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REVIEW

Systematic review on evidence-based adolescent nutrition interventions

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Adolescence is a critical stage in the life cycle, and adequate nutrition is necessary for the proper growth and development of individuals and their offspring. Here, we comprehensively review all published systematic reviews (through October 2016) on adolescents (10–19 years) and women of reproductive age, including pregnant women, which targeted interventions related to nutrition. For interventions where there was no existing systematic review on adolescents, we reviewed primary studies/trials. We included interventions on micronutrient supplementation (iron, folic acid, iron–folic acid (IFA), calcium, vitamin D, vitamin A, zinc, iodine, and multiple micronutrients), food/protein energy supplementation, nutrition education for pregnant adolescents, obesity prevention and management, and management of gestational diabetes. We identified a total of 35 systematic reviews, of which only five were conducted on adolescents, and 107 primary studies on adolescents. Our review suggests that iron alone, IFA, zinc, and multiple micronutrient supplementation in adolescents can significantly improve serum hemoglobin concentration. While zinc supplementation in pregnant adolescents showed improvements in preterm birth and low birth weight, we found a paucity of trials on calcium, vitamin D, vitamin A, and iodine supplementation. We found limited evidence on food/protein energy supplementation in adolescents. Interventions to prevent and manage obesity showed a nonsignificant impact on reducing body mass index. This review underscores the importance of adolescent nutrition interventions. It is imperative that countries design nutritional interventions, particularly for adolescents.

Keywords: adolescent; nutrition; obesity; micronutrient; malnutrition; pregnancy

Introduction

Globally, there are nearly 1.8 billion people 10–24 years of age, making up a quarter of the total population (7.3 billion) of the world, and approximately 89% of these live in low- and middle-income countries (LMICs).[1] The United Nations reports that, with such large numbers of young people, it is imperative that they should be given economic and social power, as well as the right to health and empowerment to handle their own lives and future. Unfortunately, most of the adolescent population grows up in countries with multiple adolescent health problems, including diseases of poverty, undernutrition, poor sexual and reproductive health, injury and violence, and noncommunicable diseases.[2] There has been limited focus on adolescents in global initiatives, but more recently there has been an increasing focus on adolescent health, with the launch of a *Lancet* commission on adolescent health and well-being involving a network of academics, policy makers, practitioners, and young health advocates. This Commission outlines the opportunities and challenges for investment in adolescents at both country and global levels.[2]

Adolescent development is as intricate as children's, as there is a complex interaction between

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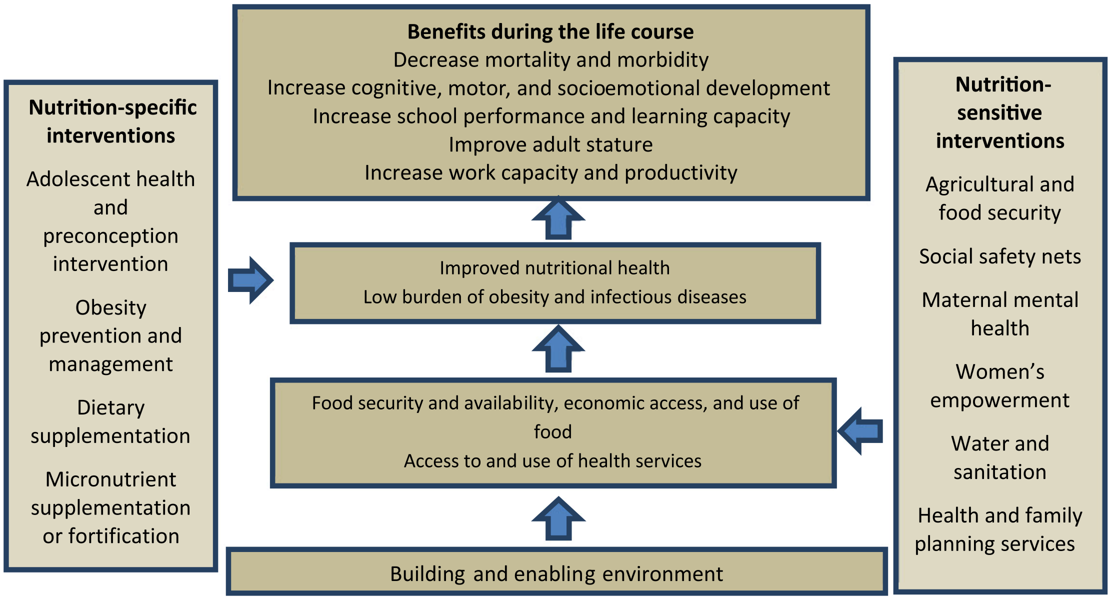


Figure 1. Framework for nutrition in adolescents and young women.

puberty, neurocognitive maturity, and social-role transitions.[3] In addition to the role of living conditions and environment, especially at home, a key contributor to normal development is nutrition. Consumption of a healthy diet is necessary for proper growth and development during puberty, which necessitates adequate macro- and micronutrition. Recently, there has been an epidemiological shift from undernutrition and growth stunting to increasing rates of obesity, and many LMICs now bear a double burden of nutritional disorders, owing to the emerging issue of overweight and obesity along with the existing high rates of stunting and other micronutrient deficiencies. There has been a growing interest in adolescent girls' nutrition as a means to improve the health of women and children, as maternal preconception nutritional deficiencies have profound consequences for fetal and infant development, with the effects extending to neonatal and early childhood development and mortality.

Adolescent nutrition is relevant for current, future, and intergenerational health, and the causes of adolescent nutritional deficiencies are complex, with contributors at the individual, household, and population levels. This underscores the need for comprehensive research on adolescent nutritional interventions. While an earlier review on adolescent nutrition intervention only included systematic reviews, it was also only limited to micronutrient supplementation, nutrition interventions for pregnant adolescents, and interventions to prevent obesity.[4] No efforts were undertaken to uncover data from women of reproductive age in cases where data were not available on adolescents.[4] Here, we review the current evidence for nutritional and related interventions from studies focused on adolescents only or as part of different population groups. These interventions include micronutrient supplementation, food/protein energy supplementation, and obesity prevention and management, and Figure 1 depicts the framework for pathways for improvement in nutrition in adolescents and young women. Our primary objective here is to analyze the existing literature exploring these interventions and their impact on the health of adolescents (aged 10–19 years), including pregnant teenagers in both high-income countries (HICs) and LMICs.

Methods

We conducted a search to identify existing systematic reviews on adolescents (10–19 years) that targeted the identified nutrition interventions. For interventions where there were no systematic reviews specific to adolescents, we searched for reviews on women of reproductive age including pregnant women. In addition, we also conducted a new review of trials for interventions where there were no adolescent-specific reviews. The following electronic reference libraries were searched to access the available data: the Cochrane Library, PubMed, CINAHL, and Google Scholar (until October 2016). Studies that included adolescents as a subpopulation along with other population groups were deconstructed to isolate the evidence on the adolescent age group. Detailed examination of cross-references and bibliographies of available data and publications was also performed to identify additional sources of information. The following interventions are reviewed here: (1) micronutrient supplementation (iron, folic acid, iron–folic acid (IFA), calcium, vitamin D, vitamin A, zinc, iodine, and multiple micronutrient (MMN) supplementation); (2) food/protein energy supplementation; (3) nutrition education for pregnant adolescents; (4) obesity prevention and management; and (5) gestational diabetes prevention and management.

For existing systematic reviews

We considered all available published Cochrane and non-Cochrane reviews of randomized or non-randomized controlled trials that fully or partly addressed nutrition-specific interventions for improving the health of adolescents. We included reviews that specifically addressed adolescents or women of reproductive age, including pregnant women. The included systematic reviews were assessed using the AMSTAR (assessment of the methodological quality of systematic reviews) criteria.[5] We resolved any disagreement by discussion, and the final decision was made by consensus within the team.

We recorded the extracted pooled effect size with 95% confidence intervals (CIs). We contacted the review authors for updated data in case each review had not recently been updated. We also contacted trial authors of studies awaiting classification for updated information. We did not update the individual review, but summary of findings tables were formulated and included for most of the reviews (where applicable). We were very cautious when comparing absolute effects across reviews, as there may be different control group risks.

For primary studies/trials

For the interventions where there was no existing systematic review on adolescent populations, we searched for trials. Pre–post study designs and observational studies were only included when no higher-quality trials could be found for a specific intervention. The team set up a triage process with standardized criteria for evaluating outputs from the search strategy and primary screening. Following an agreement on the search strategy, the abstracts (and the full sources when abstracts were not available) were screened by two abstractors to identify studies adhering to the inclusion criteria. Any disagreements on selection of studies between these two primary abstractors were resolved by the third reviewer. After full-text retrieval of all the studies that met the inclusion/exclusion criteria, each study was double data abstracted into a standardized form. We extracted the information on characteristics of included studies, including descriptions of methods, participants, interventions, outcomes, extraction of measurement of treatment effects, methodological issues, and quality of included studies.[6]

Search strategies were prepared for each intervention separately to identify the existing reviews (Table S1, online only). The same search strategy was applied to look for primary trials, with some modification, as detailed in Table S1 (Fig. 2). Data analysis of the outcomes was based on an intention-to-treat principle. For dichotomous data, we presented results as summary risk ratio (RR) and as odds ratio (OR) for observational studies with 95% CIs. For continuous data, we used the mean difference (MD), standard mean difference (SMD), or weighted mean difference between trials if outcomes were measured comparably. All the analysis was performed using Review Manager 5.[7]

The outcomes of interest included mortality (death rate, death due to any disease, fatality rate, perinatal/neonatal mortality), pregnancy outcomes (preterm births, preeclampsia, eclampsia, stillbirth, miscarriage, termination of pregnancy), morbidity (obesity, obesity-related complications, hypertension, diabetes, cardiovascular disease, infectious diseases), nutritional deficiencies (anemia or micronutrient deficiency), and anthropometrics (height, weight, body mass index (BMI), stunting).

On the basis of the findings from reviews, the quality of the evidence was assessed following the Grading of Recommendations, Assessment, Development and Evaluation methodology.[8] The following criteria were taken into account to grade the evidence: study limitations (i.e., risk of bias),

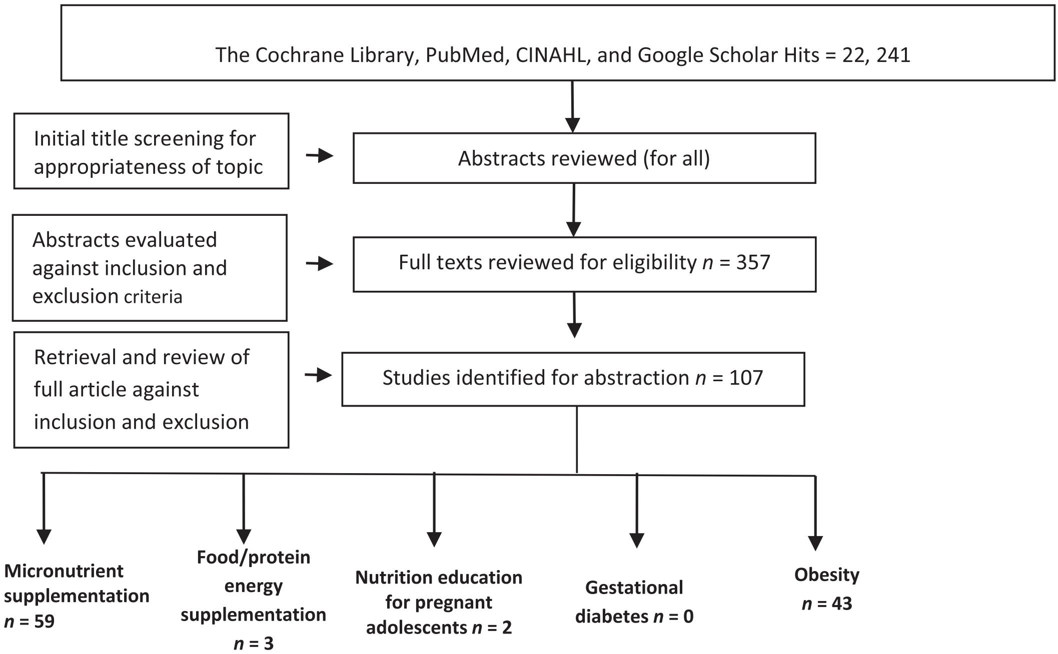


Figure 2. Flow diagram for primary studies on adolescents.

consistency of effect, imprecision, indirectness, and publication bias. The quality of the body of evidence for each key outcome was then rated as "high," "moderate," "low," or "very low."

Results

We identified 35 systematic reviews, of which five focused on children and adolescents.[9–13] These reviews examined interventions related to the prevention and management of obesity.[9–13] On the other hand, 12 reviews targeted women of reproductive age,[14–25] 12 included pregnant women,[26–37] seven included children (5–18 years),[38–44] and one included a mother/child population.[45] For interventions where evidence on adolescents was scarce, including micronutrient supplementation, food/balanced protein energy supplementation, and prevention of gestational diabetes, we identified and included evidence from primary trials.

Micronutrient supplementation

Iron supplementation. Our search found no systematic reviews of iron supplementation in adolescents; however, we identified reviews on women of reproductive age and pregnant women.[14,26,27] Our search for primary trials on iron supplementation in adolescents identified 11 studies, of which seven reported serum hemoglobin as an outcome.[46–56] Studies were conducted in India, Iran, Pakistan, Sri Lanka, Tanzania, the United States, and Vietnam and provided iron as ferrous sulfate preparations in dosages ranging from 50 to 260 mg. The pooled analysis showed a significant impact of iron supplementation on improving serum hemoglobin levels (SMD 1.83; 95% CI 0.59–3.08; seven studies; $n = 1257$) (Fig. 3A).

Although evidence from studies in adolescents was scarce, reviews focusing on women of reproductive age showed that intermittent iron supplementation (alone or with other nutrients) had a significant impact on improving anemia rates, hemoglobin, and serum ferritin concentration. However, no difference was reported for iron-deficiency anemia, serum iron deficiency, and all-cause morbidity.[14] While intermittent iron supplementation in pregnant women showed no statistically significant effect on anemia, iron-deficiency anemia, low birth weight (LBW), or preterm birth, there was a significant effect on improving serum hemoglobin concentration.[26] Daily iron supplementation in pregnant women, on the other hand, showed a significant effect on reducing maternal anemia, maternal iron deficiency, and LBW and improving mean birth weight (Table S2, online only).

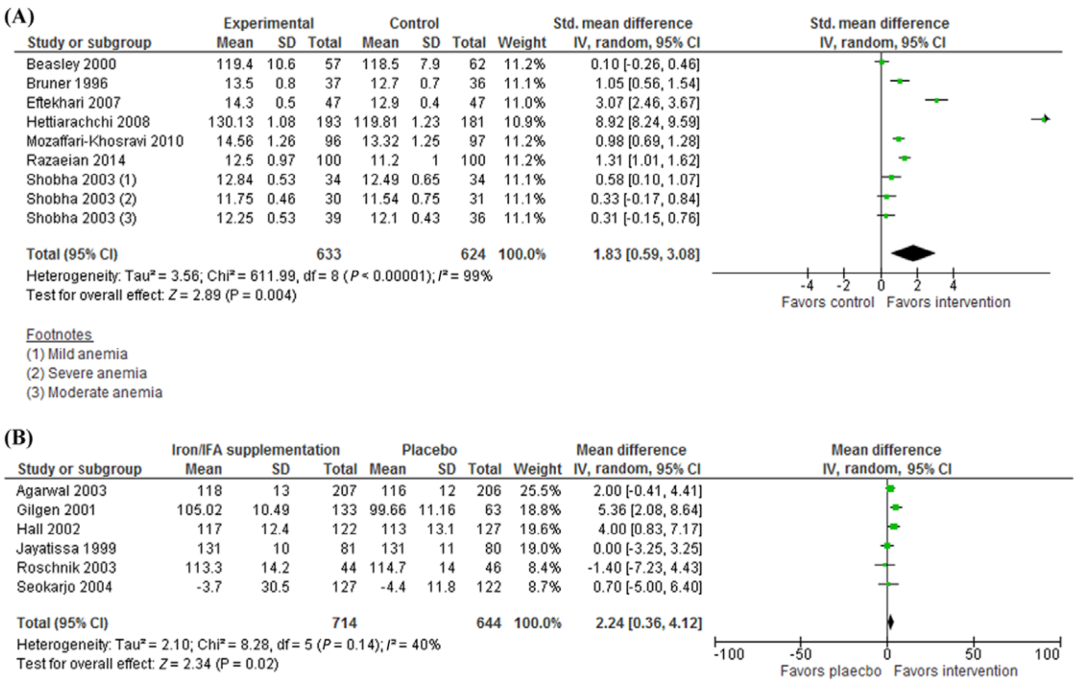


Figure 3. Iron supplementation. (A) Iron supplementation versus placebo: hemoglobin concentration (g/L) in adolescents. (B) Weekly/intermittent IFA supplementation versus placebo: hemoglobin (g/L) in adolescents. References: Beasley,[53] Bruner,[46] Eftekhari,[47] Hettiarachchi,[48] Mozaffari-Khosravi,[54] Rezaeian,[56] Shobha,[55] Agarwal,[58] Gilgen,[60] Hall,[61] Jayatissa,[62] Roschnik,[67] Soekarjo.[70]

Folic acid supplementation. We found no systematic review on the supplementation of folic acid in adolescents. However, we found a single study on folic acid supplementation among adolescents from Canada that reported a nonsignificant effect on serum folate concentration (SMD 1.89; 95% CI 1.0–2.79). We found reviews on folic acid supplementation in children,[38] women of reproductive age,[15] and pregnant women.[28]

One review reported that periconceptional folic acid supplementation alone in women of reproductive age showed significant reduction in the number of pregnancies terminated for fetal abnormality and neural tube defects (NTDs). No effects were seen for multiple pregnancy, miscarriages, stillbirths, and congenital anomalies, such as cleft palate, cleft lip, congenital cardiovascular defects, and other birth defects.[15] The same review showed that supplementation with other micronutrients had a nonsignificant effect on pregnancy termination for fetal abnormality, multiple pregnancy, miscarriages, stillbirths, NTDs, cleft palate, cleft lip, congenital cardiovascular defects and other birth defects, and LBW.[15] On the other hand, folic acid supplementation in pregnant women led to no change in anemia, serum hemoglobin, or folate concentration. However, megaloblastic anemia decreased significantly. No change was seen in stillbirth/neonatal death, preterm birth, LBW, or birth weight (Table S3, online only).[28]

Iron and folic acid supplementation. We found no systematic review on the supplementation of IFA in adolescents, but we identified two reviews on pregnant women.[29,30] In our search for primary trials on adolescents, we identified 23 moderate-quality studies from Bangladesh, Kenya, India, Indonesia, Iran, Mali, Malaysia, Mozambique, Nepal, Sri Lanka, and Tanzania.[57–78] Iron dosages across those studies ranged from 60 to 120 mg/day, and folic acid ranged from 3.5 to 500 mg/day. While there was a lot of variability in study design to detect dose–response results, the overall evidence suggests that daily IFA supplementation reduced the prevalence of anemia (RR 0.52; 95% CI 0.28–0.96; three studies; n = 1979) and improved the serum hemoglobin concentrations (MD 10.07; 95% CI 4.05–16.10; five studies; $n = 822$) among adolescent girls and that weekly IFA supplementation also led to a reduction in anemia (RR 0.73; 95% CI 0.58–0.92; nine studies) and improved the serum hemoglobin concentration (MD 2.24; 95% CI 0.36–4.12; six studies; $n = 2839$) (Fig. 3B).

Multiple micronutrient supplementation. We found no systematic reviews on MMNs among adolescents, but identified reviews on children,[39,40] general adult populations,[16] and pregnant women.[31] In our search for primary studies, we identified five moderate- to high-quality studies on adolescents.[79–83] Of these, four were conducted on nonpregnant adolescents girls from India,[84] Indonesia,[82] and Bangladesh,[80,81] while one was conducted on pregnant adolescents from Brazil.[83] MMN supplementation among nonpregnant (SMD 0.55; 95% CI 0.30–0.81) and pregnant girls (SMD 1.30; 95% CI 0.31–2.28) showed a significant improvement in serum hemoglobin concentration.

Data from pregnant women suggest that MMN supplementation, when compared with no supplements, placebo, or supplementation with two micronutrients or fewer, had a significant effect on maternal anemia (third trimester hemoglobin <110 g/L), small for gestational age (SGA), and LBW. However, no change was reported for preeclampsia, miscarriage (loss before 28 weeks), maternal mortality, perinatal mortality, neonatal mortality, and preterm births.[31] The review also suggests that MMN had similar effects when compared to IFA[31] (Table S4, online only).

Calcium supplementation. No systematic review was found in adolescent populations, while other reviews included examined children and adolescents,[41,42] women of reproductive age, and pregnant women.[32,33]

We included four studies from the primary search: two each on nonpregnant[85–87] and pregnant adolescents.[88,89] Calcium supplementation showed a nonsignificant improvement in hip bone mineral density after 1 year of supplementation for nonpregnant adolescents (SMD 1.17; 95% CI −0.45 to 2.79) and serum calcium concentration (SMD 0.17; 95% CI −0.32 to 0.67). Included studies were conducted in Israel, the United States, and China, with calcium dosages ranging from 600 to 1200 mg/day, and are considered of high quality. Calcium supplementation among pregnant adolescents showed no effect on mean birth weight (SMD 0.47; 95% CI −0.17 to 1.10).

Data from pregnant women showed that low-dose calcium supplementation alone reduces high blood pressure, preeclampsia, and preterm births. No impact was reported in caesarean births or stillbirth/death before discharge.[90] Routine high-dose calcium supplementation (>1 g/day) in women with adequate calcium diet showed significant effects in reducing high blood pressure, while, in a low–calcium intake population, high-dose calcium supplementation showed significant effects on reducing high blood pressure and preeclampsia (Table S5, online only).[90]

Vitamin D supplementation. We found no systematic review of vitamin D supplementation in adolescents. Reviews were mostly conducted on children, adults, and pregnant women.[17] We found three primary studies in our search, two were conducted in Finland[91,92] and one in India.[93] These studies reported nonsignificant change in serum 25(OH)D levels at 1, 2, and 3 years after vitamin D supplementation (Fig. 4). The data from the general pregnant population showed no change in preeclampsia (RR 0.67; 95% CI 0.33–1.35; one study, $n = 400$).[17]

Calcium and vitamin D supplementation. We found no systematic reviews on calcium and vitamin D supplementation among adolescents. We did not find any primary studies, either.

Vitamin A supplementation. No systematic reviews were found on vitamin A supplementation in adolescents. Reviews were mostly conducted in children,[43] pregnant women,[34,35] and women of reproductive age.[18] In our search for primary studies, we found three moderate-quality studies on adolescents from Bangladesh,[57] Kenya,[94] and Indonesia.[70] A study from Bangladesh on 138 nonpregnant adolescents who were provided with 2.42 mg retinol as vitamin A supplementation reported a significant reduction in anemia (RR 0.73; 95% CI 0.56–0.93).[57] The evidence from women of reproductive age showed improvements in maternal serum retinol levels (MD 0.17; 95% CI 0.06–0.28; three studies; $n = 258$).[18] One review on vitamin A supplementation during pregnancy reported

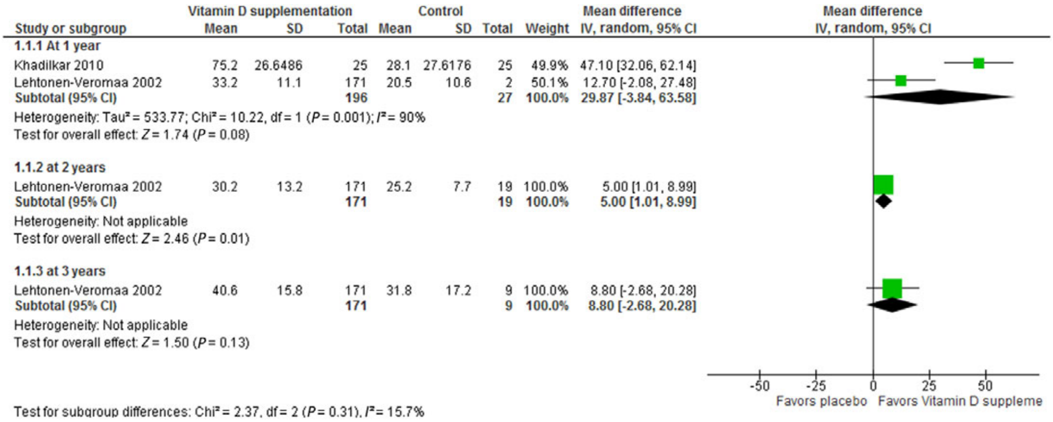


Figure 4. Vitamin D supplementation versus placebo: 25(OH)D (nmol/L) concentration in adolescents. References: Khadilkar,[93] Lehtonen-Veromaa.[91]

a significant impact on anemia (hemoglobin < 110 g/L) (Table S6, online only).[34]

Zinc supplementation. No systematic reviews were found on adolescents. Reviews evaluating zinc supplementation were found in children,[44] adults,[19] and pregnant women.[36] We identified seven studies on adolescents from a primary search.[48,84,95–100] In these studies, which were from Brazil, Chile, India, Sri Lanka, the United Kingdom, and the United States, adolescents were supplemented with zinc ranging from 14 to 20 mg/day. Of these, four studies examined pregnant adolescents.[96–100] Two studies on 494 nonpregnant adolescents reported significant increases in hemoglobin concentration (SMD 4.81; 95% CI 0.47–8.66; two studies; $n = 494$) (Fig. 5A) and serum zinc concentration (SMD 4.28; 95% CI 0.49–6.06; three studies; $n = 805$) (Fig. 5B). Studies on pregnant adolescent reported a significant reduction in preterm births (RR 0.57; 95% CI 0.46–0.69; two studies) (Fig. 5C) and LBW (RR 0.39; 95% CI 0.15–0.98, one study) (Fig. 5D).

Food fortification with zinc in women of reproductive age led to no change in offspring height growth or weight gain. Neonatal serum zinc levels did not alter significantly, nor did neonatal serum hemoglobin.[19] Zinc supplementation in pregnant women did not significantly alter stillbirth/neonatal mortality risk. Preterm birth decreased significantly. Birth weight, LBW, and SGA did not change (Table S7, online only).[36]

Iodine supplementation. We found no systematic reviews on iodine supplementation in adolescents. Reviews were mainly conducted on children and pregnant women.[45] We conducted a search for any trials of iodine supplementation in adolescents but found only one study that fulfilled the criteria. That study, from Iran, provided a single oral dose of 190 mg iodine to high school girls and reported no change in serum thyroid-stimulating hormone (TSH) (MD 0.30; 95% CI −0.06 to 0.66, $n = 47$) (Fig. 6).[47] Iodine supplementation in pregnant women led to a significant decrease in cretinism (RR 0.27; 95% CI 0.12–0.6; five studies, $n = 9500$).[45]

Food/protein energy supplementation. We found no systematic reviews of food/balanced energy protein (BEP) supplementation in adolescents; the available systematic reviews examined pregnant women and women of reproductive age, providing oral protein supplementation and nutritional education along with balanced supplementation.[20–25,101] Our search for adolescent-specific trials identified three trials.[102–105] A study from the United States provided nutritional supplementation to pregnant adolescents (provided 240 kcal of energy, 14.5 g of protein, 33.2 g of carbohydrate with 4 g of lactose and the rest as sucrose, 5.6 g of fat, 4 mg of iron, and 240 mg of calcium in 240 mL). This study reported a nonsignificant increase in birth weight (SMD 156.80; 95% CI −1.82 to 315.42).[102] Another study from Peru[103,104] consisted of participatory training with community kitchen leaders, educational materials, and increased access to heme iron (chicken liver

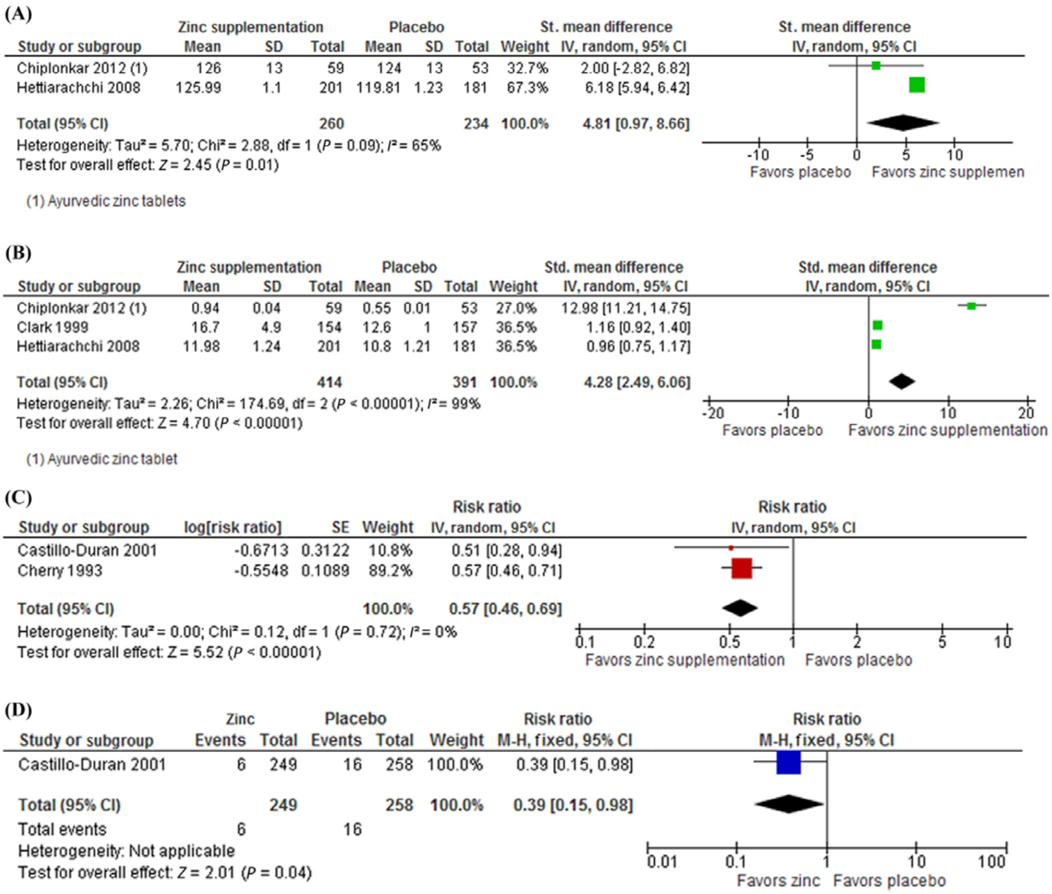


Figure 5. Zinc supplementation versus placebo: (A) hemoglobin (g/L) concentration in adolescents, (B) serum zinc (μmol/L) in adolescents, (C) preterm birth in pregnant adolescents, and (D) low birth weight in pregnant adolescents. References: Chiplonkar,[84] Hettiarachchi,[48] Clark,[95] Castillo-Duran,[99] Cherry.[96]

and blood) for adolescents in the first 5 months, and reported a reduction in anemia rates (RR 0.32; 95% CI 0.26–0.69; $n = 22$). Another study from India[105] targeted university students and provided them with iron along with energy supplementation and reported a nonsignificant effect on hemoglobin concentration (MD –0.10; 95% CI –0.46 to 0.26; $n = 30$).

The evidence from a review on children and adolescents 5–18 years of age in school-feeding programs found an increase in weight gain of 0.39 kg (95% CI 0.11–0.67) over an average of 19 months of supplementation. Similarly, the school-feeding programs improved school attendance and math scores.[101]

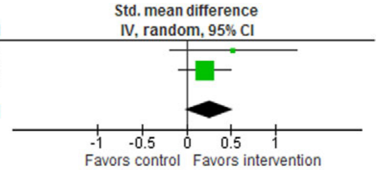
There is a paucity of information on food supplementation or protein energy supplementation among at-risk adolescents. However, evidence from studies among general pregnant women reported significant effects on reducing stillbirths, neonatal mortality, LBW, and SGA.[25] The review also showed improvement in birth weight and birth length.[25] However, Bayley mental scores at 1 year remained unchanged[25] (Table S8, online only).

Nutrition education for pregnant adolescents

We found two studies on pregnant adolescents from already established reviews,[106,107] with no studies found during the updated search. These studies involved healthy-eating education programs. Pooled analysis (three studies; $n = 288$) found no significant difference in maternal weight gain (SMD 0.20; 95% CI −0.04 to 0.45); and no difference was found in birth weight (SMD 0.25; 95% CI −0.02 to 0.52; two studies; $n = 233$) (Fig. 7).

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. mean difference IV, random, 95% CI
Hunt 2002 (1)	3,500	600	18	3,200	500	14	14.8%	0.52 [-0.19, 1.23]
Long 2002 (2)	3,328.6	588.07	136	3,206.18	616.81	65	85.2%	0.20 [-0.09, 0.50]
Total (95% CI)			**154**			**79**	**100.0%**	**0.25 [-0.02, 0.52]**

Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 1 (*P* = 0.42); *I*² = 0%
Test for overall effect: *Z* = 1.80 (*P* = 0.07)



Footnotes
(1) Comparing adult nutritional education program with adolescent
(2) Comparing nutritional education program with no intervention

Figure 6. Iodine supplementation versus placebo: TSH (μU/dL) concentration in adolescents. References: Hun,[106] Long.[107]

Gestational diabetes prevention and management

We found no systematic reviews or trials aimed specifically at preventing or managing gestational diabetes mellitus (GDM) in adolescents. Our systematic review evaluating GDM interventions on women of reproductive age in general included interventions focusing on dietary, lifestyle, and physical activity advice and interventions. Those reviews reported that preconception counseling alone for preconception women had an impact on decreasing HbA1c levels in the first trimester.[37] The reviews also reported a decrease in perinatal mortality and congenital malformations.[37] No significant change was seen in the rate of miscarriages or in preterm deliveries[37] (Table S9, online only).

A comprehensive systematic review on pregnant women found that early detection of GDM in pregnant women led to a significant decrease in GDM (RR 0.24; 95% CI: 0.16–0.37) and abnormal fasting glucose (RR 0.21; 95% CI 0.11–0.39; one study). However, the results from one study showed no significant change in the rate of caesarean sections (RR 0.83; 95% CI 0.60–1.15).[37]

Borderline diabetic care in pregnant women did not show any significant change in preterm births but did lead to a significant alteration in mean birth weight.[37] The same review reported that continuous insulin dosing compared with standard dosing did not lead to any change in caesarean sections or hypoglycemia. No change was seen in stillbirths/intrauterine fetal deaths, preterm deliveries, mean birth weight, SGA babies, or large for gestational age babies.[37]

The comparison of intensive care against standard care did not show any significant difference in stillbirths. Comparing GDM treatment with standard care showed no change in caesarean sections or in the proportion of children with birth weight above the 90th percentile.[37] Comparing optimal and suboptimal glucose control showed no significant change in stillbirths. A significant decrease was seen in perinatal deaths.[37] Exercise with or without dietary changes led to significant postpartum weight loss.[37]

Obesity prevention and management

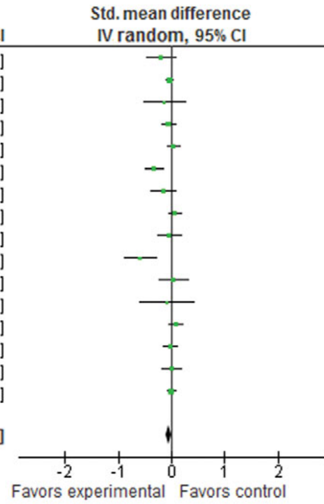
Obesity prevention. We found three systematic reviews focusing on adolescents,[11–13] of which two reported computer-mediated interventions[11,12] and one reported surgery.[13] Systematic reviews conducted in the general population of children and women of reproductive age were more comprehensive and included school-based, primary care–based, community-based, behavioral, diet, and supplementary interventions.[108–111] We identified specific trials ($n = 31$) from those reviews on adolescent populations and updated the search ($n = 28$). The interventions involved diet, physical activity, behavior change, and combinations of these. They were provided via school, community, family, technology, or a combination of those methods.

Interventions, including health promotion and education, counseling on diet, physical activity/lifestyle support, and dietary advice, showed marginal impact on reducing BMI (SMD −0.05; 95% CI −0.11 to 0.01; 15 studies; $n = 14{,}912$) (Fig. 8A) in adolescents. Moreover, there is an increasing evidence that the types of fluids that we drink can have a long-term impact on health, influencing the development of overweight, obesity, or metabolic diseases. Therefore, plain water is recommended as a healthy option over sweetened beverages for prevention of obesity.[112]

Obesity management. We identified two systematic reviews that were conducted on children.[9,10] We also identified 12 high-quality studies on adolescents[113–124] from HICs that showed a significant

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. mean difference IV random, 95% CI
Amaro 2006	0.13	0.68	153	0.26	0.64	88	3.6%	-0.19 [-0.46, 0.07]
Bonsergent 2013	-0.71	1.49	1949	-0.66	1.45	1589	11.7%	-0.03 [-0.10, 0.03]
Ebbeling 2006	0.07	1.02	53	0.21	1.06	50	1.9%	-0.13 [-0.52, 0.25]
Foster 2008	1.99	1.9	479	2.1	1.9	364	7.8%	-0.06 [-0.19, 0.08]
Gentile 2009	0.6	2.9	582	0.5	2.8	619	9.0%	0.04 [-0.08, 0.15]
Haerens 2006 (1)	1.11	1.74	381	1.66	1.61	176	6.0%	-0.32 [-0.50, -0.14]
Haerens 2006 (2)	1.42	1.62	118	1.66	1.61	176	4.3%	-0.15 [-0.38, 0.09]
Kain 2004 (3)	0.3	1.72	996	0.2	1.7	454	9.2%	0.06 [-0.05, 0.17]
Lubans 2012	0.76	1.16	141	0.81	1.17	153	4.4%	-0.04 [-0.27, 0.19]
NeumarkSztainer 2003	-0.96	3.22	84	0.75	2.59	106	3.1%	-0.59 [-0.88, -0.30]
Reed 2008	0.4	2.42	156	0.3	2.92	81	3.5%	0.04 [-0.23, 0.31]
Robinson 2003 (4)	0.5	2.43	28	0.71	2.47	33	1.2%	-0.08 [-0.59, 0.42]
Sichieri 2009	0.32	1.43	434	0.22	1.08	493	8.2%	0.08 [-0.05, 0.21]
Simon 2008	2.38	2.2	479	2.42	2.14	475	8.3%	-0.02 [-0.15, 0.11]
Singh 2009 (5)	0.5	1.3	312	0.5	1.55	208	6.1%	0.00 [-0.18, 0.18]
Webber 2008	2	2.05	1751	2	2.05	1751	11.7%	0.00 [-0.07, 0.07]
Total (95% CI)			**8096**			**6816**	**100.0%**	**-0.05 [-0.11, 0.01]**

Heterogeneity: Tau² = 0.01; Chi² = 34.89, df = 15 (P = 0.003); I^2 = 57%
Test for overall effect: Z = 1.68 (P = 0.09)



(1) Females only
(2) Interventions included parents + females only
(3) Females only
(4) Females only
(5) Females only

Figure 7. Interventions for prevention of obesity in pregnant adolescent: birth weight. References: Amaro,[113] Bonsergent,[114] Ebbeling,[115] Foster,[116] Gentile,[117] Haerens,[118] Kain,[119] Lubans,[120] Neumark-Sztainer,[121] Reed,[122] Robinson,[123] Sichieri,[124] Simon,[125] Singh,[126] Webber.[127]

reduction in BMI postintervention that involved diet, physical activity, behavior change, and combinations of those (SMD −0.24; 95% CI −0.36 to −0.13; 12 studies; n = 1541) (Fig. 8B). Subgroups showed the largest effect for family-based interventions (SMD –0.43; 95% CI −0.76 to –0.09; two studies; n = 215) and the combination of the interventions (SMD −0.23; 95% CI −0.38 to −0.08; two studies; n = 720).

Discussion

To the best of our knowledge, this is the first comprehensive systematic review on adolescent nutrition interventions. Although we aimed to include data from existing systematic reviews, we searched for primary trials when data from systematic reviews on adolescents were not available. We further summarized the data from nutritional interventions from recently published systematic reviews on women of reproductive age, including pregnant women, in order to contextualize the evidence to support nutrition among adolescent girls and young women, especially those in LMICs.

Our review suggests that iron supplementation among adolescents can significantly improve serum hemoglobin concentration. Data from women of reproductive age, including pregnant women, suggest effects on improving anemia rates, serum hemoglobin and ferritin concentrations, and birth weight. Studies on folic acid supplementation alone were scarce, but IFA supplementation showed effects on improving serum hemoglobin concentration. Data from reviews on periconceptional folic acid supplementation showed significant effects on reducing NTDs. Data from studies on MMN supplementation in adolescent and pregnant adolescent populations showed significant improvement in serum hemoglobin concentration. We found a paucity of trials on calcium and vitamin D supplementation in adolescents, and those that exist did not show improvement in bone mass density. Data from reviews on pregnant women showed that low-dose calcium improves preeclampsia and preterm birth. Limited evidence was found on vitamin A supplementation and iodine supplementation. Pooled analysis on zinc supplementation in adolescents showed improvement in serum zinc and hemoglobin concentration, whereas supplementation in pregnant adolescents showed significant improvement in preterm birth and LBW.

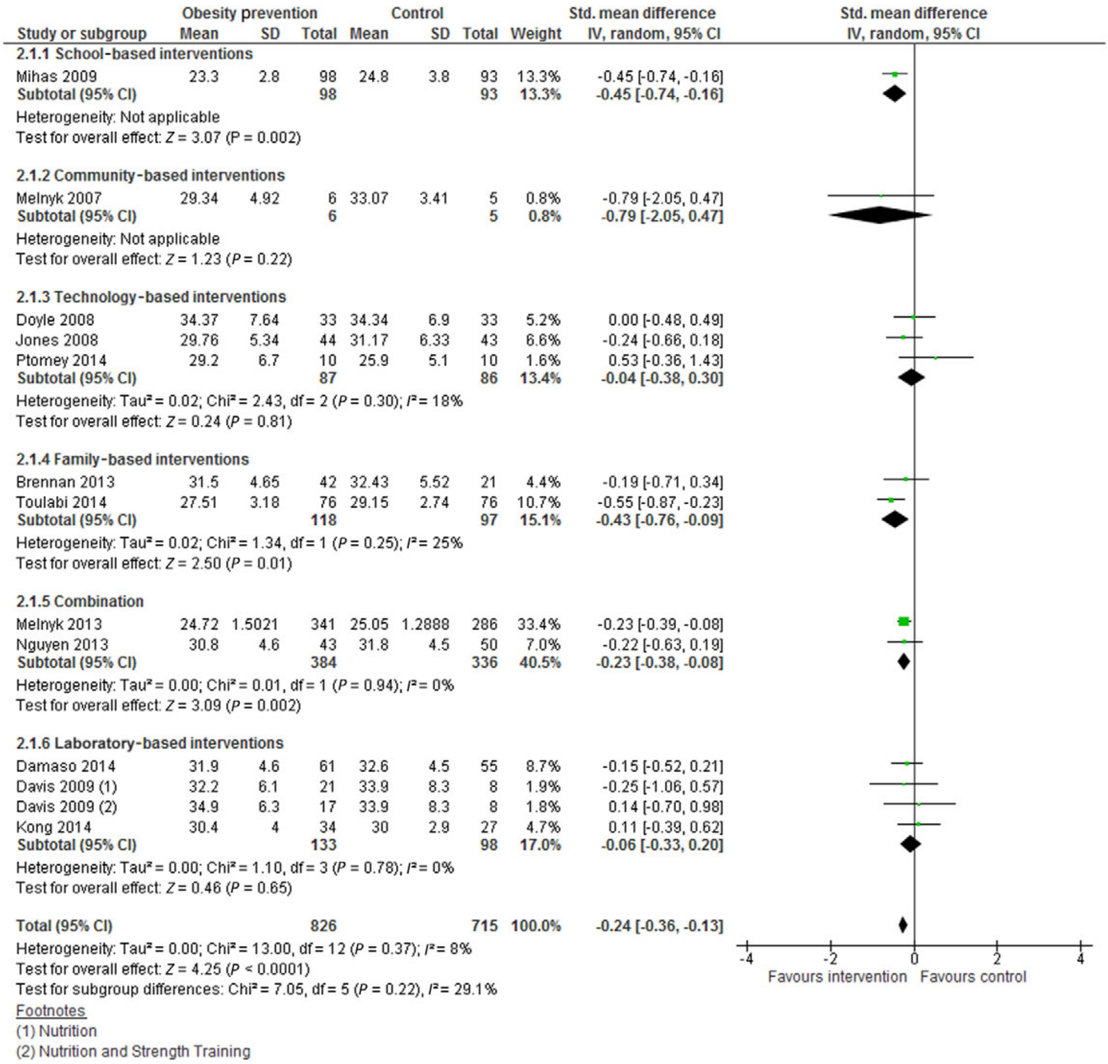


Figure 8. Interventions for management of obesity in adolescents: BMI. References: Mihas,[128] Melnyk,[129] Doyle,[130] Jones,[131] Ptomey,[132] Brennan,[133] Toulabi,[134] Nguyen,[135] Dâmaso,[136] Davis,[137] Kong.[138]

We found a limited number of studies that supplemented food/protein energy in adolescents, and one study from Peru on only a few adolescents showed a reduction in anemia rates. The data from pregnant women showed significant impact of balanced energy/protein on stillbirths, neonatal mortality, and LBW. Similarly, only two studies on very few pregnant adolescents reported the impacts of education interventions on maternal weight gain and birth weight, and those were not significant.

It should be noted that the majority of trials on adolescent micronutrient supplementation were conducted in LMICs, making the findings relevant since these countries stand the highest burden of undernutrition and micronutrient deficiencies. However, these findings should be interpreted with caution owing to imprecision and high heterogeneity. Moreover, we could not find any study on adolescents related to other micronutrients, such as vitamin B_{12}.

Adolescents are living in increasingly obesogenic environments, and the world is witnessing increasing rates of overweight and obesity. Our review suggests that interventions to promote health and prevent obesity had nonsignificant effects on reducing BMI. On the other hand, interventions to manage obesity showed significant effects on reducing BMI. The higher rates of overweight and obesity have consistently been reported in high-income settings, particularly among those who are disadvantaged and live with food insecurity. The majority of the studies that we identified were conducted in HICs, limiting the generalizability of findings to HICs only. However, with the current increasing trends of double burden of malnutrition, there is a need for research in LMICs on this issue. It is also imperative to promote health and education for those at risk of obesity and prediabetes in school/community settings. It is also important to arrange for counseling for appropriate dietary intake and dietary advice to prevent obesity and to improve and increase physical activity and lifestyle support.

We aimed to complete a review of adolescent nutritional interventions to evaluate their effectiveness; however, this review has a number of limitations. First, there was a paucity of reviews and clinical trials on adolescent population. Second, the majority of the trials conducted on women of reproductive age (including pregnant women) did not provide disaggregated findings on adolescent populations. Third, certain trials on adolescents have a varied age range and, although a majority of the study population was within our specified range, the findings need to be interpreted with caution. Fourth, a few trials were reported as quasiexperimental, but we found that they used a pre–post method of reporting final data, which limited our ability to pool those studies with other randomized trials. Fifth, some studies did not report the numbers of participants in each group or reported them only in a graph, which again limited our ability to pool the data. Sixth, there was a paucity of trials on nutrition-sensitive interventions. Seventh, most of the studies that we included were ranked as moderate in quality, owing to lack of blinding and/or the lack of reporting of randomization and allocation-concealment methods. Since most of these interventions included educational activities, blinding may have been difficult if not entirely impossible to perform. Therefore, there is a strong need for detailed and comprehensive studies evaluating nutritional interventions conducted on adolescents. Eighth, the majority of the studies that we identified contained very few adolescents, and the results presented high heterogeneity. Last, we did not include ongoing studies on trial registries; however, we plan to update the evidence on nutritional interventions for adolescents at a subsequent time.

While Figure 1 depicts the nutrition-specific and nutrition-sensitive interventions for improving the health of adolescents, it is important to underscore that our review has only assessed evidence of nutrition-specific interventions and their impact on improved adolescent nutrition and birth outcomes. It is equally important to keep in mind that nutrition-sensitive interventions also have the goals of addressing issues that are indirectly related to malnutrition, such as poverty, environmental contamination, tobacco control, infections, poor education and health literacy, and gender inequalities. Therefore, it is imperative that countries design nutritional interventions, particularly for this population. Implementation through community and school platforms may work. Interventions to reduce the rates of overweight and obesity should also be designed for rapidly urbanizing countries. Similarly, there is a need to implement micronutrient and food supplementation programs for countries with the highest burden of undernutrition and stunting.

Conclusions

This review is limited by the information available on nutrition-specific interventions in adolescents from LMICs. In relation to wasting, while we found limited evidence related to BEP supplementation among adolescents, the general evidence from pregnant women provides evidence of benefits in reducing the risk of stillbirths and neonatal mortality. Similarly, the evidence on interventions to tackle micronutrient deficiencies among adolescents is limited, although most of the studies are from LMICs. The evidence indicates that iron, IFA, and MMN supplements can significantly improve hemoglobin concentration. There is a paucity of trials on calcium and vitamin D supplementation among adolescents; however, the evidence from reviews on pregnant women at risk of low calcium intake shows positive maternal and newborn outcomes and hence could be recommended for this age group as well. Our review found some evidence supporting strategies for obesity prevention and management among adolescents, although the evidence on benefits of interventions to prevent and reduce obesity was mostly from high-income settings with limited generalizability to LMICs. The evidence summarized in this paper suggests incorporating interventions for prevention and management of obesity as well as those pertaining to food supplementation and micronutrient supplementation in at-risk populations.

Our review shows that there is a general dearth of studies on food and micronutrient supplementation in this population. Given the high proportion of adolescents in studies of nutrition interventions in pregnancy, almost all prenatal supplementation trials have included this age group, but they have not examined or reported disaggregated outcomes among adolescents. In the absence of a specific interaction with age and extra requirements for growth, one can assume that the direction of effect and possible impacts would be comparable between adolescents and young women. We therefore also included available evidence from women of reproductive age, including pregnant women, to assess plausible interventions and strategies.

Supporting Information

Additional supporting information may be found in the online version of this article.

Table S1. Search strategies.

Table S2. Summary estimates of interventions for iron supplementation in pregnant women and women of reproductive age.

Table S3. Summary estimates of interventions for folic acid supplementation in pregnant women and women of reproductive age.

Table S4. Summary estimates of interventions for MMN in pregnant women.

Table S5. Summary estimates of interventions for calcium supplementation in pregnant women.

Table S6. Summary estimates of interventions for vitamin A supplementation in pregnant women.

Table S7. Summary estimates of interventions for zinc supplementation in pregnant and women of reproductive age.

Table S8. Summary estimates of interventions for protein energy supplementation in pregnant women.

Table S9. Summary estimates of interventions for GDM in preconception women and women of reproductive age.

Competing interests

The authors declare no competing interests.

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