Rapid Evidence Review

[30th, Nov. 2020]

What can research evidence tell us about:

Fortification of staple foods with vitamin A as a policy option to reduce vitamin A deficiency

Key messages

- The findings of this review suggest that the effect of fortification of staple foods with vitamin A alone on serum retinol concentrations (an indicator of vitamin A stores in the body), subclinical vitamin A deficiency (serum/plasma retinol of 0.70 µmol/L or less), and clinical vitamin A deficiency (night blindness) is uncertain.
- In comparison with provision of unfortified foods, provision of staple foods fortified with vitamin A plus other micronutrients probably reduces the risk of subclinical vitamin A deficiency, but may not increase serum retinol concentration.
- Based on the best available evidence we found in this review (which is with high quality), vitamin A supplementation (VAS) may still be the best strategy to prevent disease and death from vitamin A deficiency (VAD) in children aged 6 to 59 months. However, the review also acknowledges that VAS may not be the long-term solution to control VAD. Food distribution programmes and horticultural developments may provide more permanent relief to VAD.

⇒ Implications for policy and practice

- It is **uncertain** whether fortifying staple foods with vitamin A alone reduces the risk of subclinical and clinical VAD as the certainty of the evidence is very low. Therefore, policy makers or programme managers should take note of this to be guided with respect to the expected outcomes as they formulate policy and plan for implementation of mandatory mass fortification.
- This review also suggests **maintaining** the policy of universal supplementation for children under five years of age in populations at risk of VAD.

⇒ Implications for research

- It is important to know if there are differences in the estimated effects by food staple. Other contextual factors that need to be checked include that the foods selected for fortification are on the basis of the food consumption practices, stability, production and marketing characteristics, and cost.

Where did this Rapid Evidence Review come from?

This document was prepared in response to a specific question from Food Science and Nutrition Directorate (FSND) of EPHI.

It was prepared by Knowledge Translation Directorate, Ethiopian Public Health Institute, Addis Ababa, Ethiopia

✚ Included:

- **Key findings** from research
- **Considerations about** the relevance of this research for policy decisions in Ethiopia.

✖ Not included:

- Recommendations
- Detailed descriptions

Short summary

Background:

Vitamin A deficiency (VAD) occurs when there is an insufficient intake or poor absorption or excessive loss of vitamin A. VAD is a major nutritional concern, especially in lower-income countries such as Sub-Saharan Africa and South Asia. It is most prevalent among young children and pregnant women. It is the leading cause of preventable blindness in children and pregnant women, and is associated with an increased risk of mortality in children.

In Ethiopia, although the prevalence of night blindness and Bitot's spot had shown a reducing pattern from 1990 to 2019, the magnitude still remains a moderate public health problem while the subclinical vitamin A deficiency (serum value ≤0.70 µmol) is a severe public health problem based on the available evidence.

Experiences from different countries and evidence from researches indicate different measures to prevent and control micronutrient malnutrition including VAD. These include **direct measures** of food-based approaches that increase vitamin A intake, including increased production and consumption of vitamin A rich foods; food fortification with vitamin A, vitamin A supplementation; and **indirect public health measures** to control disease frequency.

The primary focus of this review; however, is to assess the effectiveness of food-based approaches mainly fortification of staple foods (including edible oil) with vitamin A and vitamin A supplementation (VAS) for reducing vitamin A deficiency and improving health related outcomes among young children and women of reproductive age.

Question/s:

- Is fortification of staple foods (including edible oil) with Vitamin A effective to reduce VAD among young children and women of reproductive age?
- Is vitamin A supplementation (VAS) effective to reduce VAD and improve health related outcomes among young children and women of reproductive age?

Review findings:

The findings of the review based on the questions above are summarized as follows:

1) Impact of fortifying staple foods (including edible oil) with Vitamin A

- The findings from this review suggest that the effect of fortification of staple foods with **vitamin A alone** on serum retinol concentrations (an indicator of vitamin A stores in the body), subclinical vitamin A deficiency (serum/plasma retinol of 0.70 µmol/L or less), and clinical vitamin A deficiency (night blindness) is **uncertain**.
- In comparison with provision of unfortified foods, provision of staple foods fortified with **vitamin A plus other micronutrients** **probably reduces** the risk of subclinical vitamin A deficiency;

however, **may not increase** serum retinol concentration.

- Compared to no intervention, staple foods fortified with **vitamin A plus other micronutrients** **may increase** serum retinol concentration, although it is **uncertain** whether the intervention reduces the risk of subclinical vitamin A deficiency as the certainty of the evidence is very low.
- In this review it was not possible to estimate the effect of staple food (including edible oil) fortification on outcomes such as mortality, morbidity, adverse effects, congenital anomalies, or breast milk vitamin A, as no trials included these outcomes.

2) Impact of Vitamin A supplementation (VAS)

- Vitamin A supplementation is associated with a clinically meaningful reduction in morbidity and mortality in children. This result suggests maintaining the policy of universal supplementation for children under five years of age in populations at risk of VAD.

Conclusion:

Based on the best available evidence (which is with high quality) we conclude that, vitamin A supplementation (VAS) may still be the best strategy to prevent disease and death from VAD in children aged 6 to 59 months. However, the review recognizes that VAS may not be the long-term solution to control VAD. Food distribution programmes and horticultural developments may provide more permanent relief to VAD.

For the outcome of subclinical vitamin A deficiency, for which fortification is estimated to have a better effect, there are not enough studies for different food staples. It is also uncertain whether fortifying staple foods with vitamin A fortification alone reduces the risk of subclinical and clinical vitamin A deficiency as the certainty of the evidence is very low. Thus, policy makers and programme managers should take note of this and should be guided with respect to the expected outcomes as they formulate policy and plan for implementation of mandatory mass fortification. It is important to know if there are differences in the estimated effects by food staple. Other contextual factors that need to be checked include that the foods selected for fortification are on the basis of the food consumption practices, stability, production and marketing characteristics, and cost.

1. Introduction

1.1 Background

Vitamin A deficiency (VAD) occurs when there is an insufficient intake of vitamin A which is primarily found in milk and breast milk, eggs, and liver as well as yellow, orange, and dark green vegetables and fruits, and in fortified foods or supplements. VAD can also be caused by poor absorption or excessive loss of vitamin A (Keith P. West, Gernand and Sommer, 2007).

Vitamin A deficiency is a major nutritional concern, especially in lower-income countries such as Sub-Saharan Africa and South Asia. It is most prevalent among, young children and pregnant women (Stevens *et al.*, 2015). VAD can cause preventable night blindness in pregnant women and children and it is also associated with an increased risk of mortality in children (Imdad *et al.*, 2017).

1.2 Measurements and Indicators for VAD

A number of methods are used to assess vitamin A deficiency including dietary patterns, biomarkers, clinical examination and histopathology. All these methods have their own advantages and limitations for assessing VAD both at individual and community level (WHO, 1996). For instance, isotope dilution testing that measures vitamin A stores in the liver is the gold standard method to assess vitamin A deficiency. However, this method requires a liver biopsy, which is not available for a population-based assessment. The modified relative dose response (biomarker) that determines population level vitamin A deficiency can be used alternatively as an indirect measure of vitamin A stores in the liver. But, due to its limited commercial availability this method is not widely used. Instead, **serum/plasma retinol levels** are the most commonly used measurement for vitamin A status. This indirect measurement has been associated with the functional outcomes of vitamin A deficiency, and generally reflects the liver stores when they are depleted (WHO, 2011b).

Subclinical VAD which is measured by serum retinol level and clinical VAD which is defined as night blindness are the indicators to assess the magnitude of vitamin A deficiency at population level. The cut-off point for subclinical VAD is serum retinol concentration level of 0.70 µmol/L or less. The severity of VAD as a public health problem is explained by the prevalence of low serum retinol concentration level (≤ 0.70 µmol/L). Accordingly, the prevalence of low serum retinol level at a population level is considered to be mild public health concern if 2-9%, moderate if 10-19%, and severe if ≥20%. This applies to most age group with the exclusion of infants under six months (WHO, 2011b).

Among the several clinical indicators, night blindness, Bitot's spot, corneal scarring, and corneal ulcerations are used to assess VAD at population level. The WHO states VAD is considered as a public health problem at a cut-off point 1% for night blindness and 0.5% for Bitot's spot among preschool children (WHO, 2014).

1.3 Magnitude of VAD in Ethiopia

According to the Ethiopian National Micronutrient Survey conducted in 2015, highest prevalence of Vitamin A deficiency was observed in preschool children 6 to 59 months of age (13.9%), followed by school age children 5 to 14 years of age (10.9%) and non-pregnant women age 15 to 49 years (3.4%). As per the WHO classifications, Vitamin A deficiency could be considered as mild public health problem for women of reproductive age and moderate for children 6 to 59 months and 5 to 14 years of age (EPHI, 2016).

On the other hand a systematic review by Sahile et al indicated that the prevalence of subclinical VAD decreased from 55.7% in the period 1990-2004 to 28.3% in the period between 2005 and 2019. This review indicated that VAD is severe public health problem (>20%) in Ethiopia (Sahile *et al.*, 2020). The review also revealed that the prevalence of night blindness decreased from moderate public health problem (4.2%) in the period between 1990-2004 to mild public health problem (0.8%) in the period from 2005-2019. In the same period the prevalence of Bitot's spot has decrease from 2.2% to 1.8%. Despite the reduced proportion of night blindness and Bitot's spot, still both clinical and subclinical VAD remain to be a public health problem in Ethiopia (Sahile *et al.*, 2020).

1.4 Risk Factors for VAD

The following are considered as risk factors for VAD.

Age: clinical and subclinical VAD are most prevalent in children six months through five years of age (Underwood, 1998).

Gender: There is no consistent, clear indication in humans of a gender differential in the requirement for vitamin A during childhood. Growth rates and presumably need for vitamin A from birth to 10 years for boys are consistently higher than those for girls. Pregnant and lactating women, of course, require additional vitamin A to support maternal and fetal tissue growth and lactation losses that are not endured by other post-adolescent adults (WHO, 1995; Underwood, 1998).

Quality of Diet: Dietary sources of biologically active vitamin A are found preformed in some animal foods or as pro-vitamin carotenoids from plants. There is no specific human requirement for carotenoids apart from their potential conversion to biologically active retinoid.

Preformed vitamin A is highly bioavailable, whereas the bioavailability of pro-vitamin A carotenoids varies with the kind of plant source (Rodriguez-Amaya, 1997).

Disease Occurrence: Infectious diseases contribute to vitamin A depletion. Enteric infections may alter absorptive-surface area, compete for absorption-binding sites, and increase urinary loss (Alvarez *et al.*, 1995).

Seasonality: In endemic VAD areas, fluctuations in the incidence of VAD throughout the year reflect the balance between intake and need. Times of food shortage (particularly of vitamin A-rich foods), periods of peak incidence of common childhood infectious diseases (diarrheal, respiratory, and measles infections),and periodic seasonal growth spurts affect the balance (Underwood, 1998).

Cultural Factors: Food habits and taboos often restrict consumption of potentially good food sources of vitamin A. Culture specific practices in the feeding of children, adolescents, and pregnant and lactating women are common (Johns, Booth and Kuhnlein., 1992).

1.5 Policy Options/Intervention Programs to reduce VAD

Experiences from different countries and research evidence indicated different measures to prevent and control micronutrient malnutrition including VAD. These strategies can be grouped into two main categories (ICN, FAO and WHO, 1992; Underwood, 1998). These are:

1) Food-based approaches that directly increase vitamin A intake including increased production and consumption of vitamin A rich foods, food fortification with vitamin A, and vitamin A supplementation.

2) Indirect public health measures to control disease frequency such as Information, education, and communication (IEC), including social marketing and specific vitamin A oriented nutrition education.

The primary focus of this review; however, is to assess the effectiveness of food-based approaches. More specifically: **A**) to assess the effects of fortifying staple foods (including edible oil) with vitamin A for reducing vitamin A deficiency and improving health-related outcomes among young child and women of reproductive age or in the general population, and **B**) to assess the effects of vitamin A supplementation (VAS) for reducing vitamin A deficiency and improving health-related outcomes among young child and women of reproductive age or in the general population.

2. Approach/methods used for this review

Rapid evidence review method (adapted from SURE guide for Rapid Response Services) was applied to search, appraise and summarize the available evidence on the effectiveness of staple foods fortification with Vitamin A and Vitamin A supplementation for the control of VAD.

We identified the Population (**P**), Intervention (**I**), Comparator(**C**) and Outcome (**O**) with respect to the objective of the review to facilitate searching of relevant articles and unpublished documents. The identified PICO is presented below.

Population, Intervention, Comparator and Outcome (PICO)

P	Children 6-35 months & women of reproductive age
I	• Fortification of staple foods with vitamin A • Vitamin A supplementation
C	Any other intervention or no intervention
O	Vitamin A deficiency (VAD)

Studies included:

In this review only systematic reviews were included to ensure quality and reliability of evidence. Systematic reviews constitute a more appropriate source of evidence for decision-making than relying on the most recent or most publicized primary research study.

Data sources:

To answer the question under review we searched for high quality studies (systematic reviews) from the following international data bases: SUPPORT Summaries, Health Systems Evidence, Epistemonikos, PDQ-Evidence, the Cochrane Library, and PubMed. The searching was made with no date or no language restriction. The last search was made on November 25, 2020.

3. Review findings

Based on our search, we identified 34 documents that provide relevant evidence to answer the questions under review. Then we appraised the methodological quality of systematic reviews that are deemed to be highly relevant using AMSTAR. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. Note that AMSTAR is a tool that was developed to assess systematic reviews based on randomized clinical trials/interventions (RCTs).

Accordingly, the identified documents in this rapid evidence review were appraised and finally we found two highly relevant systematic reviews (with highest scores using the AMSTAR rates) in relation to the PICO. These were:

1. The impact of fortifying staple foods (including edible oil) with vitamin A for reducing

vitamin A deficiency among young children and pregnant women (Hombali *et al.*, 2019), and

2. The impact vitamin A supplementation (VAS) for reducing vitamin A deficiency and preventing morbidity and mortality in preschool children (Imdad *et al.*, 2017)

A) Vitamin A fortification for reducing VAD

Definition: Food fortification is the practice of deliberately increasing the content of an essential micronutrient, i.e. vitamins and minerals (including trace elements) in a food, so as to improve the nutritional quality of the food supply and provide a public health benefit with minimal risk to health (Underwood, 1998).

Impact of Vitamin A fortification for reducing VAD:
We found one highly relevant systematic review that assessed impact of fortifying staple foods (including edible oil) with vitamin A for reducing vitamin A deficiency among young children and pregnant women (Hombali *et al.*, 2019). Staple foods include edible vegetable oils and fats, refined sugar, rice, wheat flour, maize flours and corn meals, condiments and seasonings, and powdered or liquid milk (Dary and Mora, 2002).

The key findings are presented below. For a better description of the findings from the included studies in this review, we have presented the summary of findings table as well (see table 1, 2 and 3).

Key Findings:

- It is uncertain whether fortifying staple foods with vitamin A alone has an effect on serum retinol concentrations (an indicator of vitamin A stores in the body), subclinical vitamin A deficiency (serum/plasma retinol of 0.70 µmol/L or less), and clinical vitamin A deficiency (night blindness). In comparison with provision of unfortified foods, provision of staple foods fortified with vitamin A plus other micronutrients may not increase serum retinol concentration but probably reduces the risk of subclinical vitamin A deficiency.
- In comparison with provision of unfortified foods, provision of staple foods fortified with vitamin A plus other micronutrients probably reduces the risk of subclinical vitamin A deficiency; however, may not increase serum retinol concentration.
- Compared to no intervention, staple foods fortified with vitamin A plus other micronutrients may increase serum retinol concentration, although it is uncertain whether the intervention reduces the risk of subclinical vitamin A deficiency as the certainty of the evidence is very low.
- It was not possible to estimate the effect of staple food fortification on outcomes such as mortality, morbidity, adverse effects, congenital anomalies, or breast milk vitamin A, as no trials included these outcomes.

Table 1. Summary of findings on the effect of staple food fortified with vitamin A alone versus the same unfortified staple foods on VAD in general population.

Patients or population: General population above 2 years of age

Settings: LMIC (Philippines)

Intervention: Staple foods fortified with vitamin A alone

Comparison: Same unfortified staple foods

Outcomes	Impact (anticipated absolute effects (95% CI) per 1000 study population		Relative Effect, RR (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)
	Same unfortified staple	Staple foods fortified with vitamin A alone			
Serum/plasma retinol (µmol/L)	The mean serum retinol level in intervention group was 0.03 µmol/L higher (−0.06 to 0.12)		-	1829 (3 RCTs)	⊕○○○ Very low
Subclinical vitamin A deficiency (serum/plasma retinol 0.70 µmol/L or less)	189 per 1000	85 per 1000 (36 to 198)	0.45 (0.19 to 1.05)	993 (2 RCTs)	⊕○○○ Very low
Clinical vitamin A deficiency (defined as night blindness)	14 per 1000	2 per 1000 (0 to 28)	0.11 (0.01 to 1.98)	581 (1 RCT)	⊕○○○ Very low
All-cause mortality and morbidity, any adverse effect	No studies reported on this outcomes				

GRADE: GRADE Working Group grades of evidence
High certainty (⊕⊕⊕⊕): we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty (⊕⊕⊕○): we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty (⊕⊕○○): our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty (⊕○○○): we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Table 2. Summary of findings on the effect of staple food fortified with vitamin A plus other micronutrients versus the same unfortified staple foods on VAD in general population.

Patients or population: General population above 2 years of age

Settings: LMICs (Philippines, Bangladesh, India, and Thailand)

Intervention: Staple foods fortified with vitamin A plus other micronutrients

Comparison: Same unfortified staple foods

Outcomes	Impact (anticipated absolute effects (95% CI) per 1000 study population		Relative Effect, RR (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)
	Same unfortified staple	Staple foods fortified with vitamin A plus other			
Serum/plasma retinol (µmol/L)	The mean serum retinol level in intervention group was 0.08 µmol/L higher (−0.06 to 0.22)		-	1009 (4 RCTs)	⊕⊕○○ Low
Subclinical vitamin A deficiency (serum/plasma retinol 0.70 µmol/L or less)	103 per 1000	28 per 1000 (17 to 51)	0.27 (0.16 to 0.49)	923 (3 RCTs)	⊕⊕⊕○ Moderate
Clinical vitamin A deficiency (defined as night blindness), all-cause mortality and morbidity, any adverse effect	No studies reported on this outcomes				

GRADE: GRADE Working Group grades of evidence

High certainty (⊕⊕⊕⊕): we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty (⊕⊕⊕○): we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty (⊕⊕○○): our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty (⊕○○○): we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Table 3. Summary of findings on the effect of staple food fortified with vitamin A plus other micronutrients versus no intervention on VAD in general population.

Patients or population: General population above 2 years of age

Settings: LMICs (Mexico, India)

Intervention: Staple foods fortified with vitamin A plus other micronutrients

Comparison: No intervention

Outcomes	Impact (anticipated absolute effects (95% CI) per 1000 study population)		Relative effect, RR (95% CI)	Number of participants	Quality of the evidence (GRADE)
	No intervention	Staple foods fortified with			
Serum/plasma retinol (µmol/L)	The mean serum retinol level in intervention group was 0.22 µmol/L higher (0.15 to 0.30)		-	318 (2 RCTs)	⊕⊕◯◯ Low
Subclinical vitamin A deficiency (serum/plasma retinol 0.70 µmol/L or less)	78 per 1000	56 per 1000 (41 to 77)	0.71 (0.52 to 0.98)	318 (2 RCTs)	⊕◯◯◯ Very low
Clinical vitamin A deficiency (defined as night blindness), all-cause mortality and morbidity, any adverse effect	No studies reported on this outcome				

GRADE: GRADE Working Group grades of evidence

High certainty (⊕⊕⊕⊕): we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty (⊕⊕⊕◯): we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty (⊕⊕◯◯): our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty (⊕◯◯◯): we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Relevance of the research to the question being asked (Vitamin A Fortification)

➔ Findings	➢ Interpretation
APPLICABILITY	
➔ Studies included in this review are in Low- and middle-income countries ➔ The study populations included were general population above two years of age living in urban and rural areas.	➢ Although the studies included are done in LMIC the effect of Vitamin A fortification in reducing VAD is uncertain. Thus, policy makers or program implementers should be informed of this fact and should pilot (for its effectiveness) before its nationwide implementation. ➢ Policy makers choice of a food vehicle or vehicles can depend on a series of factors, including the target group, food consumption patterns of the target group, and availability and characteristics of the possible vehicle (Underwood, 1998). ➢ Fortification with vitamin A can be done in one or more staple foods that are regularly consumed by the population in sufficient amounts.
EQUITY	
➔ None of the studies reported the differential effect of the intervention by different target population/group.	➢ If the intervention is considered for implementation (pilot or nation-wide), foods should be selected for fortification on the basis of the food consumption practices (Underwood, 1998). ➢ With respect to the target group, food vehicles may differ when directed to the population as a whole (general fortification) or to specific target groups (e.g. Infants, schoolchildren, and refugees), or defined socioeconomic or geographical areas (for example, urban, rural, and ethnic group) (Underwood, 1998).
COST CONSIDERATIONS	
➔ The studies included did not report on cost and cost-effectiveness of the intervention on the given outcome	➢ After ascertaining the effectiveness of the intervention, foods should be selected for fortification on the basis of the food consumption practices (staple foods for each target group), stability, production and marketing characteristics, and cost (Underwood, 1998).
MONITORING & EVALUATION	
➔ The certainty of the evidence on the effects of the intervention are very low to low except for moderate certainty of the effect of staple food fortified with vitamin A plus other micronutrients on subclinical VAD. There is also no reported evidence on other health related outcomes.	➢ If applied, policy makers or programme implementers should monitor the effects of mass fortification through national surveys with robust evaluation (Underwood, 1998).

B) Vitamin A supplementation to reducing VAD

Definition: Supplementation refers to the addition of pharmaceutical preparations of nutrients (capsules, tablets, or syrups) to the diet (Underwood, 1998). Vitamin A supplementation is probably the most widespread intervention practiced clinically and in public health, and different studies support its effectiveness in improving vitamin A status and significantly reducing infant and child mortality and morbidity (particularly diarrhea) in infants and children aged 6 to 59 months living in low- and middle-income countries (Imdad *et al.*, 2017). The WHO currently recommends this intervention for countries where vitamin A deficiency is a public health problem (WHO, 2011a).

Impact of Vitamin A Supplementation for reducing VAD:

We found one highly relevant systematic review that assessed impact of vitamin A Supplementation for reducing vitamin A deficiency and preventing morbidity and mortality in preschool children (Imdad *et al.*, 2017). The key findings are presented below. For a better description of the findings from the included studies in this review, we have presented the summary of findings table as well.

Key Findings:

- Vitamin A supplementation (VAS) can reduce risk of illness and death in children aged 6 to 59 months of age who are at risk of VAD. This suggests maintaining the policy of universal supplementation for children under five years of age in populations at risk of VAD.

- Further placebo-controlled trials of VAS in children between six months and five years of age would not change the conclusions of this review, although studies that compare different doses and delivery mechanisms are needed.

Table 4. Vitamin A supplementation for preventing morbidity and mortality in children from 6 months to 5 years of age

Patients or population: Children aged between 6 months and 5 years

Settings: All settings

Intervention: Vitamin A supplementation

Comparison: Placebo or usual care

Outcomes	Illustrative comparative risks (95% CI) per 1000 study population		Relative Effect, RR (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
All-cause mortality rate	26 per 1000	23 per 1000 (22 to 24)	0.88 (0.83 to 0.93)	1,202,382 (19 Studies)	⊕⊕⊕⊕ High
Mortality due to diarrhea	8 per 1000	7 per 1000 (6 to 8)	0.88 (0.79 to 0.98)	1,098,538 (9 Studies)	⊕⊕⊕⊕ High
Bitot's spots incidence	35 per 1000	15 per 1000 (12 to 19)	0.42 (0.33 to 0.53)	1,063,278 (5 Studies)	⊕⊕⊕○ Moderate
Night blindness incidence	4 per 1000	1 per 1000 (1 to 2)	0.32 (0.21 to 0.50)	22,972 (2 Studies)	⊕⊕⊕○ Moderate
Vitamin A deficiency	509 per 1000	361 per 1000 (331 to 397)	0.71 (0.65 to 0.78)	2262 (4 studies)	⊕⊕⊕○ Moderate

GRADE: GRADE Working Group grades of evidence

High certainty (⊕⊕⊕⊕): we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty (⊕⊕⊕○): we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty (⊕⊕○○): our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty (⊕○○○): we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

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Conflict of interest

There is no conflict of interest

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What is Rapid Evidence Review?

Rapid evidence review address the needs of policymakers and managers for research evidence that has been appraised and contextualised in a matter of hours or days, if it is going to be of value to them. The review address questions about arrangements for organising, financing and governing health systems, and strategies for implementing changes.

Knowledge Translation Directorate: in EPHI is a drectorate that aims to translate knowledge from the research setting in to policy and practice. Since its establishment, this directorate has served as the focal unit for international networks and projects such as the Evidence-Informed Policy Network (EVIPNet), the Supporting the Uptake of Research Evidence in African Health Systems (SURE) project, and Rapid and Responsive Evidence Partnership (RREP).