,[1] the Editors lament the fact that vitamin A distribution has reached a 6-year low, according to a UNICEF report. However, vitamin A supplementation was never intended to be a long-term sustainable strategy, as reminded by Michael Latham,[2] who called attention to the "great vitamin A fiasco" in 2010.

Although the cost-effectiveness of vitamin A supplementation has been demonstrated in controlled trials, its