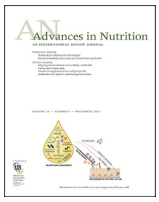
Advances in Nutrition 14 (2023) 1436–1452

American Society for Nutrition
Excellence in Nutrition Research and Practice

Advances in Nutrition
AN INTERNATIONAL REVIEW JOURNAL
journal homepage: https://advances.nutrition.org/



Review

Effects of Food-Based Approaches on Vitamin A Status of Women and Children: A Systematic Review

Joyce Nankumbi [1], Frederick Grant [2], Lindiwe Sibeko [1], Evelyn Mercado [3], Kristina O'Neil [1], Lorraine S. Cordeiro [1,*]

[1] *Department of Nutrition, University of Massachusetts, Amherst, MA, United States;* [2] *International Potato Center, Kampala, Uganda;* [3] *Department of Psychology and Brain Sciences, University of Massachusetts Amherst, Amherst, MA, United States*

A B S T R A C T

Vitamin A deficiency (VAD) increases risk for morbidity and mortality. Food-based approaches offer one strategy to improve vitamin A status. This systematic review assessed evidence of the effects of food-based approaches on the vitamin A status of women and children under 5 y. VAD was defined as clinical ocular symptoms, such as loss of vision, and/or retinol plasma or serum concentration <0.70 μmol/L. Searches on food-based approaches to improve vitamin A status were conducted for the period 2011–2022 on PubMed, CINHAL, Web of Science, and Google Scholar using PRISMA guidelines. English-language publications were included. Case studies, unpublished dissertations, and non-peer-reviewed studies were excluded. This review comprises 24 of 27,322 identified studies; 23 included studies focused on provitamin A carotenoids. There were 17,214 participants across the 24 studies with sample sizes ranging from 8 to 3571 individuals. Intervention studies spanned from 3 wk to 2 y. Fifteen (63%) studies were randomized control trials, 7 were cross-sectional, and 2 were longitudinal studies. Most studies ($N = 21$) used biochemical measurements, for example, serum retinol, to assess vitamin A status; other studies used clinical symptoms (for example, xerophtalmia) or dietary intake. Thirteen (54%) studies reported a statistically significant effect of food-based interventions ($N = 8$) or an association of diet ($N = 5$) on vitamin A status. This systematic review indicated that some food-based interventions improved vitamin A status, thus offering a safe and effective delivery mechanism for vitamin A. There appeared to be significant association between vitamin A status and consumption of foods with high concentrations of preformed vitamin A and provitamin A carotenoids. Differences across studies in regard to the period of evaluation, food approaches used, and statistical power may explain the lack of effectiveness of food-based approaches on vitamin A status in some studies.

Keywords: vitamin A, women, children, food-based approaches, vitamin A deficiency

Statement of Significance

A plethora of research on the effectiveness of vitamin A interventions exists; however, there is limited evidence on associations between dietary intake and vitamin A status, as well as the effectiveness of food-based interventions on vitamin A status. This systematic review fills a critical gap in the literature given that there is no recent review that documents and evaluates the effectiveness of the various food-based approaches in improving vitamin A status among women and children under 5 y.

Abbreviations: AGP, *α1-acid glycoprotein*; BC, ß-carotene; BOFSP, boiled orange-fleshed sweet potato; C-RID, C-retinol Isotope dilution; CRP, C-reactive protein; CSS, cross-sectional study or cross-sectional survey design; DRI, daily recommended intake; EAR, estimated average requirement; FFQ, food frequency questionnaire; LNG, longitudinal study design; LMIC, low- and middle-income country; NPNLW, nonpregnant nonlactating women; NS, not significant; OFSP, orange-fleshed sweet potato; OM, orange maize; PCS, prospective cohort design or study; RAE, retinoic acid equivalent; *RBP*, *retinol binding protein*; *RCT*, *randomized control trial*; RID, retinol isotope dilution; TAG, triacyl glycerol; TBVA, total body vitamin A; VA, vitamin A; *VAC*, *vitamin A capsule*; VAD, vitamin A deficiency; WM, white maize; WFSP, white-fleshed sweet potato.

* Corresponding author *E-mail address:* lcordeir@umass.edu (L.S. Cordeiro).

https://doi.org/10.1016/j.advnut.2023.08.009
Received 20 September 2022; Received in revised form 2 August 2023; Accepted 15 August 2023; Available online 25 August 2023

Introduction

Vitamin A is an essential micronutrient for the normal functioning of the visual system, growth, development, and maintenance of epithelial cellular integrity, immune function, and reproduction [1]. Vitamin A regulates cellular differentiation, which is highly responsive to changes in vitamin A status of rapidly dividing cells. Indicators based on the measurement of status in such cell systems may be expected to reflect vitamin A status [2]. Vitamin A deficiency is defined as clinical ocular symptoms of vitamin A deficiency, such as night blindness to permanent loss of vision, and/or retinol plasma or serum concentration <0.70 μmol/L [2].

Globally, over 127 million children, inclusive of more than one-third of children in sub-Saharan Africa, are affected by VAD [3,4]. An estimated 3 million children have clinical manifestations of xeropthalmia; a third of these cases were in Africa [5]. Between 1995 and 2005, an estimated 19 million pregnant women were affected by VAD [2,5]. VAD can occur in individuals of any age, with higher susceptibility among women and children [2,6]. Women are particularly vulnerable to VAD during pregnancy and lactation, evidenced by reports of night blindness and low vitamin A levels in breast milk [7]. VAD presents a disabling and potentially fatal public health problem for children under 6 y of age [8,9] with a high prevalence of blindness in children under 3 y [5].

In addition to the clinical manifestations of xeropthalmia and risk of irreversible blindness, nonspecific symptoms include increased morbidity and mortality, poor reproductive health, increased risk of anemia, and delayed growth and development [2]. However, the actual number of subclinical deficiencies based on the prevalence of low serum retinol levels remains uncertain because of the confounding and poorly quantified role of infections [2]. Furthermore, many nonspecific adverse effects of VAD may also be caused by other nutrient deficiencies including deficiencies in iron, zinc, and the B-vitamins [10], making it difficult to attribute nonocular symptoms to VAD alone in the absence of biochemical measurements [11,12].

Preformed vitamin A is found in fish, organ meats (for example, liver), eggs, and dairy products, whereas provitamin A carotenoids (mainly ß-carotene) can be found in plant products such as dark leafy greens, and red, orange, and yellow fruits and vegetables like sweet potatoes, pumpkins, carrots and mangos. There is a high efficiency of metabolization, absorption, and storage of preformed vitamin A. In contrast, provitamin A carotenoids, like ß-carotene, have to be converted into active vitamin A, retinol, and other retinoids in the human body and are less bioavailable. VAD prevention efforts primarily occur through vitamin A intervention approaches, including direct increase in vitamin A intake through consumption of foods with naturally high concentrations of preformed vitamin A or provitamin A, vitamin A (or ß-carotene) supplements, food biofortification, and indirect public health measures to control disease frequency [13,14]. Biofortification refers to the process of improving the nutrient quality of food through plant breeding, biotechnology, or agronomic initiatives [15]. Efforts promoting homestead food production of both biofortified and nonfortified crops can directly reduce the prevalence of vitamin A deficiency by increasing intake of food sources with high concentrations of preformed vitamin A and provitamin A [16]. Adequate intake of fruits and vegetables that are rich in provitamin A is a sustainable alternative to the provision of vitamin A supplements or fortified food [17].

Although a plethora of research on the effectiveness of vitamin A interventions exists, there is limited evidence on the effectiveness of food-based interventions such as increasing dietary intake of foods with high concentrations of preformed or provitamin A, traditional food fortification, or food biofortification on vitamin A status. Food-based interventions offer an opportunity for effective and catalytic programming to achieve global development targets, eradicate malnutrition, and improve health outcomes at scale [18–20]. Considerable efforts have been made in low- and middle-income countries (LMIC) to promote vitamin A intake through increased production and consumption of affordable provitamin A plant sources, mainly containing ß-carotene and ß-cryptoxanthin [21]. Food-based approaches, including supplementation, increased dietary diversity, and biofortification, have been identified as a key strategy in improving multi-micronutrient deficiencies [22].

This systematic review documents the scientific evidence on the effectiveness of food-based approaches on addressing VAD or improving the vitamin A status of women and children under 5 y. This review fills a critical gap in the literature base given that there is no recent review on the effectiveness of food-based approaches in combating VAD.

Methods

The authors followed the systematic review process reported by Crowther et al. [23] and adhered to the PRISMA guidelines [24]. Systematic searches and extractions were used to map the nutrition, agriculture, and public health literature and identify key concepts and primary research. A literature search was conducted using 4 large databases, including PubMed, CINHAL, Web of Science, and Google Scholar. The search strategy was developed in consultation with the University of Massachusetts Amherst Health Science librarian until we achieved saturation in the results.

Two authors, JN and KO, independently abstracted all studies in this review using a search strategy of text words, index, truncation, and Boolean operators [25]. The framework employed the following search terms in PubMed, CHNHAL, Web of Science, and Google Scholar: (“Food-based approach*” OR “strateg*” OR “program*” OR “intervention*” OR “trial” OR experiment*”) AND (“vitamin A status” OR ‘’vitamin A deficienc*”) AND (“women” OR “young child*” OR “infant*” OR “toddler*”). The * symbol serves as a wildcat that stands in for any letters to finish the word. Additional searches were conducted manually by looking at citations of full-text reviews, thus serving as a reference list search (that is, backward reference search) and cited reference search (that is, forward reference search). All searches were conducted and logged from May 2021 to March 2022.

Eligibility and exclusion criteria

Studies with publication dates between 2011 and 2022 were included in this empirical study. This time period reflects the last decade during which no systematic reviews were found on this topic. We included primary research studies that were *1*)

English-language publications in peer-reviewed journals; *2*) focused on interventions or programs of food-based approaches aimed at improving vitamin A status or VAD of women and children under the age of 5 y; and *3*) cross-sectional studies that explored the association between diet and vitamin A status of women and children. Studies were excluded if they were single case studies, unpublished theses or dissertations, not published in peer-reviewed journals, or not relevant to the objective of this review. We considered including articles in languages other than English but omitted these from this systematic review due to limited resources for translation of documents.

Study selection

Detailed information about the study selection process is provided in the PRISMA flow diagram (Figure 1).

Quality assessment

Each of the studies under review was independently assessed for quality by 2 authors, and reassessed by a third author. The team assessed risk of bias in each of the studies following recommendations of the Agency for Healthcare Research and Quality which provided evidence-based guidelines for assessing comparative effectiveness and risk of bias reviews of individual studies [26]. Recommendations applicable to this review included using a tool that is specific to the study design being evaluated, transparency in how assessments were made, and avoiding the presentation of risk of bias assessment as a numerical score. For cross-sectional studies, we used the AXIS tool as described by Downes et al. [27]. Developed in 2016, AXIS is a critical appraisal tool that addresses study design, reporting quality, and risk of bias in cross-sectional studies [27–29]. The AXIS tool includes 20 items that focus on study quality including justification of the sample, representativeness of the sample, use of validated measures, description of statistical methods, discussion of no response bias, funding statement, and conflict of interest disclosures [27]. For intervention studies, we determined risk of bias in randomized control trials using a tool that assessed study quality including trial design, conduct, and reporting [30]. For each domain, a series of questions elicited information about features of the trial that could result in risk of bias [31].

Data extraction

The research team used a standard form to extract information from each article on authors, year of publication, study design, study objective, sample size, recruitment method(s), sample eligibility criteria, geographical location, measures of vitamin A status and/or VAD, type of food-based approach,

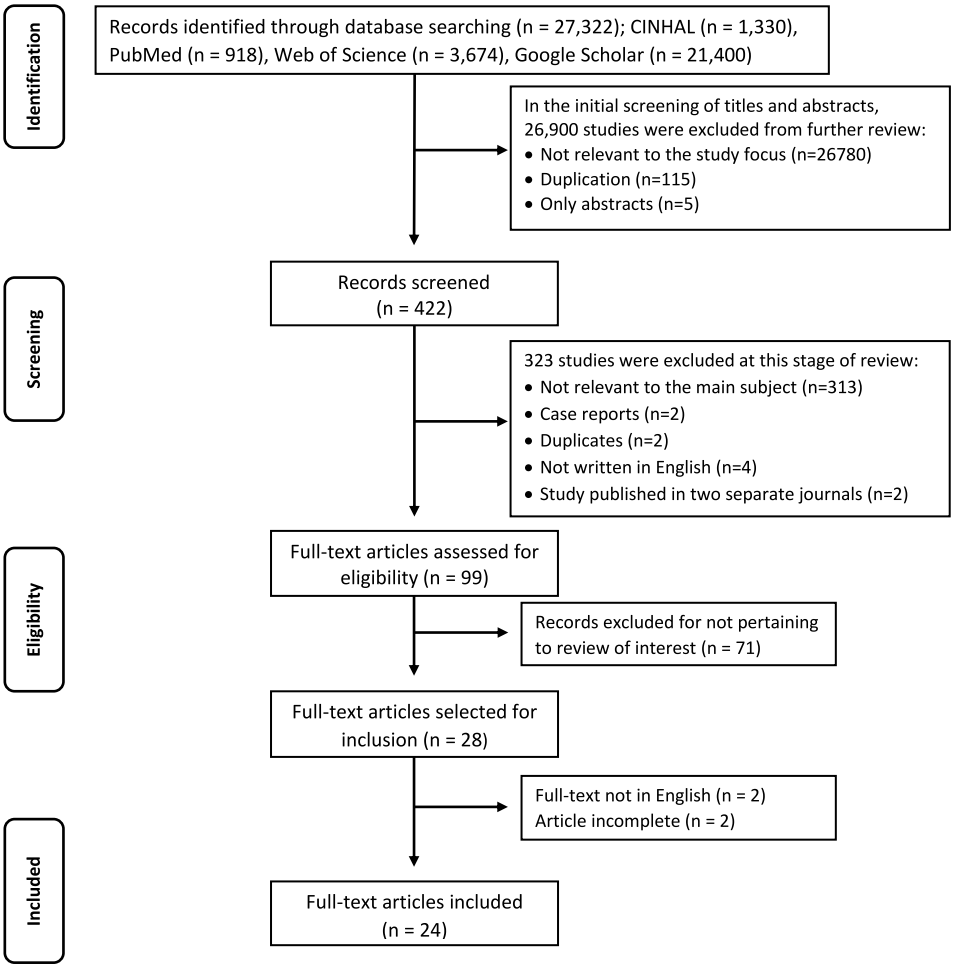


FIGURE 1. PRISMA flow diagram detailing the database searches, records screened and excluded, full-text articles retrieved and reviewed, and full-text articles included.

sociodemographic characteristics, statistical methods, and the effects on or relationship of the food-based approach to vitamin A status/VAD. Data were independently extracted from articles by 2 authors and later reconciled by the same authors by comparing extracted data with the original research articles. Discrepancies that arose between the 2 primary readers were resolved through review and discussion with a third author until consensus was reached. A protocol was not prepared for this review and this review was not registered.

Results

A total of 27,322 studies were identified and screened for this systematic review (PubMed: 918 articles; CINAHL: 1330; Web of Science: 3674; Google Scholar: 21,400 articles). After all titles and abstracts were examined, 26,780 studies did not meet the inclusion criteria. An additional 115 studies were excluded because of duplication and 5 were excluded because they were solely abstracts. Consequently, a total of 422 studies were screened. Of these, 2323 studies were excluded due to being irrelevant to the main subject ($n = 313$), single case reports ($n = 2$), duplication ($n = 2$), not English-language articles ($n = 4$), and because the same study was published in 2 different journals ($n = 2$) (Figure 1). Ninety-nine full-text articles were assessed further and of these, 71 records were excluded for not pertaining to the review of interest. Twenty-eight full-text articles were considered for inclusion and after excluding 4 articles, 24 empirical studies were included for the final systematic review (Figure 1).

General characteristics and main methodological properties of the 24 studies included in this systematic review are described in Table 1. Twenty-three studies focused on plant-based foods as sources of provitamin A/beta carotene and one study examined micronutrient-fortified milk, a source of preformed vitamin A. Interventions featured in this review spanned from 3 wk to 2 y. One study was conducted in each of the following countries: Uganda [32], Tanzania [33], Cameroon [34], Mozambique [35], Mexico [36], Philippines [37], Indonesia [38] and Thailand [39]. Two studies were conducted in each of the following countries: Kenya [40,41] Nigeria [42,43], Zambia [44,45], India [46,47], and United States [48,49]. Three studies were conducted in Bangladesh [50–52] and 3 studies were conducted in Brazil [53–55].

Participant characteristics

In total, there were 17,214 participants across the 24 studies in the final analytical sample. The number of participants ranged from 8 [49] to 3571 [47]. Four studies recruited less than 100 participants with a range from 8 to 70 participants [39,48,49,56]. All other studies ($N = 20$) recruited more than 100 participants [32–35,37,38,40–47,50–55]. Two studies recruited participants that were well-nourished with adequate vitamin A intake [48,49], whereas 9 studies reported that the participants had mild to moderate or marginal VAD [32,37,39,42–45,50,51]. Three studies indicated lower baseline vitamin A breast milk concentrations [34,44,51].

Eight studies recruited only women [33,39,40,48–51,53], 8 studies included only children [37,41,42,45–47,54,57], and 8 studies included both women and children [32,34,35,38,43,44,52,55]. Women included in the studies were in the reproductive age group ranging from 15 to 49 y, with a mean of 34.0 ± 0.5 y. Fourteen studies included children [32,34,35,37,38,41–43,45–47,52,54,55,57], most ($n = 12$) of which included children ≤60 mo [32,34,35,37,38,42,43,46,47,52,54,55]. The lowest and highest reported mean ages for children were 20.8 ± 0.5 mo and 8.9 ± 2.4 y, respectively.

Risk of bias in individual studies

Eligible studies were assessed for risk of bias (Table 2). Most studies explicitly stated the study objective as food-based approaches and vitamin A status or VAD; the population of interest; and the exposure and outcome of the study [32,34,37,39,40,42,44,45,48–51,54,57]. In the process of assessment, studies were identified as having a risk for sampling bias if they had loss to follow-up [32,39–41]. We noted 3 studies where measuring the exposure or the outcome was based on participant recall which increases bias [43,44,51]. Studies with stringent inclusion criteria or greater than 15% loss to follow-up were considered to have a higher risk of sampling bias [32,37,39,40,56]. One study explicitly reported a high risk of measurement bias as one of its limitations [46].

Methodological features of the studies

All studies reviewed were empirical and quantitative. Of the 24 studies, 14 studies (58.3%) were experimental studies [32,35,37,39–42,44,45,48–51,56]. Ten of the experimental studies were randomized control trials with 2 arms or groups [32,35,39–44,51,56]; 2 studies had 3 arms [41,44] and 2 studies had 4 arms [50,51]. Two randomized crossover trials [48,49], with a minimum of 2 wk between food-based treatments, and one pre- and post-evaluation study were also included [38]. Ten studies (41.7%) were nonexperimental [33,34,38,43,46,47,52–55], with one study being a prospective cohort study [53] and one with a longitudinal design that had an intended intervention [33]. The remaining were cross-sectional studies [34,38,43,46,47,52,54,55].

Sampling techniques

The reviewed studies employed various sampling techniques at different stages of the design including multistage cluster sampling [34,43,45,52], cluster sampling [32,35,46], simple sampling at the village or household level [38,44,51], and simple random sampling of participants [37,39,51]. Other studies employed purposive sampling of participants [33,41,42,48,49,53,55] or the sampling techniques were not clearly articulated in the articles [40,50,54,57]. All 14 experimental studies employed randomization of participants to the study arms. Among the nonexperimental studies, 4 studies purposively selected women who met the inclusion criteria [37,40,47,50]. In 7 studies, only children under the age of 5 y were included in the study [37,42,45–47,54,57].

Food-based approaches

Food-based approaches identified in this review included examination of tubers, citrus, rice, maize, fruit, oil, peanuts, and milk. Biofortified foods included orange-fleshed sweet potatoes (600 μg) [32,35,40,50,51], provitamin A-fortified cassava (1mg ß-carotene) [41–43,48,49], tangerines (13 RAE/100g) [51], vitamin A fortified rice (6–31 μg/g) [39], and orange maize

TABLE 1
Characteristics of the studies included in the review of food-based approaches on vitamin A status of women and children under 5 y

	Study	Country	Study design	Sample size	Age range and mean age	Exposure/intervention	Outcome
RCT	Hotz et al., 2012 [32]	Uganda	• Randomized control trial with 2 arms • 2-y intervention	$N = 1416$ children 843, women 573	Children 6–35 mo, mean age 20.8 ± 0.5 mo; 3–5 y, mean age 51.4 ± 0.4 mo; women 13–45 y, mean age 34.0 ± 0.5 y	OFSP distribution and consumption	Serum retinol adjusted for inflammation/infection
RCT	Mason et al., 2011 [37]	Philippines	• Randomized control study with 3 groups • 18 mo intervention	$N = 342$ children	Children 1–5 y, mean age 32.4 ± 9.8 mo	3-monthly and 6-monthly VAC dosing vs. vitamin A fortified coconut oil promotion (3-mo and 9-mo) plus 6-monthly VACs	Serum retinol
RCT	Pinkaew et al., 2021 [39]	Thailand	• Randomized control trial • 70-d intervention	$N = 70$ lactating women recruited during pregnancy; 35 women in each group	Women 20–40 y, mean age 28.9 ± 5.2	Rice consumption (50 μg RAE/50g) with other foods vs. unfortified rice	Change in vitamin A status measured using the C-RID [4] test
RCT	Girard et al., 2017 [40]	Kenya	• Intervention study with control • 1-y intervention	$N = 505$ women. 250 intervention arm and 255 control arm	Women, mean age 24.3 ± 5.5 y Prime gravidity at 30%	Distribution of OFSP vines, enhanced nutrition education about OFSP and vitamin A vs. clinic-based nutrition only	Serum retinol adjusted for infection
RCT	Talsma et al., 2016 [41]	Kenya	• Randomized control trial with 3 arms, 6/d for 18 mo • 5-wk intervention	$N = 342$ children	Children 5–13 y, mean age 8.9 ± 2.4 y	Yellow cassava vs. ß-carotene supplement vs. white cassava	Serum retinol level
RCT	Palmer et al., 2016 [44]	Zambia	• Randomized control trial, with 3 arms • 6-wk intervention	$N = 149$ lactating women with children aged 4–12 mo	Women 20–30 y, mean age 22 y	White maize and placebo verses orange maize (600μg RAE/d) vs. Vitamin A capsule (600ug) retinyl palmitate	Milk retinol concentration adjusted for CRP and AGP
RCT	Palmer et al., 2016 [45]	Zambia	• Randomized control trial, with 2 arms • 6-mo intervention	$N = 1024$ children	Children 4–8 y, mean age 5.7 ± 1.3 y	Biofortified orange maize verses white maize	Serum retinol, response to grade light stimuli
RCT	La Frano et al., 2013 [48]	United States	• Randomized, single blind crossover study • 3 meals with 2 wk washout period • 6 sample collection between 0.5 and 9.5 h	$N = 12$ nonpregnant women	Women 21–44 y, mean age 29.3 ± 8.8 y	Biofortified cassava, each participant consumed 3 randomized cassava porridges, 3 meals separated by 2 wk wash out	Post prandial plasma triacylglycerols retinol lipoprotein
RCT	Zhu et al., 2015 [49]	United States	• Randomized crossover trial • Three gari preparations separated by 2 wk washout periods	$N = 8$ women	Women 19–43 y, mean age 27.1 ± 2.9 y	Three gari preparations separated by 2-wk washout periods; treatments (containing 200–225.9 g gari) were biofortified gari (containing 1 mg ß-	Post-ingestion Triacylglycerol-rich plasma and drawn 6 times from 0.5 to 9.5 h

(*continued on next page*)

TABLE 1 (*continued*)

	Study	Country	Study design	Sample size	Age range and mean age	Exposure/intervention	Outcome
			• 6 sample collection between 0.5 and 9.5 h			carotene), red palm oil-fortified gari (1 mg ß-carotene), and unfortified gari with a 0.3 mg retinyl palmitate reference dose	
RCT	Jamil et al., 2012 [50]	Bangladesh	• Randomized control trial, with 4 arms • 10-wk intervention	$N = 120$ nonpregnant, nonlactating women	Women 18–45 y, mean age 28.4 ± 6.5 y	WFSP + a corn oil capsule, 600ug of boiled OFSP + capsule 150 uL corn oil (BOFSP); boiled WFSP + a capsule containing 600 ug RAE of retinyl palmitate; 600 ug as boiled and fried OFSP and a corn oil capsule (FOFSP)	Plasma retinol concentrations
RCT	Turner et al., 2013 [51]	Bangladesh	• Randomized placebo-controlled trial with 4 arms • 3-wk intervention	$N = 136$ lactating women; 34 women in each of the 4 groups	Women 18–45 y, mean age 24.0 ± 5 y	Vitamin A capsule + white-fleshed sweet potatoes vs. tangerine + placebo capsule vs. OFSP + placebo capsule vs. white-fleshed sweet potatoes + placebo capsule; assessed using FFQ	Serum retinol level
RCT	Lopez-Teros et al., 2013 [57]	Mexico	• Randomized control trial • 3-mo intervention	$N = 27$ children	Children 3–6 y, mean age 5.5 y	Daily consumption of 250 mL of VA fortified milk providing 196 RAE/d	TBVA; serum retinol
RCT	Afolami et al., 2020 [42]	Nigeria	• Randomized control trial • 93-d intervention	$N = 176$ preschool children	Children 36–60 mo, mean age 49 ± 12.4 mo	Children were fed on either yellow or white cassava twice a day, 6 d a week for 93 d providing 221 RAE/d of the yellow cassava vs. 74 RAE/mcg of the white cassava	Serum retinol adjusted for inflammation
RCT	Hotz et al., 2012 [35]	Mozambique	• Randomized control trial • 2.5 y intervention	$N = 432$ women and children	Children 6–35 mo; 3–5.5 y, mean 22.4 ± 0.4 mo, pregnant and women, mean age 28.9 ± 0.5 y	Distribution of OFSP vine, intake of vitamin A foods including OFSP	OFSP consumption and vitamin A intake by children and women
LNG	Ndau et al., 2016 [33]	Tanzania	Longitudinal intervention design	$N = 569$ lactating women	Lactating women 15–49 y	Consumption of vitamin A rich foods, knowledge about vitamin A and fortified oil	Serum retinol
CSS and PCS	Jus'at et al., 2014 [38]	Indonesia	Cross-sectional survey, pre-post design with independent samples. Study also collected semi-weekly oil	N =1518 women and children	Lactating mothers, mean age 28.9 ± 6.7 y; children 12–23 mo, mean age 17.1 ± 3.8 mo; 24–59 mo, mean age 38.3 ± 10; women	Dietary intake of vitamin A and consumption of vitamin A fortified cooking oil	Serum retinol adjusted for subclinical infection of women and children

(*continued on next page*)

TABLE 1 (*continued*)

	Study	Country	Study design	Sample size	Age range and mean age	Exposure/intervention	Outcome
			samples from 2 cohorts, *1*) children (5–9 y) and *2*) women (15–29 y), between surveys		15–29 y, mean age 23.0 ± 6.6 y		
CSS	De Moura et al., 2015 [43]	Nigeria	Cross-sectional survey	N = 578 Mother-child dyads	Women 18–49 y mean age 28.2 ± 7.9 y; children 6–59 mo mean age 32.5 ± 14.9 mo	Dietary intake including consumption of provitamin A biofortified cassava, assessed using multiple 24-h recall	Serum retinol adjusted for inflammation/ infection
CSS	Sachdeva et al., 2011 [47]	India	Cross-sectional survey	N = 3571 children	Children 0–60 mo, mean age 36.0 ± 21 mo	Dietary intake and Vitamin containing foods	Xeropthalmia; ocular examination and proxy report from mothers
CSS	Suri et al., 2017 [46]	India	Cross-sectional survey	N = 750 children	Children 12–60 mo, mean age 33.45 ± 12.7 mo	Dietary intake assessed using the Hellen Keller FFQ	VAD as deduced from the dietary intake
RCT	Rahman et al., 2017 [52]	Bangladesh	Cross-sectional survey	N= 1176 women and children	Children 6–59 mo, Children 6–14 y, NPNLW 15–49 y	Dietary intake was assessed using the FFQ	serum retinol levels adjusted for CRP and AGP
LNG	Neves et al., 2018 [53]	Brazil	Prospective cohort study	N = 442 pregnant women	Women, mean age 24.7 ± 6.4 y	Dietary intake including Amazon fruits	Serum retinol
CSS	Lira et al., 2018 [55]	Brazil	Cross-sectional study	N = 134 pairs of mother-infant dyad, lactating women	Women 18–40 y 24.9 ± 6.6 y Children <1 y	Dietary intake in the last 3 mo using an FFQ	Serum retinol and ß-carotene
CSS	Lima et al., 2017 [54]	Brazil	National survey	N = 3417 children	Children 6–59 mo	Dietary intake	VAD as measured using serum retinol levels
CSS	Engle-stone et al., 2017 [34]	Cameroon	Cross-sectional survey, pre-post design with independent samples: 2 y before and 1 y after cooking oil fortification program	N = 300 women 15–49 y and children 12–59 mo	Children 12–59 mo, mean age 32.9 ± 0.8 mo; women 15–49 y, mean age 29.1 ± 0.4 y	Vitamin A fortified coconut oil intake measure using FFQ	Serum RBP, breast milk retinol adjusted for inflammation

Abbreviations: AGP, α1-acid glycoprotein; BOFSP, boiled orange-fleshed sweet potato; C-RID, C-retinol Isotope dilution; CRP, C-reactive protein; CSS, cross-sectional study; FFQ, food frequency questionnaire; LNG, longitudinal study; OFSP, orange-fleshed sweet potatoes; PCS, prospective cohort design; RAE, retinoic acid equivalent; RBP, retinol binding protein; RCT, randomized control trial; VAC, vitamin A capsule; WFSP, white-fleshed sweet potato.

TABLE 2
Findings, study limitations, and risk of biases of the studies included in the review of food-based approaches on vitamin A status of women and children

	Study	Main findings	Baseline and end data for Vit A levels	Study limitations	Risk of bias
NS	Hotz et al., 2012 [32]	Significant increase in OFSP consumption; no impact of intervention on serum retinol for women One-third reduction in serum retinol <0.7mmol/L, 9.5% reduction in the prevalence of children with retinol <1.05 mmol/L	Vit A RAE, μg/d Children 6-35 mo: Baseline IP 315 ± 49, RP 242 ± 39, Control 315 ± 59. Follow-up IP 443 ± 61, RP 425 ± 70, Control 279 ± 40 Women: Baseline IP 692 ± 73, RP 683 ± 87, Control 855 ± 120. Follow-up IP 1390 ± 170, RP 12205 ± 170, Control 762 ± 90	Unable to tease out the contribution of vitamin A levels from other sources such as red palm oil	Sampling bias due to significant loss to follow-up, potentially resulting into differential misclassification
Sig	Mason et al., 2011 [37]	No difference in baseline serum retinol was observed between VAC groups, and no significant change in serum retinol and VAD was observed from baseline to endpoint for VAC groups. Promotion of vitamin A-fortified oil over 9 mo plus 6-monthly VACs seemed most effective with a significant increase in serum retinol (5–6 mcg, $P < 0.001$) and decrease in the prevalence of low serum retinol	Blood samples were collected to assess serum retinol and hemoglobin status. Mean serum retinol across all groups was 22.5 ± 6.6 mcg/dL at baseline. No significant changes in serum retinol at endpoint for VAC groups. An 5–6 mcg increase in serum retinol was observed over 18 mo for the promotion of vitamin-A fortified oil (9 mo) plus 6 monthly VACs ($P < 0.001$).	Changes in the initial methods, the intervention arm of oil promotion picked momentum at a later point therefore at the end of 18 mo, there was no comparison/control group. The results are not generalizable due to the lack of a comparison group.	Sampling and measurement bias due to changes in study methodology along the course of the intervention.
Sig	Pinkaew et al., 2021 [39]	Total body vitamin A stores were significantly higher in the intervention than the control group. An estimated total liver VA reserves indicated high levels of VA deficiency	TBS of VA, μmol retinol VA rice: Baseline = 240 (182, 316), Endpoint = 331 (251, 447), Change = 52.9 (−74, 453). Control: Baseline = 257 (199, 339), Endpoint = 275 (214, 355), Change = −4.3 (−106, 275)	Metabolic differences among women impacting on the assumptions used for the stable isotope technique (RID) equation. The necessity to validate the results since accuracy reduces as due to losses through breast milk	Sampling bias due to loss to follow-up
Sig	Girard et al., 2017 [40]	No impact of the intervention on the mean RBP, however with reduced odds of RBP <1.17 mmol/L ($P = .001$) at 9 mo. Higher odds of VA adequacy as measured by EAR or DRI ($P < .001$)	VA, μg RAEs/d. Intervention: 451 (251–810) Control: 321 (173–533) Adjusted 95% CI: 287 (82, 513) $p < .01$	Minimal bias due to geographical clustering, logistical constraints	Sampling bias due to losses to follow-up in either group of the study
NS	Talsma et al., 2016 [41]	An increase in serum retinol concentration by 0.04 μmol/L was observed for both yellow cassava and ß-carotene. No marked difference was observed in the prevalence of VAD for yellow cassava or ß-carotene	Baseline prevalence of serum retinol concentration <0.7 μmol/L was 27% Intake of yellow cassava and supplementation with ß-carotene increased serum retinol concentration by 0.04 μmol/L	Sample size might have been a limitation of the study. Furthermore, serum retinol concentration as a primary measure may result in overestimation of deficiency and underestimation of effect	Sampling bias due to loss to follow-up, however not significant
NS	Palmer et al., 2016 [45]	The mean ±SD pupillary threshold did not differ significantly between WM and OM clusters at baseline (−1.94 ± 0.71 compared with −1.82 log cd/m^2 ± 0.79, respectively; $p = 0.16$)	Baseline: At baseline, 11.7% of the children had serum retinol <0.7 mmol/L, 14.4% had impaired dark adaptation (pupillary threshold 21.1 log cd/m^2), and 2.3% had night blindness. <0.7	Significant differences were identified in the subsample of children by intervention group including pupillary baseline response, this may have affected the results	Measurement bias due to differences in the 2-intervention group were likely to regress the mean of the pupillary response

(*continued on next page*)

TABLE 2 (*continued*)

	Study	Main findings	Baseline and end data for Vit A levels	Study limitations	Risk of bias
		and at end line (−1.98 ±0.79 compared with −1.88 log cd/m^2 ± 0.73) respectively	µmol/L was 12.9% for the WM group and 10.4% for the OM group. No endline data reported		
NS	Palmer et al., 2016 [44]	The mean milk retinol concentration was higher in the orange maize group vs. the VA capsule group. However, the difference was not statistically significant	Milk retinol µmol/L, WM + placebo/Initial: 0.93 (0.76, 1.14)/Final: 0.91 (0.72, 1.14) OM + placebo/Initial: 0.95 (0.78, 1.16)/Final: 1.15 (0.96, 1.39) White maize + VA/ initial= 1.01 (0.85, 1.20)/ Final: 1.17 (0.99, 1.38)	The intervention period was short, probably results would be different if longer	Measurement bias as a result of discrepancies in the outcome indicator, the milk sampling method has an effect on the retinol concentration
Sig	La Frano et al., 2013 [48]	The plasma TAG retinol lipoproteins were higher with the biofortified meal compared to the other 2 meals. Similar bioavailability was observed for the 3 meals; however, the rate at which ß-carotene was detected in blood was significantly different	No baseline and end data were collected regarding VA concentration of participants	The participants in the study were well-nourished, probably with adequate vitamin A reserves, this affects the effect of the intervention	Measurement bias as a result of possible carry-over effects
Sig	Zhu et al., 2015 [49]	There was an increase in ß-carotene and alpha-carotene and retinyl palmitate at the end of the meal. The retinyl palmitate induced by the red palm oil supplement added to biofortified cassava gari was greater than that induced by the red palm oil added to unfortified cassava gari ($P < .05$) (4.12 ± 1.5 vs. 2.4 ± 0.3 µg provitamin A carotenoid:1 µg retinol) (means ± SEM)	Conversion of vitamin A for red palm oil was 2.4 ± 0.3 and for biofortified gari 4.2 ± 1.5 µg provitamin A carotenoid/ 1 µg retinol. Both resulted in increased levels of ß-carotene, α-carotene, and retinyl palmitate in triacylglycerol-rich plasma concentrations of participants	The study was conducted among well-nourished American women, probably the results would have been different in a vitamin A deficient population	Measurement bias due to possible carry-over effects
NS	Jamil et al., 2012 [50]	Mean plasma ß-carotene concentrations were higher in groups that received OFSP ($P < .001$), and final mean plasma ß-carotene was marginally higher in the group that received fried OFSP compared with boiled OFSP ($P = 0.07$). No significant differences observed between baseline and final total body VAs. Despite BC concentration, there was a limited impact of OFSP on vitamin A status	Initial and final total body VA pool sizes were 0.071 ± 0.081 mmol and 0.153 ± 0.356 mmol, respectively, for all groups combined ($P = 0.50$, $N = 115$)	Differences in the diets for the 2 study populations may have painted a different picture of the results compared to if the 2 groups were initially as close as possible	Measurement bias due to differences in the diets for the 2 study population groups
NS	Turner et al., 2013 [51]	Plasma retinol increased in the VA group. Plasma BC in the OFSP group and ß-cryptoxanthin in the tangerine group increased 250% and 830%, respectively; apparent relative absorption in the	Retinol (mmol/L): Control: Baseline 0.83±0.03, Final 0.86± 0.03 OFSP: Baseline 0.85±0.04, Final 0.96± 0.04 VA: Baseline 0.9 ±0.05,	Self-reporting of factors such as intake of foods other than treatments, the relatively short intervention time, and the inability to measure changes in VA status directly	Measurement bias due to dietary intake assessment errors

(*continued on next page*)

TABLE 2 (*continued*)

	Study	Main findings	Baseline and end data for Vit A levels	Study limitations	Risk of bias
		ß-cryptoxanthin group, considering the amounts consumed, was 4 times that in the BC group. OFSP and tangerines did not contribute to increased VA concentration in breastmilk	Final 1.21±0.05 Tangerine: Baseline 0.88±0.05, Final 0.93± 0.04		
Sig	Lopez-Teros et al., 2013 [57]	Median changes in the serum retinol concentration for the intervention and control groups were 0.13 and 20.21 mmol/L, respectively ($P = 0.009$). Median changes in the TBVA stores were 0.06 and 0.01 mmol, respectively ($P = 0.006$) and estimated median changes in the liver VA concentration were 0.09 and 0.01 mmol/g, respectively ($P = 0.002$)	Serum retinol mmol/L Intervention: Baseline 1.19, 3 mo 1.38 Control: Baseline 1.29, 3 mo 10.9	Lack of placebo milk to the children in the control group	Measurement bias due to dietary intake assessment errors
NS	Afolami et al., 2020 [42]	No significant treatment effect for adjusted ß-carotene was detected (3.9%; 95%CI: −0.6%, 8.6%). But a significant effect for the hemoglobin concentration (adjusted effect: 3.08 g/L; 95% CI: 0.38,5.78 g/L)	β-carotene, µmol/L White cassava group/ Baseline 1.82 (1.25, 2.48), Follow-up 2.51 (1.76, 3.36) Yellow cassava group/ Baseline 1.90 (1.35, 2.42), Follow-up 2.64 (2.10, 3.57)	Challenging to control for the foods consumed by the children outside the intervention meals. Low prevalence of VAD in the study population contributing to a nondetectable treatment effect	Measurement bias due to lack of control of other food consumed
Sig	Hotz et al., 2012 [35]	There was a significant net increase in OFSP and vitamin A intake by children 6-35 mo, 3-5.5 y, and women, OFSP provided 80% of the total vitamin A intakes	Women Vit A intake (µg RAE/d) Mean: Model 1: Baseline 504.4, Follow-up 1053.9 Model 2: Baseline 523.7, Follow-up 1240.2 Control: Baseline 541.3, Follow-up 599.2	Biochemical or clinical indicators of vitamin A status were not included, therefore it was not possible to predict the impact of the increase of vitamin A intake on change in vitamin A status, instead relied on other smaller studies in the same area that reported improvement in serum retinol concentration	Measurement bias due to dietary intake assessment errors
N/A	Ndau et al., 2016 [33]	Mothers had a positive attitude toward vitamin A consumption though consumption of vitamin A rich foods was generally low; 40% of the mothers consumed animal products and 20% consumed plant products; Residence was significantly associated with vitamin A status ($P <$ .001). Prevalence of VAD was highest in the younger age group 15–19 at 88.5%	No baseline and end data were collected regarding vit A concentration of participants	subclinical infection/ inflammation was not controlled for, possibly could have had an effect on the prevalence of VAD	Measurement bias due to lack of measurement for possible confounding factors
Sig	Jus'at et al., 2014 [38]	Fortified oil improved vitamin A intake of	Mean (CRP/AGP-adjusted) serum retinol	Uncertainty in the extrapolation of vitamin A	

(*continued on next page*)

TABLE 2 (*continued*)

	Study	Main findings	Baseline and end data for Vit A levels	Study limitations	Risk of bias
		children, lactating and nonlactating women. Serum retinol was 2–19% higher at end line than baseline ($P<\cdot001$). After adjusting for socioeconomic differences, vitamin A intake from fortified oil predicted retinol status for children aged 6–59 mo ($P=\cdot003$) and 5–9 y ($P=\cdot03$)	concentrations at baseline ranged from 30·7 μg/dl among children aged 6–11 mo and lactating mothers, to 42·7 μg/dl among nonlactating women at endline, mean retinol was higher among all groups, with $P<0\cdot001$ among all groups except children aged 12–23 mo ($P=0\cdot529$) and 24–59 mo ($P=0\cdot057$)	content in oil from a subsample of households. Potential measurement errors in the measurement might have diluted the associations between vitamin A intake from oil and vitamin A status	Measurement bias due to possible errors recording dietary intake
N/A	De Moura et al., 2015 [43]	Vitamin A intake was adequate with a high median of intake children 1038 μg RAE/d for children and 2441 μg RAE/d for women. VAD was 16.9% among children and 3.4% among women. Fortified cassava and dark leafy vegetables were the primary sources of VA	No baseline and end data were collected regarding vit A concentration of participants	Study limitations were not highlighted	Measurement bias as by design
Sig	Sachdeva et al., 2011 [47]	Overall prevalence was at 9.1%. Low intake of proteins and vitamin A containing foods as well as predominant maize diet were significant dietary factors. Rural dwelling, lower social class, maternal illiteracy were significant antecedent sociodemographic risk factors	No baseline and end data were collected regarding vit A concentration of participants	Inability to determine cause and effect being a cross-sectional study	Measurement bias due to errors recording dietary intake
N/A	Suri et al., 2017 [46]	Plant and animal sources such as eggs and butter were the major sources of vitamin A in the study population. Consumption of animal foods was low to negligible. 80% of villages exhibited subclinical VAD, with 9/15 identified using the animal protein intake criteria and 12/15 using a weighted intake score. Three villages did not have subclinical VAD	No baseline and end data were collected regarding VA concentration of participants	Possibility of overestimation of the outcome because breastmilk was not taken into consideration	Measurement bias as a result of the exclusion of other vitamin A sources
Sig	Rahman et al., 2017 [52]	VAD prevalence was highest among preschool (6-59 mo) 20.5% vs. 20.8% and school-age (6-14 y) children compared to 5.3% NPNLW. Higher consumption of animal foods was significantly associated with VA status, while higher consumption of leafy green vegetables was associated with lower retinol status	No baseline and end data were collected regarding vit A concentration of participants	Inability to establish the cause-effect relationship given the study design, exclusion of foods from the FFQ which are part of the participants' diet	Measurement bias due to errors recording dietary intake

(*continued on next page*)

TABLE 2 (*continued*)

	Study	Main findings	Baseline and end data for Vit A levels	Study limitations	Risk of bias
Sig	Neves et al., 2018 [53]	Serum retinol levels were associated with the consumption of Amazon fruits (β = 0·087: 95% CI: 0.012, 0.162)	First evaluation week (16–20 wk): IQR = 1.00–2.60 Second evaluation week (~28 wk): IQR = 1.20–2.70	Lack of data on other biochemical indicators such as the retinol binding protein, the actual nutrient intake was also not estimated	Sampling bias due to nonprobability sampling techniques
Sig	Lira et al., 2018 [55]	16% of the women had insufficient intake of VA and ß-carotene. Mean retinol levels were low in 8% of the mothers though they were adequate overall. Retinol and ß-carotene levels were positively associated in cord serum ($P = 0.004$), maternal serum ($P = 0.041$), and colostrum ($P< 0.001$) but not associated with dietary intake	No baseline and end data were collected regarding vit A concentration of participants	Use of mean retinol concentrations to support biochemical and nutritional risk of VAD can mask	Measurement bias due to possible errors recording dietary intake
Sig	Lima et al., 2017 [54]	After adjusting for confounders, consumption of meat at least once in the 7 d was a protective factor (PR: 0.24; 95% CI: 0.13, 0.42).	No baseline and end data were collected regarding vit A concentration of participants	Overestimation of serum retinol levels since inflammation was not measured and controlled for	Measurement bias due to possible errors in dietary intake recording
NS	Engle-stone et al., 2017 [34]	Evaluation after a year of VA fortified oil no significant changes were observed in plasma RBP or breastmilk VA status	Women Pre-Fortification (2009) RBP, μmol/L 1.41± 0.02 Post-Fortification (2012) RBP, μmol/L 1.40 ± 0.02 Children Pre-Fortification (2009) RBP, μmol/L 0.87 ± 0.02 Post-Fortification (2012) RBP, μmol/L 0.88 ± 0.02	the sample size was probably inadequate, the picture would be different for a larger sample size	Measurement bias

Abbreviations: AGP, *α1-acid glycoprotein;* BC, ß-carotene; BOFSP, boiled orange-fleshed sweet potato; C-RID, C-retinol Isotope dilution; CRP, C-reactive protein; DRI, daily recommended intake; EAR, estimated average requirement; FFQ, food frequency questionnaire; NPNLW, nonpregnant nonlactating women; NS, not significant; OFSP, orange-fleshed sweet potatoes; OM, orange maize; RAE, retinoic acid equivalent; *RBP, retinol binding protein;* RID, retinoic isotope dilution; Sig, statistically significant; TAG, triacyl glycerol; TBVA, Total body vitamin A; VA, vitamin A; *VAC, vitamin A capsule*; VAD, vitamin A deficiency; WFSP, white-fleshed sweet potato; WM, white maize.

(17–24 μg/g, [44,45]. Other food-based approaches used micronutrient-fortified milk [57], red palm oil (1mg ß-carotene) [49], vitamin A fortified cooking oil [33,38], and vitamin A fortified coconut oil [34,37]. Fruits from the Amazon rain forest with high concentrations of provitamin A carotenoids were included in one study [53]. Four studies focused on the associations between dietary intake of foods rich in provitamin A carotenoids and vitamin A status or VAD [33,47,52,54]. Four intervention studies compared vitamin A supplements to food-based approaches or dietary intake of foods with high concentrations of preformed or provitamin A [37,44,50,51]. Interventions included distribution of supplemental foods to participants for daily consumption [39,56] and plant materials, such as orange-fleshed sweet potato vines [32,35,40]. Interventions designed as controlled experiments included prepared meals distributed to participants on top of their daily diets [41,42,48,49,57]; dietary intake effects on vitamin A status [33,38,47,54,55]; take-home uncooked foods for consumption with the other foods/meals [39,51]; or vitamin A supplementation compared to dietary intake of foods with high concentrations in provitamin A carotenoids [37,41,44,50,51].

In randomized controlled trials, the intervention period ranged from 3 wk [51] to 2 y [32], with 3 interventions extending beyond 12 mo [32,35,37]. Three experimental studies included more than one intervention and comparison arm [41,50,51]. Dietary intake, as an exposure variable, was assessed with either a food frequency questionnaire (FFQ) [34,35,46,52,53,55] or 24-h dietary recall [32,38,40,47,48].

Vitamin A status/vitamin A deficiency measurement

Outcomes of interest in the reviewed studies were vitamin A status and VAD. Measurement methods for these variables included high-performance liquid chromatography [32,35,37,41,44,48,51–55,57], enzyme-linked immunosorbent assay [33,34,38,40,41], or the retinol isotope dilution (RID) [39]. Vitamin A status was also estimated using postprandial plasma TAG retinol lipoprotein [48,49], response to grade light stimuli [45], xeropthalmia through ocular examination [47], or post-ingestion

and VAD deduced from dietary intake [46]. Eleven of 24 studies (45.8%) reported adjusting serum retinol levels for inflammation or subclinical infection [32,34–36,38–40,42–44,52].

Effect of food-based approaches on vitamin A status of women and children

A significant difference in vitamin A status was observed between the intervention and control groups ($P < 0.05$) in 8 intervention studies [35,37,39,40,48,49,52,57]. In another 7 intervention studies, no statistically significant differences were observed between groups, although vitamin A levels were higher in the intervention group compared to the control group in some studies [32,41,42,44,45,50,51]. Some of these studies found a statistically significant ($P < 0.05$) improvement in the vitamin A status or serum retinol levels [37,39,52], or improvement in TAG retinol lipoproteins [48], or improvement in total body vitamin A stores [40,57], or increase in beta ß-carotene, α-carotene, and retinyl palmitate in triacylglycerol-rich plasma concentrations [49] of the participants in the intervention groups. While an additional 2 studies reported a statistically significant positive association between dietary intake of foods with high concentrations of preformed vitamin A or provitamin A and vitamin A status [48,52]. In one study, a significant mean difference in retinol levels was noted in children but not among the women studied [32]. Another study reported a significant change in retinol levels at 18 mo as opposed to the 3-mo follow-up period [37].

In 5 cross-sectional studies, dietary intake of foods with high concentrations of provitamin A carotenoids was associated with higher serum retinol levels or other indicators or vitamin A status [38,47,53–55]. One cross-sectional study reported nonsignificant associations between vitamin A intake and serum levels [34]. Retinol levels were adjusted for inflammation or subclinical infection in 12 of the 24 studies [32,34,38–41,43,44,50–53].

Limitations of individual studies

A major limitation of this review is that studies derived from the search terms comprised plant-based food approaches, with the exception of one study on vitamin A fortified milk [57]. Individual studies included in the review highlighted a number of design and sampling-related limitations (Table 2). Cross-sectional studies could not establish a causal relationship. Three studies noted an inadequate amount of time (that is, 3–18 mo) to observe effects in intervention studies [37,42,56]. Four studies had low-powered designs with insufficient sample sizes to comprehensively examine the effects of food-based approaches on the retinol levels or vitamin A status of the populations [34,48,49,56]. Three studies did not include biochemical measurements of serum retinol and instead, deduced vitamin A status from dietary intake or ocular examination thus increasing the likelihood of estimation error and bias associated with self-reports [35,46,47].

Another study noted the possibility of underestimation of the outcome as a limitation considering the nutrition contribution of breast milk was not measured [46]. Similarly, the lack of precision in the estimation of the 600 μg capsule of vitamin A in another study may have resulted in overestimated changes in retinol levels hence reducing the power to detect an effect [44]. Two studies reported that additional confounding factors for vitamin A status were not measured [33,54], thus increasing the likelihood of overestimation of the outcome. In one study, the physiological status of women who were breastfeeding may have impacted the assumptions used in RID calculations [39], hence suggesting a need to further validate the results due to issues with accuracy related to losses through breast milk. Two studies identified the inability to delineate the effect of the intervention as the sole contributor to the vitamin A status as a study limitation [32,42]. Another 2 studies were conducted among adequately nourished women suggesting optimal vitamin A status compared to studies examining VAD among participants [48,49]. Change in the initial methods of one study was documented as a limitation [37].

Discussion

This systematic review examined and synthesized research on the effects of food-based approaches on vitamin A status or VAD of women and children. The studies included in this review focused on women who were pregnant or lactating, and/or children under 5 y of age. These are critical stages of the life cycle with increased demand for vitamin A [58]. Vitamin A is necessary for cell differentiation and organ formation during pregnancy, for tissue repair in the postpartum period [59,60], and during fetal growth and development [58]. This systematic review assessed evidence of the effects of food-based approaches on the vitamin A status of women and children, and aimed to serve as a reference for future research and policy development. Previous reviews on vitamin A interventions have reported inconsistent results for improvements in vitamin A status [60] and none reported improvement in the absorption of other micronutrients [61].

There is high rate of mortality among children under 5 y of age in LMIC [62,63]. Almost three-fourths (72%) of children aged 6–23 mo are not fed a minimally diverse diet to meet their nutrition needs resulting in a high risk of not meeting their vitamin A requirements [64]. Food-based approaches provide opportunities to integrate the delivery of successful evidence-based interventions in maternal health and childhood programs for early identification, prevention, and control of VAD. Furthermore, evaluating interventions that can enhance nutrient intakes for desired health outcomes in resource-constrained settings can inform national policies to reduce malnutrition and improve health outcomes.

This systematic review found that some food-based approaches focusing on vitamin A had the potential to improve the vitamin A status of affected populations. Fifty-four percent ($N = 13$) of the studies in this review reported statistically significant results in interventions aimed at improving serum retinol levels [35,37,39,40,48,49,52,57] or in cross-sectional studies examining associations between dietary intake and vitamin A status or serum retinol levels [38,47,53–55]. In one cross-sectional study, consumption of animal source foods had an advantage over dark leafy green vegetables as protective factor for vitamin A status [52]. Household income and place of residence (urban compared with rural) were also significant variables attributable to higher serum retinol levels [47], suggesting that a multitude of factors influence vitamin A intake. The limitation of cross-sectional designs is that they cannot ascertain causal pathways. However, these studies still provide important information on determinants of intake of foods with high concentrations of preformed or provitamin A.

When a focus on and engagement of the population of interest is central to programming, the benefits of food-based approaches are likely to reach the poorest populations, while being more sustainable and environmentally friendly [65]. In addition, such food-based approaches are less likely to cause toxicity compared to high dose vitamin A supplementation programs [66,67]. Nevertheless, there are challenges in the design and assessment of the multiple input variables that go into a comprehensive food-based intervention [68]. Considerations have to be made to assess the quality of studies. Examination of the variety of approaches and crops used, including dietary modification of traditional foods, combinations of supplement and food-based interventions, and biofortification of widely consumed staple foods such as rice, maize, orange-fleshed sweet potatoes, and cassava, is also needed. Most importantly, this review presents mixed findings and recommends more research to determine the most successful food-based approaches, including an understanding of what length of time or dose-response is needed in a food-based intervention. Furthermore, more studies on the effectiveness of preformed vitamin A on VAD are needed, as well as comparative studies that examine the effect of various dietary patterns on VAD.

A key recommendation derived from this systematic review was that the need for comparative research on communities with intakes of similar staple foods or crops. Focusing on staple crops, while taking into consideration the dietary and cultural practices of the intended communities, can optimize the intended benefits such as uptake, improvement of vitamin A status, and assessment of the potential of food-based approaches [69]. Of importance is the observation that some interventions resulted in other benefits to the study communities in addition to improved levels of vitamin A [32,42]. These included improvements in livelihoods [32]; income generation derived from selling part of the harvest and increased intake of other micronutrients, such as iron [42]. The latter is of particular interest to both vitamin A and iron programs as vitamin A has a regulatory role in the expression of genes involved in iron metabolism, and supports the mobilization and transportation of iron [59].

Our examination of the quality of studies or risk of bias assessment is a strength of this review. Studies that included randomization or simple random sampling were representative of the targeted populations thus minimizing selection bias and sampling error. Although randomization can effectively capture allocation bias, it also counteracts preference effects and can decrease the potential generalizability of the study findings [70]. In addition to these quality issues, the inability to collect biochemical data to establish serum retinol levels or vitamin A status created a greater window for estimation errors from the proxy indicators used. However, the challenges in collecting serum retinol concentration directly through high-performance liquid chromatography as recommended by the WHO is challenging in resource-constrained settings. Such assays are expensive, technically demanding, and rarely available in LMIC [71]. The different approaches in estimating serum retinol levels across studies may make the comparison of study results in this review challenging due to inconsistencies. Besides other assessment methods such as estimating a combination of transthyretin, retinol binding protein and C-reactive protein concentrations [71], clinical examination for xeropthalmia [72], and the estimation of vitamin A status from dietary intake assessment, the Helen Keller International assessment tool is considered to be an effective measure of vitamin A intake [73].

Comparison with a previous systematic review and limitations

Our review corroborates a previous systematic review [74] which recommended more randomized controlled trails to assess the effectiveness of food-based approaches on improving vitamin A status or alleviating VAD among women and children. Randomized trials of food-based approaches tend to be complex during the implementation phase [75]. Evidence of efficacy, the measure of the degree of success of an intervention, rather than effectiveness, the degree of success of an intervention in ideal conditions, might provide a more meaningful understanding of improvements in vitamin A status in population-based studies [76].

Although 54% of studies in our systematic review reported significant improvements in the vitamin A status of the participants in the intervention groups, 33% did not find this effect. The vast differences across studies in the period of evaluation across interventions, food approaches used, and statistical power, may serve as possible explanatory factors for the lack of demonstrated effectiveness of food-based approaches on vitamin A status in these studies. Previous reviews noted a lack of statistical power as one of several methodological weaknesses in studies [61,74]. This is partly a consequence of the complexity of the settings in LMIC rather than a reflection of the skills of the research team or the rigor of study designs.

The intricacy of the chain of factors that lead from the implementation of a food-based approach program to improved vitamin A status warrants a greater understanding of the circumstances under which people participate in such interventions, the immediate effects on their diets, and interpretation of findings. In addition, confounding factors such as health and environmental conditions, as well as cultural beliefs and practices, can influence each stage of food-based interventions from planning, to implementation and uptake of the intervention [75]. A number of studies in our review considered the effects of health conditions, such as inflammation, in the interpretation of serum retinol levels.

Insufficient data limited our ability to provide a comparative analysis of the effectiveness of traditional fortification and biofortification approaches. Such a comparison is of interest due to implications related to sustainability, maintenance of traditional food knowledge, nutrition and food security, cost-effectiveness, stability of the fortificant and fortified food, market impact, cost, and effectiveness in reducing VAD.

Conclusion

This systematic review examined the literature on food-based approaches as a possible strategy in improving vitamin A status among pregnant or lactating women and children under 5 y. Overall, most studies presented in this review illustrated a positive trend toward improving vitamin A status using food-based approaches, with 54% finding significant improvements in the intervention groups or statistically significant associations between diet and vitamin A status. These findings suggest that food-based approaches may provide a useful public health

strategy in addressing VAD and improving vitamin A status. The lack of statistical significance in some of these studies combined with mixed results on the effects of food-based approaches on vitamin A status or improvement in VAD indicates that more research is needed for a robust analysis of this relationship. Further research could improve the quality of literature by a continued application of rigorous approaches to study design and extending the evaluation period of interventions to determine effect. We contend that the wide variety of implementation methods and lengths of interventions created challenges in assessing effect size.

Food-based approaches command large resources and improvements in their programmatic design have the potential to maximize the nutritional outcomes outlined in the Sustainable Development Goals [77,78]. Further comparative research on the delivery of vitamin A to intended communities through food-based approaches is needed. In conclusion, this systematic review suggests there is sufficient evidence to support food-based approaches as a potential strategy to improving vitamin A status among pregnant or lactating women and children under 5 y.

Acknowledgments

We acknowledge the support of Ellen Lutz, Librarian, University of Massachusetts Amherst.

Author contributions

The authors' responsibilities were as follows—JN, LSC: conceived the study; JN, LSC, LS, FG: contributed to the conception of the study; JN, KO: conducted the initial article searches together with the librarian and conducted the review; LSC, KO: conducted a secondary review of articles included in this study; LSC: reviewed and approved the search protocol; JN, KO, LSC: reviewed the articles selected for inclusion; LSC, LS, EM, KO, FG: reviewed the manuscript and critically revised it for important content; LSC: led substantive revisions of the manuscript; and all authors: read and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

Funding

The authors reported no funding received for this study.

References

[1] H. Bennasir, S. Sridhar, T.T. Abdel-Razek, Vitamin A from physiology to disease prevention. Research in Autism Spectrum Disorders, Int. J. Pharm. Sci. Rev. 1 (1) (2010) 68–73.
[2] WHO, Global prevalence of vitamin A deficiency in populations at risk 1995–2005. WHO Global Database on Vitamin A Deficiency, World Health Organization, Geneva, Switzerland, 2009.
[3] J.C. Sherwin, M.H. Reacher, W.H. Dean, J. Ngondi, Epidemiology of vitamin A deficiency and xerophthalmia in at-risk populations, Trans. R. Soc. Trop. Med. Hyg. 106 (4) (2012) 205–214.
[4] S. Bastos Maia, A.S. Rolland Souza, M.d.F. Costa Caminha, S. Lins da Silva, R.d.S.B.L. Callou Cruz, C. Carvalho dos Santos, et al., Vitamin A and pregnancy: a narrative review, Nutrients 11 (3) (2019) 681.
[5] World Health Organization, Global Prevalence of vitamin A Deficiency, World Health Organisation (WHO), Geneva, Switzerland, 2009.
[6] A.I. Rice, K.P. West Jr., R.E.J. Black, Vitamin A deficiency [Internet], Comparative Quantification of Health Risks, 2004 [date cited 25 April 2003]. 1:0211–0256. Available from: http://www.who.int/publications/cra/chapters/volume1/0211-0256.pdf.
[7] UNICEF, WFP, WHO, Preventing and Controlling Micronutrient Deficiencies in Populations Affected by an Emergency, 2007.
[8] G.A. Stevens, J.E. Bennett, Q. Hennocq, Y. Lu, L.M. De-Regil, L. Rogers, et al., Trends and mortality effects of vitamin A deficiency in children in 138 low-income and middle-income countries between 1991 and 2013: a pooled analysis of population-based surveys, Lancet Glob. Health. 3 (9) (2015) e528–e536.
[9] M.G.V. Mannar, R.F. Hurrell, Need and approach: Food fortification: past experience, current status, and potential for globalization In Food fortification in a globalized world, Academic Press, Cambridge, UK, 2018.
[10] U. Ramakrishnan, P. Nguyen, R. Martorell, Effects of micronutrients on growth of children under 5 y of age: meta-analyses of single and multiple nutrient interventions, Am. J. Clin. Nutr. 89 (1) (2009) 191–203.
[11] E.M.G. Ribeiro, L.M. Jaeger, G.M.D. Ortiz, Vitamin A: Dietary Sources and Health Consequences, in: L. De Smet, M. Claes (Eds.), Vitamin A and Vitamin E., 3, Nova Science Publishers, Inc., 2013, pp. 85–103.
[12] Vitamin and Mineral Requirements in Human Nutrition. Joint FAO/WHO Expert Consultation Report, second ed., World Health Organization, Geneva, 2004 (accessed 7/25/2022).
[13] M. Bruins, K. Kraemer, Public health programmes for vitamin A deficiency control, Community Eye Health 26 (84) (2013) 69–70.
[14] B.A. Underwood, C. Howson, E. Kennedy, A. Horwitz, in: P.H. Christopher, T.K. Eileen, H. Abraham (Eds.), Prevention of vitamin A deficiency. Institute of Medicine Prevention of micronutrient Deficiencies: Tools for Policymakers public health workers. Institute of Medicine (US) Committee on Micronutrient Deficiencies, National Academies Press (US), Washington (DC), 1998, pp. 103–166.
[15] J.A. Kellogg, E.F. Klarquist, A.D. Waziri, D. Luftig, F. Carbonero, P. Solverson, et al., Developing a definition of biofortification through the synthesis of food biofortification publications: a scoping review protocol, JBI Evid. Synth. 20 (8) (2022) 2109–2116.
[16] D. Pee, W. Bloem, The bioavailability of (pro) vitamin A carotenoids and maximizing the contribution of homestead food production to combating vitamin A deficiency, Int. J. Vitam. Nutr. Res. 77 (3) (2007) 182–192.
[17] B.J. Burri, Evaluating sweet potato as an intervention food to prevent vitamin A deficiency, Compr. Rev. Food Sci. Food Saf. 10 (2) (2011) 118–130.
[18] M. Arabi, L.M. De-Regil, Large-scale food fortification is a game-changing solution to tackling global malnutrition. But we have work to do. Multisectoral Action in Food Systems, World Health Organization, 2021 [date cited 8 September 2022]. Available from: https://www.nutritionintl.org/news/all-blog-posts/large-scale-food-fortification-game-changing-solution-to-tackling-global-malnutrition/.
[19] D. Nabarro, Global child and maternal nutrition—the SUN rises, Lancet 382 (9893) (2013) 666–667.
[20] R.E. Black, H. Alderman, Z.A. Bhutta, S. Gillespie, L. Haddad, S. Horton, et al., Maternal and child nutrition: building momentum for impact, Lancet 382 (9890) (2013) 372–375.
[21] S. Mitra, Nutritional status of orange-fleshed sweet potatoes in alleviating vitamin A malnutrition through a food-based approach, J. Nutr. Food Sci. 2 (8) (2012) 1–3.
[22] R. Gibson, Strategies for preventing multi-micronutrient deficiencies: a review of experiences with food-based approaches in developing countries, Combating micronutrient deficiencies: food-based approaches, CAB International, Wallingford, UK, 2011, pp. 7–27.
[23] M. Crowther, W. Lim, M.A. Crowther, Systematic review and meta-analysis methodology, Blood 116 (17) (2010) 3140–3146.
[24] D. Moher, L. Shamseer, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, et al., Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement, System, Rev 4 (1) (2015) 1–9.
[25] C. Lefebvre, J. Glanville, S. Briscoe, A. Littlewood, C. Marshall, M.I. Metzendorf, et al., Technical Supplement to Chapter 4: Searching for and selecting studies, in: JPT Higgins, J Thomas, J Chandler, MS Cumpston, T Li, MJ Page, VA Welch (Eds.), Cochrane Handbook for

Systematic Reviews of Interventions, 2022 (updated February 2022). Cochrane, Version 6.3.
[26] M. Viswanathan, C.D. Patnode, N.D. Berkman, E.B. Bass, S. Chang, L. Hartling, et al., Assessing the risk of bias in systematic reviews of health care interventions. Methods Guide for Effectiveness and Comparative Effectiveness Reviews, Agency for Healthcare Research and Quality (US), Rockville (MD), 2017, 2008.
[27] M.J. Downes, M.L. Brennan, H.C. Williams, R.S. Dean, Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS), BMJ Open 6 (12) (2016) e011458.
[28] M.S. Allen, E.E. Walter, C. Swann, Sedentary behaviour and risk of anxiety: a systematic review and meta-analysis, J. Affect. Disord. 242 (2019) 5–13, https://doi.org/10.1016/j.jad.2018.08.081.
[29] J.N. Wong, E. McAuley, L. Trinh, Physical activity programming and counseling preferences among cancer survivors: a systematic review, Int. J. Behav. Nutr. Phys. Act. 15 (1) (2018) 48.
[30] J.A. Sterne, J. Savović, M.J. Page, R.G. Elbers, N.S. Blencowe, I. Boutron, et al., RoB 2: a revised tool for assessing risk of bias in randomised trials, BMJ 366 (2019) l4898.
[31] J.P.T. Higgins, J. Savović, M.J. Page, R.G. Elbers, J.A.C. Sterne, Chapter 8: assessing risk of bias in a randomized trial [updated February 2022]. Cochrane, in: J.P.T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M.J. Page, V.A. Welch (Eds.), Cochrane Handbook for Systematic Reviews of Interventions version 6.3, 2022. Available from: www.training.cochrane.org/handbook.
[32] C. Hotz, C. Loechl, A. Lubowa, J.K. Tumwine, G. Ndeezi, A.N. Masawi, et al., Introduction of beta-carotene-rich orange sweet potato in rural Uganda resulted in increased vitamin A intakes among children and women and improved vitamin A status among children, J. Nutr. 142 (10) (2012) 1871–1880.
[33] E. Ndau, D. Walters, D. Wu, N. Saleh, T. Mosha, S. Horton, et al., Factors influencing vitamin A status of lactating mothers in Manyara and Shinyanga Regions of Tanzania, Tanzania J. Agric. Sci. 15 (1) (2016) 21–32.
[34] R. Engle-Stone, M. Nankap, A. Ndjebayi, M.-M. Gimou, A. Friedman, M.J. Haskell, et al., Vitamin A status of women and children in Yaoundé and Douala, Cameroon, is unchanged one year after initiation of a national vitamin A oil fortification program, Nutrients 9 (5) (2017) 522.
[35] C. Hotz, C. Loechl, A. de Brauw, P. Eozenou, D. Gilligan, M. Moursi, et al., A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women, Br. J. Nutr. 108 (1) (2012) 163–176.
[36] E.F. Talsma, K.J. Borgonjen-van den Berg, A. Melse-Boonstra, E.V. Mayer, H. Verhoef, A.Y. Demir, et al., The potential contribution of yellow cassava to dietary nutrient adequacy of primary-school children in Eastern Kenya; the use of linear programming, Public Health Nutr 21 (2) (2018) 365–376.
[37] J.B. Mason, M.A. Ramirez, C.M. Fernandez, R. Pedro, T. Lloren, L. Saldanha, et al., Effects on vitamin A deficiency in children of periodic high-dose supplements and of fortified oil promotion in a deficient area of the Philippines, Int. J.Vitam. Nutr. Res. 81 (5) (2011) 295–305.
[38] I. Jus'at, A.B. Jahari, M.K. Htet, R.L. Tilden, D. Soekarjo, B. Utomo, et al., Vitamin A-fortified cooking oil reduces vitamin A deficiency in infants, young children and women: results from a programme evaluation in Indonesia, Public Health Nutr 18 (14) (2015) 2511–2522.
[39] S. Pinkaew, E. Udomkesmalee, C.R. Davis, S.A. Tanumihardjo, Vitamin A-fortified rice increases total body vitamin A stores in lactating Thai women measured by retinol isotope dilution: a double-blind, randomized, controlled trial, Am. J. Clin. Nutr. 113 (5) (2021) 1372–1380.
[40] A.W. Girard, F. Grant, M. Watkinson, H.S. Okuku, R. Wanjala, D. Cole, et al., Promotion of orange-fleshed sweet potato increased vitamin A intakes and reduced the odds of low retinol-binding protein among postpartum Kenyan women, J. Nutr. 147 (5) (2017) 955–963.
[41] E.F. Talsma, I.D. Brouwer, H. Verhoef, G.N. Mbera, A.M. Mwangi, A.Y. Demir, et al., Biofortified yellow cassava and vitamin A status of Kenyan children: a randomized controlled trial, Am. J. Clin. Nutr. 103 (1) (2016) 258–267.
[42] I. Afolami, M.N. Mwangi, F. Samuel, E. Boy, P. Ilona, E.F. Talsma, et al., Daily consumption of pro-vitamin A biofortified (yellow) cassava improves serum retinol concentrations in preschool children in Nigeria: a randomized controlled trial, Am. J. Clin. Nutr. 113 (1) (2021) 221–231.
[43] F.F. De Moura, M. Moursi, A. Lubowa, B. Ha, E. Boy, B. Oguntona, et al., Cassava intake and vitamin A status among women and preschool children in Akwa-Ibom, Nigeria, PLOS ONE 10 (6) (2015) e0129436.
[44] A.C. Palmer, J. Chileshe, A.G. Hall, M.A. Barffour, N. Molobeka, K.P. West Jr., et al., Short-term daily consumption of provitamin A carotenoid-biofortified maize has limited impact on breast milk retinol concentrations in Zambian women enrolled in a randomized controlled feeding trial, J. Nutr. 146 (9) (2016) 1783–1792.
[45] A.C. Palmer, K. Healy, M.A. Barffour, W. Siamusantu, J. Chileshe, K.J. Schulze, et al., Provitamin A carotenoid-biofortified maize consumption increases pupillary responsiveness among Zambian children in a randomized controlled trial, J. Nutr. 146 (12) (2016) 2551–2558.
[46] S. Suri, D. Kumar, R. Das, Dietary deficiency of vitamin A among rural children: a community-based survey using a food-frequency questionnaire, Natl Med. J. India. 30 (2) (2017) 61–64.
[47] S. Sachdeva, S. Alam, F.K. Beig, Z. Khan, N. Khalique, Determinants of vitamin A deficiency amongst children in Aligarh District, Uttar Pradesh, Indian Pediatr 48 (11) (2011) 861–866.
[48] M.R. La Frano, L.R. Woodhouse, D.J. Burnett, B.J. Burri, Biofortified cassava increases ß-carotene and vitamin A concentrations in the TAG-rich plasma layer of American women, Br. J. Nutr. 110 (2) (2013) 310–320.
[49] C. Zhu, Y. Cai, E.R. Gertz, M.R. La Frano, D.J. Burnett, B.J. Burri, Red palm oil–supplemented and biofortified cassava gari increase the carotenoid and retinyl palmitate concentrations of triacylglycerol-rich plasma in women, Nutr. Res. 35 (11) (2015) 965–974.
[50] K.M. Jamil, K.H. Brown, M. Jamil, J.M. Peerson, A.H. Keenan, J.W. Newman, et al., Daily consumption of orange-fleshed sweet potato for 60 days increased plasma ß-carotene concentration but did not increase total body vitamin A pool size in Bangladeshi women, J. Nutr. 142 (10) (2012) 1896–1902.
[51] T. Turner, B.J. Burri, K.M. Jamil, M. Jamil, The effects of daily consumption of ß-cryptoxanthin-rich tangerines and ß-carotene-rich sweet potatoes on vitamin A and carotenoid concentrations in plasma and breast milk of Bangladeshi women with low vitamin A status in a randomized controlled trial, Am. J. Clin. Nutr. 98 (5) (2013) 1200–1208.
[52] S. Rahman, A.S. Rahman, N. Alam, A.S. Ahmed, S. Ireen, I.A. Chowdhury, et al., Vitamin A deficiency and determinants of vitamin A status in Bangladeshi children and women: findings of a national survey, Public Health Nutr 20 (6) (2017) 1114–1125.
[53] P.A. Neves, C.A. Campos, M.B. Malta, B.H. Lourenço, M.C. Castro, M.A. Cardoso, et al., Predictors of vitamin A status among pregnant women in Western Brazilian Amazon, Br. J. Nutr. 121 (2) (2019) 202–211.
[54] D.B. Lima, L.P. Damiani, E. Fujimori, Vitamin A deficiency in Brazilian children and associated variables, Rev. Paul. Pediatr. 36 (2018) 176–185.
[55] L.Q. Lira, A.F. de Souza, A.d.M. Amancio, C.G. Bezerra, J.B. Pimentel, M.N. Moia, et al., Retinol and betacarotene status in mother-infant dyads and associations between them, Ann, Nutr 72 (1) (2018) 50–56.
[56] V Lopez-Teros, L Quihui, J Esparza-Romero, M. Grijalva-Haro, R.O. Méndez Estrada, B. Pacheco-Moreno, O. Tortoledo, M. Duarte-Figueroa, H. Garcia, Vitamin a status and associated variables in mexican lactating women, FASEB J. 27 (2013), https://doi.org/10.1096/fasebj.27.1_supplement.850.3.
[57] V. Lopez-Teros, L. Quihui-Cota, R.O. Méndez-Estrada, M.I. Grijalva-Haro, J. Esparza-Romero, M.E. Valencia, et al., Vitamin A-fortified milk increases total body vitamin A stores in Mexican preschoolers, J. Nutr. 143 (2) (2013) 221–226.
[58] E. Eilender, Nutrition Throughout the Lifecycle, Momentum Press, New York, NY, 2016.
[59] E.M. Wiseman, S. Bar-El Dadon, R. Reifen, The vicious cycle of vitamin A deficiency: a review, Crit. Rev. Food Sci. Nutr. 57 (17) (2017) 3703–3714.
[60] A.W. Girard, J.L. Self, C. McAuliffe, O. Olude, The effects of household food production strategies on the health and nutrition outcomes of women and young children: a systematic review, Paediatr. Perinat. Epidemiol. 26 (2012) 205–222.
[61] E. Masset, L. Haddad, A. Cornelius, J. Isaza-Castro, Effectiveness of agricultural interventions that aim to improve nutritional status of children: systematic review, BMJ 344 (2012) d8222.
[62] Z. Li, O. Karlsson, R. Kim, S. Subramanian, Distribution of under-5 deaths in the neonatal, postneonatal, and childhood periods: a multicountry analysis in 64 low-and middle-income countries, Int. J. Equity Health. 20 (1) (2021) 1–11.
[63] WHO, Child Mortality and Causes of Death, The Global Health Observatory, 2021.

[64] A. Hasman, G. Moloney, V. Aguayo, Regular vitamin A supplementation: prioritizing the youngest children, Am. J. Clin. Nutr. 114 (1) (2021) 390–391.
[65] H.E. Bouis, A. Saltzman, Improving nutrition through biofortification: a review of evidence from HarvestPlus, 2003 through 2016, Glob. Food Sec. 12 (2017) 49–58.
[66] B.J. Burri, F. Safety, Evaluating sweet potato as an intervention food to prevent vitamin A deficiency, J. Comprehensive Rev. Food Sci. 10 (2) (2011) 118–130.
[67] A. Nguyen, D. Grover, K. Sun, V. Raju, R. Semba, D. Schaumerg, Coverage of the vitamin A supplementation programme for child survival in Nepal: success and challenges, Paediatr. Int. Child Health. 32 (4) (2012) 233–238.
[68] T.L. Blasbalg, B. Wispelwey, R. Deckelbaum, Econutrition and utilization of food-based approaches for nutritional health, Food Nutr. Bull. 32 (1_suppl) (2011) S4–S13.
[69] M.N. Garcia-Casal, J.P. Peña-Rosas, H. Pachón, L.M. De-Regil, E.C. Tablante, M.C. Flores-Urrutia, Staple crops biofortified with increased micronutrient content: effects on vitamin and mineral status, as well as health and cognitive function in the general population, Cochrane Database Syst. Rev. 8 (2016) 1–17.
[70] J.F. Trepanowski, J.P. Ioannidis, Perspective: limiting dependence on nonrandomized studies and improving randomized trials in human nutrition research: why and how, Adv. Nutr. 9 (4) (2018) 367–377.
[71] E.F. Talsma, H. Verhoef, I.D. Brouwer, A.S. Mburu-de Wagt, P.J. Hulshof, A. Melse-Boonstra, Proxy markers of serum retinol concentration, used alone and in combination, to assess population vitamin A status in Kenyan children: a cross-sectional study, BMC Med 13 (1) (2015) 1–9.
[72] WHO, Xerophthalmia and night blindness for the assessment of clinical vitamin A deficiency in individuals and populations, World Health Organization, 2014.
[73] N.J. Haselow, D.S. Rosen, N.L. Sloan, How to use the HKI food frequency method to assess community risk of vitamin A deficiency, Helen Keller International, 1993.
[74] C. Bassey, H. Crooks, K. Paterson, R. Ball, K. Howell, I. Humphries-Cuff, et al., Impact of home food production on nutritional blindness, stunting, wasting, underweight and mortality in children: a systematic review and meta-analysis of controlled trials, Crit. Rev. Food Sci. Nutr. Cancer 62 (2022) 1856–1869.
[75] P. Mirmiran, Z. Bahadoran, Z. Gaeini, Common limitations and challenges of dietary clinical trials for translation into clinical practices, Int. J. Endocrinol. Metab. 19 (3) (2021) e108170.
[76] M.T. Ruel, H. Alderman, Maternal Child Nutrition Study Group, Nutrition-sensitive interventions and programmes: how can they help to accelerate progress in improving maternal and child nutrition? Lancet 382 (9891) (2013) 536–551.
[77] FAO, in: B. Thompson, L. Amoroso (Eds.), Improving Diets and Nutrition: Food-based Approaches, The FAO of United Nations & *CABI*, 2014, 2014.
[78] B. Burlingame, S. Dernini, in: B. Burlingame, S. Dernini (Eds.), Sustainable diets and biodiversity directions and solutions for policy, research and action, Food and Agriculture Organization of the United Nations; Bioversity International, FAO Headquarters, Rome, 2012, p. 309.