World Health Organization

Guideline:

Vitamin A supplementation in postpartum women

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Contents

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WHO Guideline[1] Vitamin A supplementation in postpartum women

Summary

Approximately 1000 women die from pregnancy and childbirth complications worldwide every day. Vitamin A deficiency also affects about 19 million pregnant women, mostly from the World Health Organization (WHO) regions of Africa and South-East Asia. Vitamin A plays an important role in vision, growth and physical development, and immune function. Deficiency of vitamin A increases the risk of night blindness and other ocular conditions such as xerophthalmia. Member States have requested guidance from WHO on the effects and safety of vitamin A supplements for postpartum women as a public health strategy.

WHO has developed the present evidence-informed recommendation using the procedures outlined in the *WHO handbook for guideline development*. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including future research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was followed to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews. An international, multidisciplinary group of experts participated in two WHO technical consultations, held in Geneva, Switzerland, on 19–20 October 2009 and 16–18 March 2011, to review and discuss the evidence and draft recommendation, and to vote on the strength of the recommendation, taking into consideration: (i) desirable and undesirable effects of this intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings. All guideline group members completed a Declaration of Interests Form before each meeting. An External Experts and Stakeholders Panel was involved throughout the process.

Vitamin A supplementation in postpartum women is not recommended as a public health intervention for the prevention of maternal and infant morbidity and mortality (strong recommendation). The quality of the available evidence for maternal mortality, maternal morbidity and adverse effects was graded as low or very low. The quality of evidence for all-cause infant mortality was high and for cause-specific infant mortality and morbidity was very low. Postpartum women should continue to receive adequate nutrition, which is best achieved through consumption of a balanced healthy diet.

[1] This publication is a WHO guideline. A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

Scope and purpose

This guideline provides global, evidence-informed recommendations on the use of vitamin A supplements in postpartum women for the reduction of maternal and infant morbidity and mortality.

The guideline will help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Millennium Development Goals, in particular, reduction in child mortality (MDG 4) and improvement in maternal health (MDG 5). The guideline is intended for a wide audience including policy-makers, their expert advisers, and technical and programme staff in organizations involved in the design, implementation and scaling-up of nutrition actions for public health.

This document presents the key recommendation and a summary of the supporting evidence. Further details of the evidence base are provided in Annex 1 and other documents listed in the references.

Background

Approximately 1000 women die from complications related to pregnancy or childbirth worldwide every day (*1*). Almost all of these deaths occur in developing countries, and most could be averted by preventing complications such as severe bleeding (haemorrhage), infections and high blood pressure, and diseases such as malaria, anaemia and human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) during pregnancy and postpartum (*2*). Neonatal deaths account for 36% of deaths among children under 5 years of age worldwide (*3, 4*). These deaths are mainly due to prematurity and low birth weight (31%), neonatal infections (26%), birth asphyxia (lack of oxygen at birth) and birth trauma (23%). A non-negligible proportion of neonates die because of congenital anomalies (6.8%), other non-infectious perinatal causes (5.7%), tetanus (5%) and diarrhoeal diseases (2.6%).

Vitamin A deficiency also remains a public health problem among women and children, affecting an estimated 190 million preschool-age children and 19 million pregnant women (*5*), with the highest burden found in the World Health Organization (WHO) regions of Africa and South-East Asia. During lactation, vitamin A is essential for maternal health and vision (*6*). The recommended nutrient intake of vitamin A for postpartum women is 850 µg retinol equivalents (RE)/day (*7*), which may be difficult to achieve through the diet alone in some areas. Dietary sources of provitamin A include vegetables such as carrot, pumpkin, papaya and red palm oil; animal foods rich in preformed vitamin A include dairy products (whole milk, yogurt, cheese), liver, fish oils and human milk (*6, 7*).

Infants are usually born with low body stores of vitamin A. Breast milk of well-nourished mothers is rich in vitamin A and is its best source for the infant (*8*). Therefore, mothers are encouraged to exclusively breastfeed for the first 6 months postpartum. The concentration of vitamin A in breast milk is highest in the first 21 days postpartum, that is, in the colostrum in the first 4–6 days and in the transitional milk in the next 7–21 days (*9*). Following this, in industrialized countries, the concentration of vitamin A usually remains stable during the remainder of lactation (*10*).

In areas where vitamin A deficiency is common, mothers may produce breast milk with lower concentrations of vitamin A (*9*). However, if a mother cannot meet the increased vitamin A requirements during lactation through the diet, her body will attempt to compensate for the low levels of vitamin A in the breast milk by drawing on the vitamin A reserves in the liver (*11)*. Vitamin A plays an important role in vision, growth and physical development, and immune function, and deficiency of vitamin A increases the risk of night blindness and other ocular conditions such as xerophthalmia (*12*), especially during times when infectious disease rates are high and/or during seasons when food sources rich in vitamin A are scarce (*13*).

Maternal dietary intake is an important determinant of breast milk vitamin A concentrations and an infant's vitamin A status (*9, 14*). Programmes such as postpartum supplementation, dietary diversification and food fortification with vitamin A have been used to improve women's vitamin A status and to increase the vitamin A content of breast milk (*15*). This protects the vitamin A reserves of lactating women while addressing the problem of low intakes of vitamin A from breast milk in infants (*16*).

Vitamin A supplements are mostly well tolerated by postpartum women (*17*); however, maternal supplementation with high doses (more than 50 000 IU) can have side-effects such as nausea, headache, fever, vomiting, increased cerebrospinal fluid pressure, blurred vision, drowsiness and lack of muscle coordination (*18*). However, these symptoms are generally transient with no long-term adverse effects (*19*).

Summary of evidence

Three systematic reviews (*20–22*) have addressed the effects and safety of vitamin A supplementation in postpartum women. The first review evaluated the effect of postpartum vitamin A supplements on maternal and infant health (*20*). It included 12 studies comparing maternal vitamin A supplementation (β-carotene or retinyl palmitate or water miscible formulation) alone or in combination with other micronutrients, with placebo, no intervention, or administration of other micronutrients or a lower dose of vitamin A, commencing at any time during the postpartum period (within 24 hours of giving birth until 6 weeks after giving birth). The studies included mothers residing in low-income settings in India, Bangladesh, Indonesia, Tanzania, the Gambia, Zimbabwe, Kenya, Ghana and Peru. Thus the women were likely to have low vitamin A levels as well as low nutritional status. One study evaluated maternal mortality at 12 months postpartum and reported no significant effect of administration of 400 000 IU vitamin A within 24–96 hours of giving birth (hazard ratio (HR) 1.11; 95% confidence interval (CI) 0.81–1.51). Only one study assessed adverse effects and it found no difference in the incidence of vomiting within 30 hours of administering a single dose of 400 000 IU vitamin A or a placebo (risk ratio (RR) 0.33; 95% CI 0.03–3.14). Four trials reported no difference overall in infant mortality following vitamin A supplementation compared with placebo (RR 1.14; 95% CI 0.84–1.57).

The other reviews (*21, 22*) evaluated the effect of vitamin A supplementation in postpartum mothers on mortality, morbidity and adverse effects in their infants until

the age of 1 year. Seven studies from low- and middle-income countries (three in Asia and four in Africa) were included in the meta-analysis, which revealed no impact on infant mortality (RR 1.00; 95% CI 0.94–1.06). Only two trials documented information on the cause of death and there was no evidence of a reduced risk of death due to respiratory causes (RR 1.59; 95% CI 0.84 to 2.99) or diarrhoea (RR 2.57; 95% CI 0.72 to 9.12). The one trial that reported morbidity found no effect on the risk of diarrhoea (RR 1.10; 95% CI 0.99–1.23) or acute respiratory infection (rate ratio 0.96; 95% CI 0.85–1.08). Two trials reported adverse effects, but in both studies no adverse effects were observed in either the intervention or the control group during the follow-up. These reviews included three studies that were not included in the first review mentioned above (*20*). These additional studies involved supplementation with smaller, weekly doses of vitamin A before or during pregnancy until delivery or 12–24 weeks' postpartum. The cumulative vitamin A dose received by the mother over this period was reported in one of these studies, as less than or equal to 200 000 IU, and in the remaining six studies it was greater than 200 000 IU. No significant differences were identified with regard to outcomes when the data were stratified based on either the total vitamin A dose (units) received by the mothers (less than or equal to 200 000 IU versus greater than 200 000 IU) or by the number of vitamin A doses received (single versus multiple).

The overall quality of available evidence for maternal mortality, maternal morbidity and adverse effects was graded as low or very low (Annex 1). Data for all-cause infant mortality was graded as high quality, however, the quality of evidence for cause-specific infant mortality and morbidity was graded as very low.

Recommendation

Vitamin A supplementation in postpartum women is not recommended for the prevention of maternal and infant morbidity and mortality (*strong recommendation*[1]).

Remarks

- This guideline replaces and updates previous recommendations on vitamin A supplementation in mothers for the prevention of vitamin A deficiency (*23*) and for improving the vitamin A status of mothers and their infants (*8*).
- Postpartum women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a balanced healthy diet, and to refer to guidelines on healthy eating during lactation (*24*).
- Recommendations for the treatment of xerophthalmia are not covered in this guideline. Existing guidelines for the treatment of xerophthalmia in women of reproductive age should be referred to in these cases (*23*).

[1] A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. The recommendation can be either in favour of or against an intervention. Implications of a strong recommendation for patients are that most people in their situation would desire the recommended course of action and only a small proportion would not. For clinicians the implications are that most patients should receive the recommended course of action and that adherence to this recommendation is a reasonable measure of good-quality care. With regard to policy-makers, a strong recommendation means that it can be adapted as a policy in most situations.

Dissemination

The current guideline will be disseminated through electronic media such as slide presentations, CD-ROMs and the World Wide Web, either through the WHO Micronutrients and United Nations Standing Committee on Nutrition (SCN) mailing lists or the WHO nutrition web site. Currently, the WHO Department of Nutrition for Health and Development is developing the WHO electronic Library of Evidence for Nutrition Actions (eLENA). This library aims to compile and display WHO guidelines related to nutrition along with complementary documents such as systematic reviews and other evidence informing the guidelines, biological and behavioural rationales, and additional resources produced by Member States and global partners.

Implications for future research

- Research is needed on the effect of vitamin A supplements (200 000 IU) on breast milk retinol concentrations when given specifically at 6 weeks postpartum to a breastfeeding mother (as opposed to immediately after delivery).
- Research is also needed on the metabolism of a high dose of vitamin A (200 000 IU) given to postpartum women. In addition, information is needed on how a dose of vitamin A is distributed within the body (e.g. does it get stored or is it secreted in the breast milk) and how it is excreted.

Guideline development process

This guideline was developed in accordance with the WHO evidence-informed guideline development procedures, as outlined in the *WHO handbook for guideline development* (*25*).

Advisory groups

A WHO/United Nations Children's Fund (UNICEF) Steering Committee for Guidelines on Vitamin A Supplementation was established in 2009 with representatives from the WHO departments of Child and Adolescent Health and Development; Immunizations, Vaccines and Biologicals; Making Pregnancy Safer; Nutrition for Health and Development; Reproductive Health and Research; and the Nutrition Section of UNICEF (Annex 2). The Steering Committee guided the development of this guideline and provided overall supervision of the guideline development process. Two additional groups were formed: an advisory guideline group and an External Experts and Stakeholders Panel.

The Vitamin A Supplementation Guideline Group included experts from various WHO expert advisory panels and those identified through open calls for specialists, taking into consideration a balanced gender mix, multiple disciplinary areas of expertise, and representation from all WHO regions (Annex 3). Efforts were made to include content experts, methodologists, representatives of potential stakeholders (such as managers and other health professionals involved in the health-care process) and consumers. Representatives of commercial organizations may not be members of

a WHO guideline group. The role of the guideline group is to advise WHO on the choice of important outcomes for decision-making and the interpretation of the evidence.

The External Experts and Stakeholders Panel was consulted on the scope of the document, the questions addressed and the choice of important outcomes for decision-making, as well as with regard to review of the completed draft guideline (Annex 4). This was done through the WHO Micronutrients and SCN mailing lists, which together include over 5500 subscribers, and through the WHO nutrition web site.

Scope of the guideline, evidence appraisal and decision-making

An initial set of questions (and the components of the questions) to be addressed in the guideline was the critical starting point for formulating the recommendation; the questions were drafted by technical staff at the Micronutrients Unit, Department of Nutrition for Health and Development, in collaboration with the Nutrition Section of UNICEF, based on policy and programme guidance needs of Member States and their partners. The population, intervention, control, outcomes (PICO) format was used (Annex 5). The questions were discussed and reviewed by the Steering Committee and feedback was received from 45 stakeholders.

The first guideline group meeting was held on 19–20 October 2009 in Geneva, Switzerland, to finalize the scope of the questions and rank the critical outcomes and populations of interest. The guideline group members discussed the relevance of each question and modified them as needed. They scored the relative importance of each outcome from 1 to 9 (where 7–9 indicated that the outcome was critical for a decision, 4–6 indicated that it was important and 1–3 indicated that it was not important). The final key question on vitamin A supplementation in postpartum women, along with the outcomes that were identified as critical for decision-making, are listed in PICO format in Annex 5.

The Cochrane Collaboration was commissioned to search, review and generate systematic reviews, evidence profiles and the "Summary of findings" table[1] (Annex 1). Two Cochrane reviews were updated, and one additional non-Cochrane review on postpartum vitamin A supplementation was identified. The up-to-date Review Manager Software (RevMan) files, obtained from the Cochrane Editorial Unit, were customized in order to reflect the critical outcomes previously identified (outcomes not relevant to this guideline were excluded). The RevMan files were exported to the GRADE profiler software in order to prepare evidence summaries according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessing the overall quality of the available evidence (*26*) (Annex 1). GRADE considers: the study design; the limitations of the studies in terms of their

[1] As part of the Cochrane pre-publication editorial process, reviews are commented on by external peers (an editor, and two referees external to the editorial team) and the group's statistical adviser (http://www.cochrane.org/cochrane-reviews). The *Cochrane handbook for systematic reviews of interventions* describes in detail the process of preparing and maintaining Cochrane systematic reviews on the effects of healthcare interventions.

conduct and analysis; the consistency of the results across the available studies; the directness (or applicability and external validity) of the evidence with respect to the populations, interventions and settings where the proposed intervention may be used; and the precision of the summary estimate of the effect.

Both the systematic reviews and the GRADE evidence profiles for each of the critical outcomes were used for drafting the guideline. A second guideline group meeting was held on 16–18 March 2011 in Geneva, Switzerland, to review the evidence, discuss the draft recommendation, and to determine its strength, taking into consideration: (i) desirable and undesirable effects of this intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings (Annex 6). Consensus was defined as agreement by simple majority of the guideline group members. WHO staff present at the meeting as well as other external technical experts involved in the collection and grading of the evidence were not allowed to vote. There were no strong disagreements among the guideline group members.

The External Experts and Stakeholders Panel was again consulted on the draft guideline. Feedback was received from 12 stakeholders. WHO staff then finalized the guideline and submitted it for clearance by WHO before publication.

Management of conflicts of interest

According to the rules in the *WHO Basic documents* (*27*), all experts participating in WHO meetings must declare any interest relevant to the meeting prior to their participation. The conflicts of interest statements for all guideline group members were reviewed by the responsible technical officer and the relevant departments before finalization of the group composition and invitation to attend a guideline group meeting. All guideline group members and participants of the guideline development meetings submitted a Declaration of Interests Form along with their curriculum vitae before each meeting. In addition, they verbally declared potential conflicts of interest at the beginning of each meeting. The procedures for management of conflicts of interests strictly followed the WHO *Guidelines for declaration of interests (WHO experts)* (*28*). The potential conflicts of interest declared by members of the guideline group are summarized below.

- Professor Michael Clarke declared being Director of the UK Cochrane Centre and a member of The Cochrane Collaboration. Professor Clarke was not personally involved in the preparation or management of the systematic reviews on vitamin A supplementation used for this guideline, although some of his colleagues were involved.
- Dr Jean Humphrey declared that her research unit received research grants from 1996 to 2009 for the Zimbabwe Vitamin A for Mothers and Babies Project (ZVITAMBO) from various organizations, including the Nestlé Foundation, BASF and the Pediatric AIDS Foundation, which receives its core funds from various organizations including Johnson & Johnson and the Abbott Fund. Sub-studies were also supported by Support for Analysis and

Research in Africa (SARA) and Linkages Projects, both managed by the Academy for Educational Development (AED). To our knowledge, other than BASF, none of these companies nor their commercial sponsors directly or indirectly produce vitamin A supplements.

- Dr Charles Stephensen declared receiving research funds from WHO for the conduct of a human study on the efficacy of newborn vitamin A supplementation in improving immune function and from the United States National Institutes of Health for the conduct of studies on vitamin A and immune function in mice.
- Dr Sherry Tanumihardjo declared receiving remuneration as a technical consultant for the International Atomic Energy Agency (IAEA) and an honorarium from HarvestPlus. She also received research support from: HarvestPlus for a vitamin A efficacy study in Zambian children fed orange maize and for a banana study in gerbils to determine the vitamin A value of provitamin A carotenoids; the United States National Institutes of Health for developing a 13C retinol isotope dilution test; the United States Department of Agriculture (USDA) for the use of α-retinol as a chylomicron tag in rats and pigs; and WHO for mechanistic studies to understand neonatal vitamin A supplementation using the sow-piglet dyad model. In addition, she received reimbursement for travel expenses from IAEA, HarvestPlus and WHO to attend meetings. To our knowledge, neither HarvestPlus nor its commercial sponsors directly or indirectly produce vitamin A supplements.

External resource persons were invited to the meeting as observers and to provide technical input, but they did not participate in the decision-making processes.

Plans for updating the guideline

The recommendation in this guideline will be reviewed in 2015. If new information is available at that time, a guideline review group will be convened to evaluate the new evidence and revise the recommendation. The Department of Nutrition for Health and Development at the WHO headquarters in Geneva, along with its internal partners, will be responsible for coordinating the guideline update following the formal *WHO Handbook for guideline development* (*25*) procedures. WHO welcomes suggestions regarding additional questions for evaluation in the guideline when it is due for review.

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Annex 1 GRADE "Summary of findings" table

Vitamin A supplementation in postpartum women

Patient or population: Postpartum women
Settings: Countries where vitamin A deficiency may be a public health concern
Intervention: Vitamin A supplementation

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)*	Comments
Maternal mortality Follow-up: mean 12 months	**HR 1.11** (0.81– 1.51)	8577 (1 study)	⊕⊕⊖⊖ **low**[1,2]	Only one study reported on this outcome
Maternal morbidity: infections (total days of illness per days of follow-up) Follow-up: mean 3 months		50 (1 study)	⊕⊖⊖⊖ **very low**[3–6]	30 episodes out of 2281 days of follow-up (vitamin A) versus 28/2281 (placebo); no statistical comparison performed in the study Only one study reported on this outcome
Maternal adverse effects after administration: vomiting	**RR 0.33** (0.03–3.14)	786 (1 study)	⊕⊕⊖⊖ **low**[5,7,8]	Only one study reported on this outcome
Maternal adverse effects after administration: nausea	**RR 1.38** (0.44–4.31)	786 (1 study)	⊕⊕⊖⊖ **low**[5,7,8]	Only one study reported on this outcome
Maternal adverse effects after administration: headache	**RR 1.21** (0.74–1.99)	786 (1 study)	⊕⊕⊖⊖ **low**[5,7,8]	Only one study reported on this outcome

CI, confidence interval; RR, risk ratio; HR, hazard ratio.
*GRADE Working Group grades of evidence:
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We have moderate confidence 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 quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.
[1] Estimates of control group risk inferred from data presented in trial report.
[2] Result compatible with benefit and harm.
[3] No analysis performed on the raw data.
[4] Roy (1997): unclear allocation concealment and unblinded control group (no placebo).
[5] Since there is only one study in the analysis, inconsistency is unknown rather than unobserved.
[6] Sparse data in the original study.
[7] ZVITAMBO Study Group: Unclear why only 766 women out of the 14 110 women randomized were included in the assessment of adverse effects.
[8] The confidence intervals around the pooled effect are compatible with benefit and harm.

(Continued overleaf)

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Vitamin A supplementation in postpartum women

Patient or population: Postpartum women
Settings: Countries where vitamin A deficiency may be a public health concern
Intervention: Vitamin A supplementation

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)*	Comments
Infant mortality (all-cause) in the first year of life Follow-up: 6-12 months	**RR 1.00** (0.94–1.06)	59 402 (7 studies)	⨁⨁⨁⨁ **high**	
ARI-related infant mortality in the first year of life Verbal autopsy or lay reporting Follow-up: 12 months	**RR 1.59** (0.84–2.99)	5207 (2 studies)	⨁⨀⨀⨀ **very low**[1–3]	
Diarrhoea-related infant mortality in the first year of life Verbal autopsy or lay reporting Follow-up: 12 months	**RR 2.57** (0.72–9.12)	5207 (2 studies)	⨁⨀⨀⨀ **very low**[1, 3, 4]	
Measles-related infant mortality in the first year of life	**Not estimable**	0 (0 studies)		None of the studies reported on this outcome
Infant morbidity due to acute respiratory infections Follow-up: mean 12 months	**Rate ratio 0.96** (0.85–1.08)	598 (1 study)	⨁⨀⨀⨀ **very low**[5,6]	Estimates of morbidity not available from external sources Only one study reported on this outcome
Infant morbidity due to diarrhoea Follow-up: mean 12 months	**RR 1.10** (0.99–1.23)	598 (1 study)	⨁⨀⨀⨀ **very low**[5,6]	Estimates of morbidity not available from external sources Only one study reported on this outcome

CI, confidence interval; RR, risk ratio; ARI, acute respiratory infection.
*GRADE Working Group grades of evidence:
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We have moderate confidence 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 quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.
[1] One study had inadequate concealment of allocation. Both studies failed to address missing data appropriately.
[2] The confidence intervals include a 16% reduction and 300% increase (appreciable harm) in the risk of ARI-related death
[3] Only two trials reported this outcome, and the meta-analysis may be affected by the non-disclosure of cause-specific mortality in the remaining studies.
[4] The confidence intervals include a 28% reduction (appreciable benefit) and 900% increase (appreciable harm) in the risk of diarrhoea-related death.
[5] One single study, in which randomization procedure and method of allocation concealment were not described, and the incompleteness of the outcome data was not addressed adequately.
[6] A single small trial reported this outcome.

For details of studies included in the reviews, see references (*20–22*).

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Annex 5

Questions in Population, Intervention, Control, Outcomes (PICO) format

Effects and safety of vitamin A supplementation in postpartum women

a. Should vitamin A supplements be given to postpartum women?
b. If so, at what dose and time after delivery?

Population:

- Postpartum women living in countries where vitamin A deficiency may be of public health concern
- Subpopulations:
  - By infant mortality rates: countries with low versus high rates
  - By maternal mortality rates: countries with low versus high rates
  - By prevalence of HIV in the general population: countries with a low versus high prevalence
  - By exposure to additional vitamin A: mothers who received vitamin A supplementation during pregnancy versus others/unknown

For infant outcomes only

- By breastfeeding initiation: early initiation (within 1 hour of birth versus other)
- By breastfeeding practices: exclusively breastfed at 3 versus 6 months versus others as defined using the WHO Indicators for assessing infant and young child feeding practices

Intervention:

- Any oral vitamin A supplement alone
- Oral vitamin A supplement given in combination with other micronutrients
- Subgroup analyses:
  - By dose: 200 000 IU or 400 000 IU versus other doses (daily or weekly doses)
  - By timing: immediately after birth versus 4–8 weeks postpartum

Control:

- Placebo or no treatment
  - Micronutrient supplements without vitamin A (to assess the additive effect of vitamin A)

Outcomes:

Critical

Maternal

- Mortality within the first postpartum year
- Morbidity, infections
- Adverse effects within 72 hours of receiving supplement:
  - Vomiting
  - Other

Infant

- Mortality within 0–6 and 0–12 months of life
  - Any cause
  - Acute respiratory infections
  - Diarrhoea
  - Measles
- Morbidity during 0–6 and 0–12 months of life
  - Acute respiratory infections
  - Diarrhoea

Setting: All countries

Annex 6 Summary of considerations for determining the strength of the recommendation

Quality of evidence:	• High-quality evidence for infant mortality only • All other critical outcomes had very low or low quality evidence
Values and preferences	• More information is needed on adverse effects
Trade-off between benefits and harm:	• There are no benefits related to the critical outcomes reviewed • Potential negative effects are uncertain (unable to rule out an increase in mortality related to respiratory infections or diarrhoea)
Costs and feasibility:	• Minimal cost • Feasible to provide supplement at time of birth or shortly after birth in women delivering in a facility. May also be able to reach postpartum mother at the first infant follow-up visit

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