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Overnutrition is a risk factor for iron, but not for zinc or vitamin A deficiency in children and young people: a systematic review and meta-analysis

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ABSTRACT

Introduction Traditionally associated with undernutrition, increasing evidence suggests micronutrient deficiencies can coexist with overnutrition. Therefore, this work aimed to systematically review the associations between iron, zinc and vitamin A (VA) status and weight status (both underweight and overweight) in children and young people.

Methods Ovid Medline, Ovid Embase, Scopus and Cochrane databases were systematically searched for observational studies assessing micronutrient status (blood, serum or plasma levels of iron, zinc or VA biomarkers) and weight status (body mass index or other anthropometric measurement) in humans under 25 years of any ethnicity and gender. Risk of bias assessment was conducted using the American Dietetic Association Quality Criteria Checklist. Where possible, random effects restricted maximum likelihood meta-analyses were performed.

Results After screening, 83 observational studies involving 190 443 participants from 44 countries were identified, with many studies having reported on more than one micronutrient and/or weight status indicator. Iron was the most investigated micronutrient, with 46, 28 and 27 studies reporting data for iron, zinc and VA status, respectively. Synthesising 16 records of OR from seven eligible studies, overnutrition (overweight and obesity) increased odds of iron deficiency (ID) (OR (95% CI): 1.51 (1.20 to 1.82), $p<0.0001$, $I^2=40.7\%$). Odds appeared to be higher for children living with obesity (1.88 (1.33 to 2.43), $p<0.0001$, $I^2=20.6\%$) in comparison to those with overweight (1.31 (0.98 to 1.64), $p<0.0001$, $I^2=40.5\%$), although between group differences were not significant ($p=0.08$).

Conclusions Overnutrition is associated with increased risk of ID, but not zinc or VA deficiencies, with an inverted U-shaped relationship observed between iron status and bodyweight. Our results highlight significant heterogeneity in the reporting of micronutrient biomarkers and how deficiencies were defined. Inflammation status was rarely adequately accounted for, and the burden of ID may well be under-recognised, particularly in children and young people living with overnutrition.

PROSPERO registration number CRD42020221523.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Low-income and middle-income countries are increasingly facing a double burden of malnutrition, that is, the coexistence of undernutrition (stunting, wasting, underweight) with overnutrition (overweight and obesity).

⇒ While the relationship between undernutrition and critical micronutrients for childhood growth and development (eg, iron, zinc and vitamin A (VA)) is well established, less is known about the risk of micronutrient deficiencies (MNDs) in children and adolescents with overweight or obese, a hidden form of malnutrition.

⇒ There are limited data summarising associations between biomarkers of the most commonly limiting micronutrients and body weight status, particularly in children and young people.

WHAT THIS STUDY ADDS

⇒ Overnutrition increases the risk of iron deficiency (ID), but not zinc or VA deficiencies.

⇒ There is an inverted U-shaped relationship observed between iron status and bodyweight in children and young people, with IDs observed more frequently in both undernutrition and overnutrition.

⇒ Studies conducted to date have been heterogeneous in terms of populations studied, diagnostic criteria and approaches to data analysis; few studies followed current guidelines for measuring inflammation and defining MNDs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Healthcare practitioners will increasingly recognise that children and young people living with overweight or obesity are likely to be iron deficient, resulting in improved clinical practice and care.

⇒ More research needs to be conducted to examine MNDs and the double burden of malnutrition from currently under-represented countries.

⇒ In future research investigating MNDs, there is a critical need for enhanced reporting and higher-quality evidence.

INTRODUCTION

Deficiencies in micronutrients contribute to impaired immune function, poor growth and physical development and increased morbidity and mortality in children.[1 2] Public health prevention strategies such as supplementation, fortification and nutrition education are therefore strongly encouraged by the WHO and UNICEF in low-income and middle-income countries (LMICs).[3 4] Although great strides have been made in the last century to address micronutrient deficiencies (MNDs) and reduce childhood mortality rates, disappointingly in 2013 (median year of data collection), the global prevalence of deficiency in one or more micronutrients was estimated to be 56% in children under 5 years, although rates vary across countries.[5 6]

Among the micronutrients, deficiencies in iron, zinc and vitamin A (VA) remain particularly prevalent and causally associated with adverse health outcomes for children. Iron deficiency (ID) and ID anaemia (IDA) are major global health challenges affecting more than 1.2 billion people worldwide.[7] In addition to ID, it is estimated that more than 25% of South Asia and sub-Saharan African populations are at risk of insufficient dietary zinc intake, with some countries particularly deficient.[8] In a large population survey in Ethiopia, for example, the prevalence of zinc deficiency among young children was shockingly found to be 89%, improving somewhat in school children to 71%.[9] Similarly, in Southeast Asia in Vietnam, in 2010 the prevalence of zinc deficiency was remarkably high (68%) in young children, improving to 42% in children over 5 years of age.[10] Moreover, although large-scale VA supplementation programmes have been implemented in many countries,[2] subclinical VA insufficiency is still prevalent in Vietnam (10.1%, young children aged 5–75 months, data from Vietnam nationwide food consumption survey[10]), and Africa (Ethiopia, 45.4% for 6–72-month-old children, from meta-analysis in 2020[11]), and often observed in the context of multiple MNDs.[12]

Historically, MNDs were considered as one of the four forms of undernutrition, alongside wasting, stunting and underweight,[13] and a particular concern for LMICs where undernutrition may be the leading cause of childhood mortality for children under 5.[2 14] However, increasingly, it is recognised that MNDs also occur in the context of overweight and obesity.[15] Deficiencies in iron,[16] zinc[17] and VA[18] have been observed in adults living with overweight and obesity and associated metabolic diseases. Typically associated with nutrient-poor, energy-dense diets, the presence of multiple MNDs in the absence of an energy-deficit diet has been described as 'hidden hunger'.[19] While in high-income countries obesity is associated with ultra-processed foods that are high in fat, sugar, salt and energy, in LMICs overweight and obesity are often associated with poverty and monotonous diets with limited choices of low-cost energy-dense staples such as corn, wheat, rice and potatoes.[19 20] Even in high-income countries, childhood obesity is strongly linked to poverty and socioeconomic and health disparities.[21]

Moreover, many LMICs are now facing a double burden of malnutrition with the coexistence of an increasing prevalence of overnutrition alongside undernutrition.[22] This is intricately linked to the rapid increase in the global prevalence of obesity, especially in children aged 5–19 years in recent decades.[23] Deficiencies in multiple micronutrients including iron,[24 25] zinc[17 26] and VA[27 28] have also been observed in children living with malnutrition. Indeed, the term 'triple burden of malnutrition' aims to underscore the coexistence of MNDs alongside undernutrition (stunting, wasting, underweight) and overnutrition.[29]

While increasing evidence now suggests MNDs are associated with overnutrition as well as undernutrition, to date there have been only a limited number of reports summarising associations between biomarkers of micronutrient status and obesity in children and young people. In one meta-analysis of multiple comorbidities associated with obesity in children, higher OR for both vitamin D deficiency (OR (95% CI): 1.9 (1.4 to 2.5)) and ID (OR 2.1, 95% CI 1.4 to 3.2) were found in children under age 10 living with obesity.[30] Similarly, a separate meta-analysis of vitamin D deficiency in children and adolescents aged 0–18 years also found a positive association between obesity and vitamin D deficiency (OR 1.4, 95% CI 1.3 to 1.6).[31] However, to our knowledge the risks of iron, zinc and VA deficiencies, the most frequently limiting micronutrients in children and young people, have not been collectively examined. Therefore, in this work, we aimed to systematically review the associations between iron, zinc and VA status and body weight in children and young people, using meta-analyses to summarise where sufficient data existed.

METHODS

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[32] and was registered at PROSPERO (CRD42020221523).

Search strategy

The Ovid Medline, Ovid Embase, Scopus and Cochrane databases were systematically searched through 19 April 2023. A combination of keywords and related medical subject headings were used from three main themes: (1) population: infants, children, adolescents and young adults; (2) malnutrition indicators, including undernutrition and overnutrition; and (3) blood micronutrient indicators for iron, zinc and VA. The specific search strategies developed for each database are reported in online supplemental tables 1–4.

Inclusion and exclusion criteria

Observational studies in humans under 25 years of age,[33] of any nationality, gender or ethnicity, with undernutrition or overnutrition diagnosed by body mass index

(BMI) or other anthropometric measurement, were included. In addition to be included, studies had to have reported as primary outcomes either: a blood or serum test of micronutrient level, the OR or relative risk of MNDs, or the linear regression between a micronutrient indicator and weight status. Records excluded from this review were: non-English articles, short reports, communications, address, case reports, comments, letters, editorial matters, meta-analyses, news, reviews, conference abstracts, studies with unrepresentative samples (either convenience sampling or n<100), studies not reporting primary outcomes of interest, studies reporting associations with combined MNDs and studies of micronutrient supplement interventions. Studies that assessed anaemia diagnosed with only haemoglobin (Hb) were excluded, as not specific to ID.

Study selection

The screening of identified studies was managed using the web-based Rayyan software.[34] The selection of the eligible studies for inclusion in this review was assessed and agreed by two independent reviewers (XT and PYT). Disagreement between reviewers was resolved by discussion or by third reviewer if necessary.

Data extraction

A standardised data extraction form was used to extract the following information: first author, year of publication, year of study, study design, country, participants' characteristics (eg, sample size, recruitment, gender, age, socioeconomic status, etc), exposure (eg, anthropometric indicators and blood/serum levels of micronutrients of interest), control or non-exposure (eg, children who were not malnourished), outcome measures (eg, changes in anthropometric indicators in the presence of MNDs or otherwise changes in the blood micronutrients levels in different anthropometry groups), main findings (eg, differences in mean, β coefficient, OR, relative risk) and funding or sponsorship.

Risk of bias assessment

Risk of bias was assessed by two reviewers using the Quality Criteria Checklist developed by the Academy of Nutrition and Dietetics.[35] Any disagreement was resolved by discussion and by a third reviewer if necessary. This tool has 10 validity questions: (1) clear research question, (2) non-biased participant recruitment, (3) group comparability, (4) report of withdrawals/participant ratio, (5) blinding, (6) study procedures description, (7) outcome, (8) appropriate statistical method and adequate adjustments, (9) conclusion supported by results and (10) conflict of interest. The overall rating was defined as either positive (majority of criteria above were met, in which criteria 2, 3, 6 and 7 must be met), neutral (any one criterion of criteria 2, 3, 6 and 7 was not met) or negative (six or more of the criteria not being met).

Data analysis

The associations (eg, OR, relative risk, linear regression) between the blood micronutrient levels of interests and anthropometry status were curated in tables according to micronutrient. If no association data was provided, the comparison of mean micronutrient levels between different anthropometry groups was included in the table. For the convenience of summarising, the main findings of each study were concluded as either direct associations (micronutrient levels increased with increasing weight status indicators) or inverse associations (decreased micronutrient levels—increasing risk of MNDs—with increasing weight status indicators).

Weight status indicators included BMI-for-age z score (BAZ) and BMI used to categorise overnutrition. While for undernutrition, height-for-age z score, weight-for-age z score and weight-for-height z score were used to categorise stunting, wasting and underweight, respectively, following the WHO growth chart, obesity work taskforce or national standard in respect to each country. Micronutrient status indicators included blood micronutrient levels (iron, zinc, retinol), Hb, iron profile, β-carotene, retinol binding protein or diagnosis of ID, IDA, zinc deficiency or vitamin D deficiency (VAD). The diagnostic criteria of MNDs mostly followed either WHO criteria or the International Zinc Nutrition Consultative Group standard or country-specific standards for defining MNDs.

Where there were at least five studies[36] assessing the risk of MNDs in malnutrition groups comparing with normal weight group, random effects restricted maximum likelihood meta-analyses were conducted to estimate the OR with 95% CI using Stata V.18 (Stata Corporation, College Station, Texas, USA). Heterogeneity across the studies was evaluated using I^2. Sensitivity analysis was conducted by using the leave-one-out method, to compare the pooled OR before and after eliminating each study at a time. To detect publication bias, the asymmetry of the funnel plot was examined. Statistical significance was set at $p<0.05$. To avoid overestimation of power, the gender-stratified data were not included in meta-analysis if overall population data were reported by the study. All graphics were produced in either Stata or using the R-package ggplot2,[37] ggalluvial[38] and rworldmap[39] in the R environment.[40]

Patient and public involvement

It was not appropriate to involve patients or the public in the design or conduct of our research. However, members of the general public, including children and young people, were consulted about dissemination materials.

RESULTS

Using systematic search strategies, a total of 9711 articles were initially identified from four databases, of which 5459 articles remained after deduplication. After title and abstract screening, the full texts of 151 articles were assessed to check for eligibility. From these, 83 observational studies met the inclusion criteria and 7 studies were eligible for meta-analysis (figure 1).

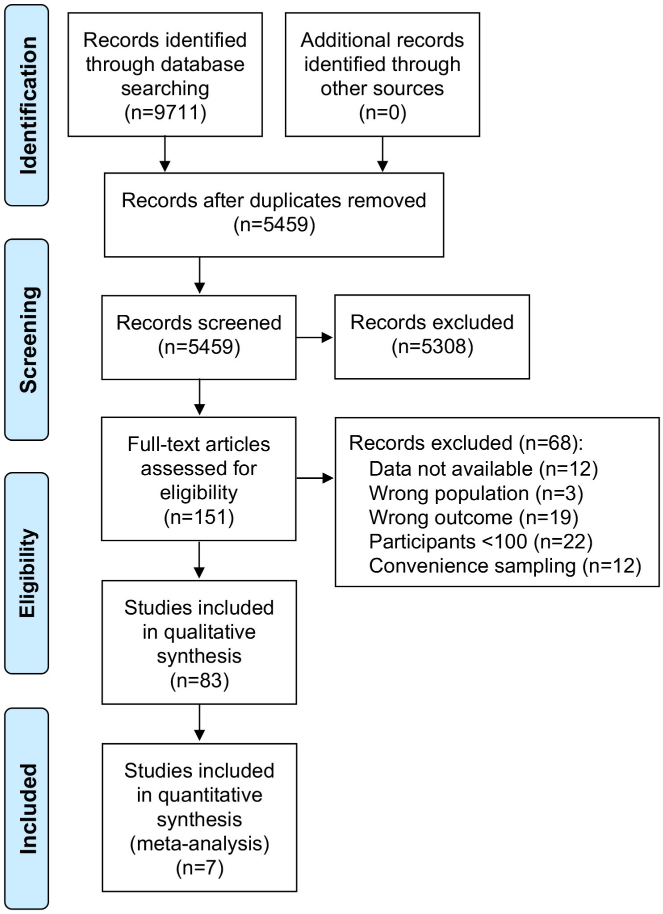

Figure 1 Flow diagram of the systematic identification and selection of articles.

Overall, the 83 studies involved a total of 190 443 participants from 44 countries (figure 2). The majority (n=74, 89.1%) were cross-sectional studies, and the number of participants in individual studies ranged from n=101[41] to n=64 850 (the China National Nutrition and Health Survey of Children and Lactating Mothers study, 2016–2017[42]), with a median n=675 participants. Notably, many studies assessed more than one micronutrient and/or weight status indicator at the same time. Iron was the most investigated micronutrient, with a total of 46 (n=10, 21 and 15 for both overnutrition and undernutrition, respectively), 28 (n=4, 8 and 16 for both overnutrition and undernutrition, respectively) and 27 (n=5, 12, 10 for both overnutrition and undernutrition, respectively) studies identified for iron (online supplemental table 5), zinc (online supplemental table 6) and VA (online supplemental table 7), respectively.

Associations between iron and weight status

The characteristics and findings of the studies that reported associations between iron status and weight status in children and young people (n=46) are summarised in online supplemental table 5. 10 studies assessed both sides of malnutrition, whereas 21 studies focused on overnutrition and 15 studies focused on undernutrition. A broad range of biomarkers for ID were used by the different studies, and most studies reported more than one (online supplemental table 5). In 2020, the WHO revised their guidance on the use of ferritin to assess iron status in individuals and populations, providing thresholds of <15 µg/L for healthy individuals above 5 years of age and <70 µg/L for individuals with infection or inflammation (<12 µg/L or <30 µg/L are used for children under 5). While current WHO guidance is that ferritin, both an iron storage protein and an acute phase reactant associated with inflammation,[43] should not be used alone to diagnose ID without other iron profile biomarkers or corrections for inflammation,[44] a minority of studies did

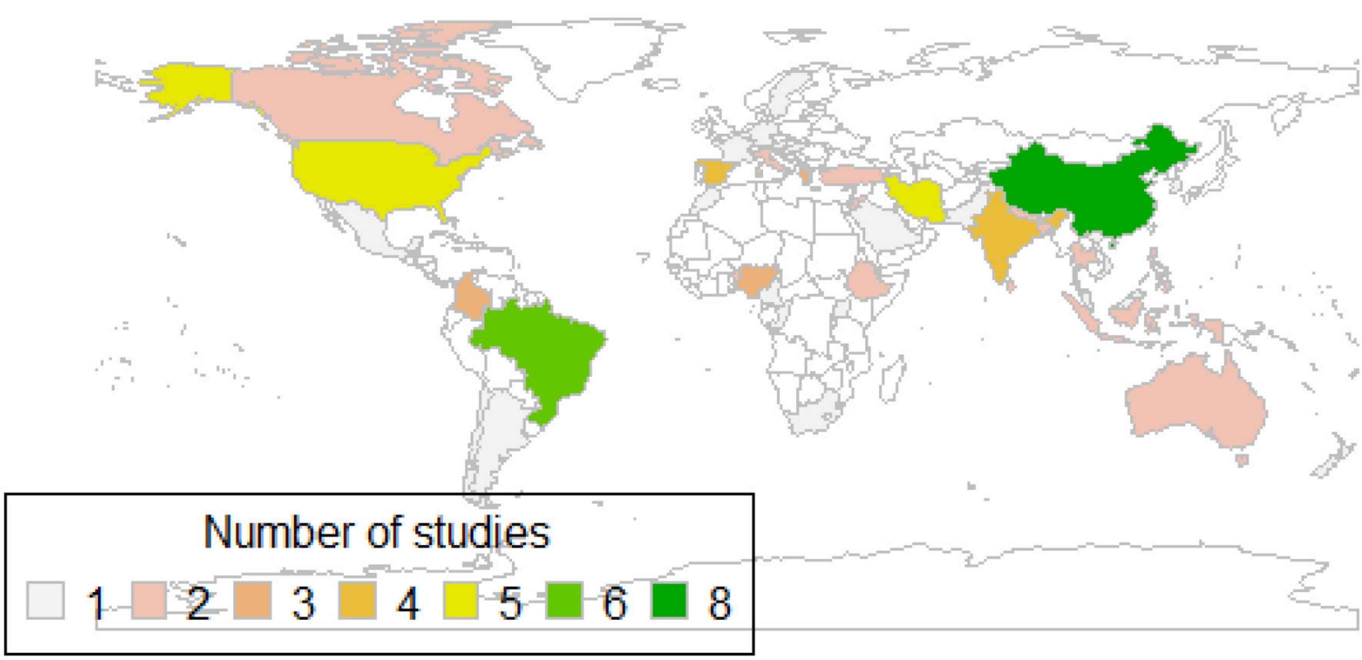

Figure 2 World map showing the populations represented in the included articles.

rely on ferritin alone.[25 45–48] Likewise, serum iron alone should not be used in isolation to diagnose ID as serum iron levels will be reduced in the context of infection or inflammation,[49] but was used in a handful of studies.[43 50 51] In risk of bias assessment, most studies were found to be of positive quality (28 out of 46; online supplemental table 5). Only three studies were found to be of negative quality.[50–52] Overall, the most common reasons for studies being rated either neutral or negative quality were either the lack of: (1) an appropriate statistical approach, such as multivariate logistic or linear regression with adequate adjustments, eg, inflammation status or menarche, or (2) essential information such as group comparability, information of withdrawals or limitation of the study (online supplemental table 8).

A total of 16 records reported OR from seven eligible studies enabling our calculation of the pooled OR for ID with overnutrition (overweight or obesity) using the normal weight groups as reference. These studies assessed overnutrition and ID in North American (USA[45 53 54] and Mexico[55]) and European (Spain[56] and Greece[57 58]) populations, and, in risk of bias assessment, all were assessed as positive (good) quality. The random-effects model meta-analysis indicated a pooled OR (95% CI) of 1.51 (1.20 to 1.82), p<0.0001, for ID with overnutrition (figure 3). Heterogeneity was moderate with an I^2 value of 40.73%, likely a result of the diversity of ethnicities, ages and genders studied as well as the broad range of biomarkers for ID and overnutrition used by the different studies. Subgroup analyses suggested increased risk of ID in those living with obesity OR (95% CI): 1.88 (1.33 to 2.43), p<0.0001, compared with overweight OR (95% CI): 1.31 (0.98 to 1.64), p<0.0001; however between group differences were not statistically different (p=0.08), likely driven by greater heterogeneity in the overweight versus obesity data (I^2: 40.46% vs 20.0%, figure 3).

Similarly, no differences were observed between studies that reported data separately for males and females versus those that reported data from mixed-gender populations (p=0.47, online supplemental figure 1). Funnel plot analyses suggested some asymmetry driven by two outliers (online supplemental figure 2). These

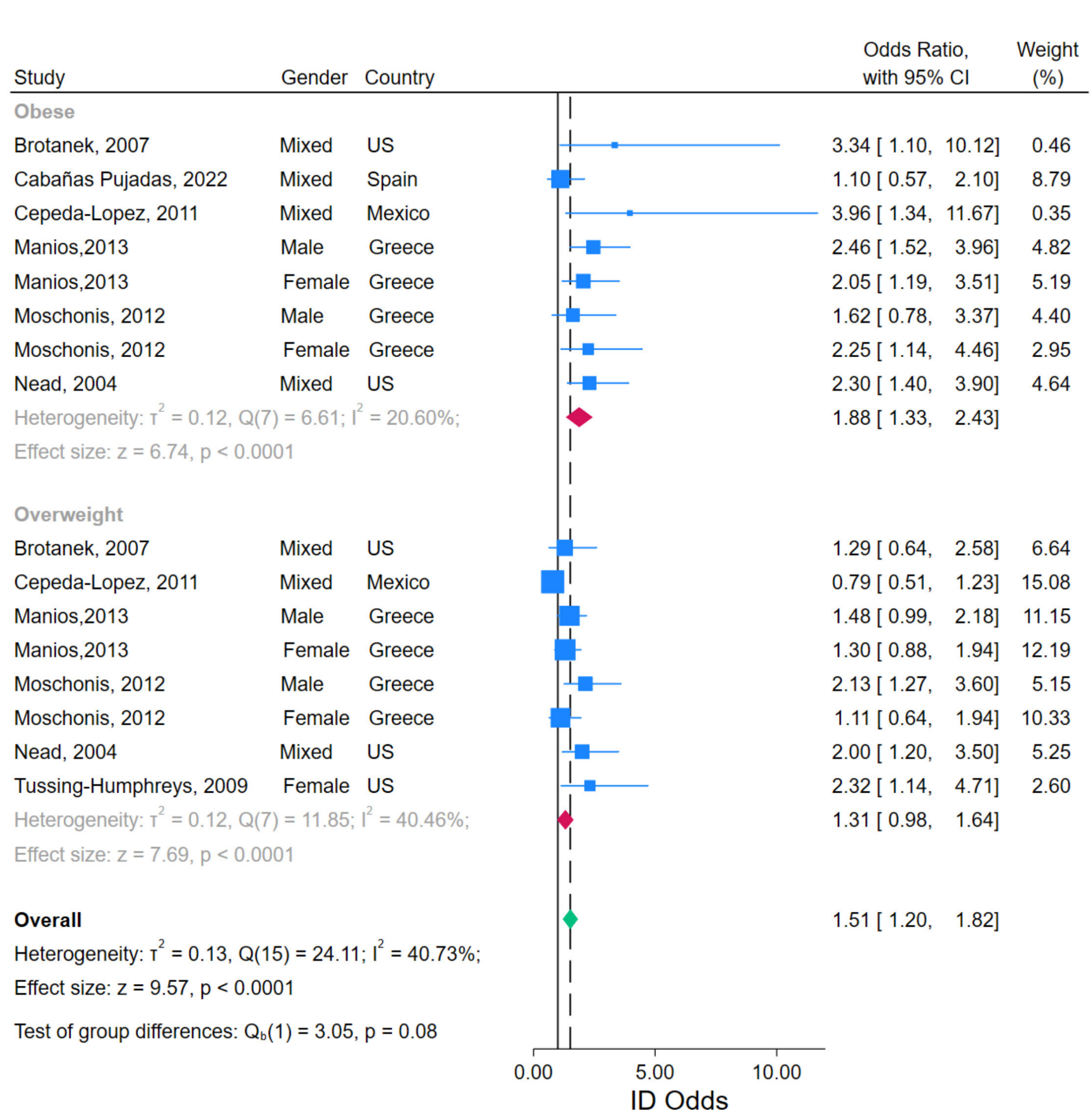

Figure 3 Forest plot of reported associations between overnutrition and odds of iron deficiency (ID).

studies reported higher prevalence of ID in both overweight and obese mixed-gender populations, with much larger SEs observed in the (fewer) children with obesity (figure 3).[53 55] As they contributed only small weights to the meta-analysis (Brotanek *et al*: 0.46%, Cepeda-Lopez *et al*: 0.35%), this is a small-study effect rather than non-reporting bias, and indeed funnel analyses with fewer than 10 studies should be interpreted cautiously.[59] Sensitivity analyses indicated robustness in the overall results as the effect size was not significantly changed after removing any of the studies (online supplemental figure 3).

Given that the meta-analysis incorporated only a small subset (7 of 46) of iron studies, to synthesise the findings across all studies, we examined the numbers of participants in the reports concluding either direct, inverse or no significant associations between ID and nutrition status (figure 4A). These data illustrate surprising heterogeneity in the conclusions of individual studies and show where individual studies contributed disproportionally larger populations. In the case of iron and undernutrition, while 13 reports that included 15 335 participants found a direct association (ie, better iron status found with normal bodyweight in comparison to undernutrition), surprisingly 10 studies that included 30 705 participants found no association and 2 concluded an inverse association (figure 4A). Notably, the two studies that found an inverse association had reported linear regression between iron and both undernutrition and overnutrition (BMI 14–32[60] and BAZ between −4 and 2[57]). However, the associated scatter plots suggest piecewise regression would be more appropriate as very low ferritin values were observed in both the lowest and highest quintiles of nutrition status. While the data for overnutrition appear clearer, with 19 reports including 27 894 participants concluding an inverse relationship (ie, worsening iron status as weight status moves from normal to overweight and obesity), nonetheless 9 reports with 8884 participants concluded a direct association and 3 found no association (figure 4A).

While these conflicting results likely reflect different populations studied and the challenges of ID diagnosis, nonetheless, we conclude the data collectively suggest an inverted U-shaped relationship between iron status and bodyweight, with children and young people living with overnutrition having a higher risk (pooled OR (95% CI): 1.51 (1.20 to 1.82)) of ID alongside those with undernutrition.

Associations between zinc and weight status

The 28 studies that examined zinc status and either undernutrition or overnutrition were similarly diverse in their approaches and findings (online supplemental table 6). In particular, how authors compared groups statistically (eg, mean, median, quartile (Q): Q2–4 vs Q1) varied between studies and precluded any meta-analysis. Although the majority of studies (27 out of 28) measured either plasma or serum zinc, 1 study used whole blood

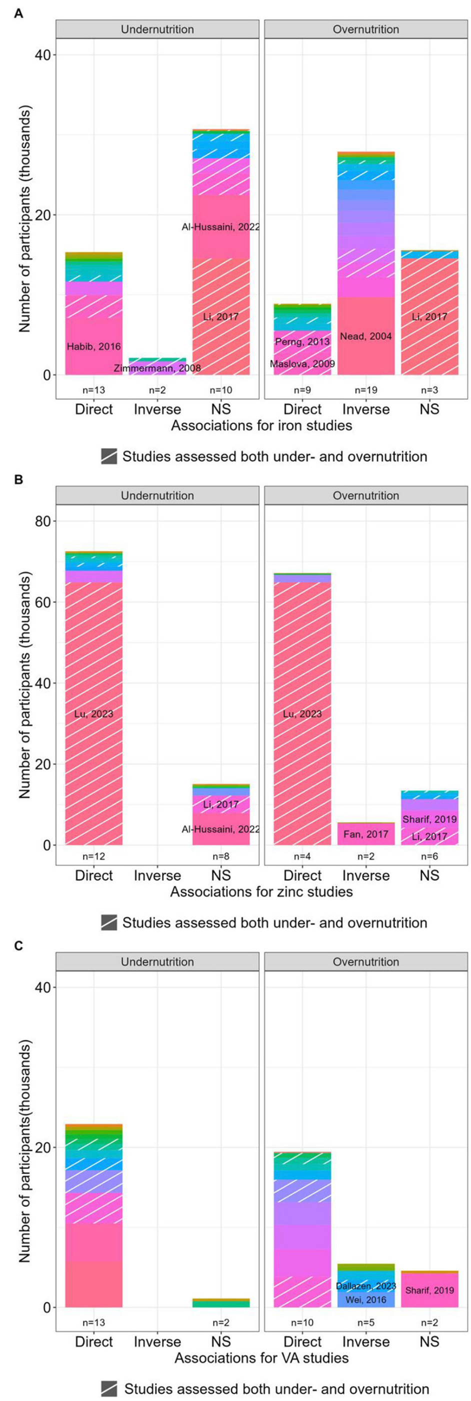

Figure 4 Summary stacked bar plots showing participant numbers, grouped by the direction of associations, in studies examining overnutrition or undernutrition: (A) iron, (B) zinc and (C) VA. Studies where participants represented >25% of the total population in each category were labelled. NS: not significant VA: vitamin A.

and concluded a direct association,[61] however, measurements of zinc in whole blood may overestimate zinc levels as whole blood zinc level was five-fold higher than plasma due to red blood cells.[62] We note only two studies[26 63] used international consensus-based thresholds (57–74 µg/dL depending on age group, sex, time of day and time since last meal[64]) for defining deficiency, which may explain some of the heterogeneity in conclusions between studies here. In addition, although plasma or serum zinc concentration is the most used biomarker of zinc status, there are well-described issues with sensitivity and specificity, as well as challenges with sample collection and storage, that render the assessment of dietary zinc status in humans challenging.[65] In the risk of bias assessment, most studies (17 out of 28) received a positive quality rating.

Although a direct relationship between zinc status and undernutrition was concluded by the majority of studies (12 of 20 accounting for 72 537 participants; figure 4B), the results from reports on overnutrition were more contradictory. While four studies concluded direct associations between zinc levels and BMI,[42 61 66 67] two found inverse relationships[68 69] and six studies, accounting for 13 440 participants in four countries (three from Iran,[70–72] and one from Colombia,[73] Australia[74] and China[75]), concluded no association between zinc status and overweight (figure 4B). Among the studies reporting direct associations with both undernutrition and overnutrition was an exceptionally large population study from China with >64 000 participants.[42] While in this cohort stunting conferred a higher risk of zinc deficiency (OR (95% CI): 1.44 (1.19 to 1.75)), and overweight and obesity appeared to confer protection (overweight: 0.88 (0.84 to 0.96); obesity: 0.78 (0.70 to 0.86)), serum zinc values were not hugely different between groups and within adequate population ranges,[64 76] with 86.0 µg/dL (77.0 to 96.0) reported for children with stunting and 91.0 µg/dL (82.0 to 101.0) for children living with obesity.[42] Relatedly, in a large American cohort (n=5404 children aged 5–19 years) the overall population mean (range) of zinc levels was similarly adequate, 82.7 µg/dL (38.9 to 198.6).[68]

In sum, while the data were more limited for zinc, they suggest an exponential plateau curve relationship between zinc status and bodyweight, with children and young people living with severe undernutrition having the highest risk for zinc deficiencies, and no evidence for a higher risk for zinc deficiency with overnutrition.

Associations between VA and weight status

The studies that investigated VA status in relation to body weight were similarly heterogenous in their approaches to assessing both VA and nutrition status (online supplemental table 7). VA was commonly assessed by measuring plasma/serum retinol levels, although some studies measured either serum carotenoids, b-carotene or retinal binding protein levels. However, plasma/serum retinol concentration is under tight homeostatic control and does not reflect VA status until body stores are extremely low or very high.[77] Where low serum retinol was defined, WHO cut-offs (retinol<0.7 µmol/L, equivalent to 20 µg/dL[78]) were most often but not always used. These values are not sensitive to moderate VA deficiencies, and, similarly, with zinc, studies often examined results by comparing bottom and top quartiles of the biomarkers measured. As with the zinc studies, variability in the outcomes measured and statistical approaches between studies prevented us from performing meta-analysis, and the majority of studies received positive quality ratings (17 out of 27; online supplemental table 7).

While a direct relationship between undernutrition and VA deficiency was clear with 13 of 15 studies concluding a direct association, the other 2 reported no association (figure 4C), the data for associations between overnutrition and VA deficiency were more contradictory. Although in favour of a direct relationship between VA status (n=10 of 17 studies, accounting for 19 443 participants), 5 found an inverse association and 2 found no association (figure 4C). In the 10 studies that found a direct relationship, these were reported in a variety of ways, such as, lower risk of VAD in the context of overweight or obese[75 79–83] or elevated serum levels of VA or plasma retinol in children with overweight or obesity.[73 84–86] Interestingly, of the five studies that concluded an inverse association between overnutrition and VA deficiency, four focused on Brazilian children. The associations were reported either as increased risk of VAD[28] or risk of low carotenoids,[87 88] for overweight children aged 5–19 years with around 500 participants in each study. While in one case, low plasma retinol (<0·70 µmol/L) was associated with overweight in Brazilian children aged 12–59 months (n=1503).[89] The fifth, non-Brazilian, study assessed 7–11 years old children (n=1928) in Chongqing, China,[90] and found that obesity increased the risk of VAD, OR (95% CI): 2.37 (1.59 to 3.55).

In the context of the tight homeostatic mechanisms for plasma retinol levels,[77] we conclude that similar to zinc, the data suggest an exponential plateau curve relationship between VA status and bodyweight, with children and young people living with severe undernutrition having the highest risk for VA deficiency and no evidence for a higher risk for VA deficiency with overnutrition.

Lastly, regional differences were observed both in terms of which micronutrients were more frequently investigated and whether populations with undernutrition or overnutrition or both were investigated (figure 5). Studies from North America and Europe (figure 5A) focused entirely on overnutrition and largely on iron, whereas reports from the Western Pacific (figure 5B), Asia (figure 5C) and Latin America (figure 5D) assessed both undernutrition and overnutrition and most studies in Africa (figure 5E) focused on undernutrition.

DISCUSSION

To our knowledge, this is the first systematic review of the associations between weight status in children and young people and iron, zinc and VA deficiencies, to concurrently examine associations with both undernutrition and overweight, that is, the double burden of malnutrition. Notably, our results suggest an inverted U-shaped relationship between iron status and bodyweight, with both undernutrition and overnutrition increasing risk for ID. In meta-analyses, children and young people living with

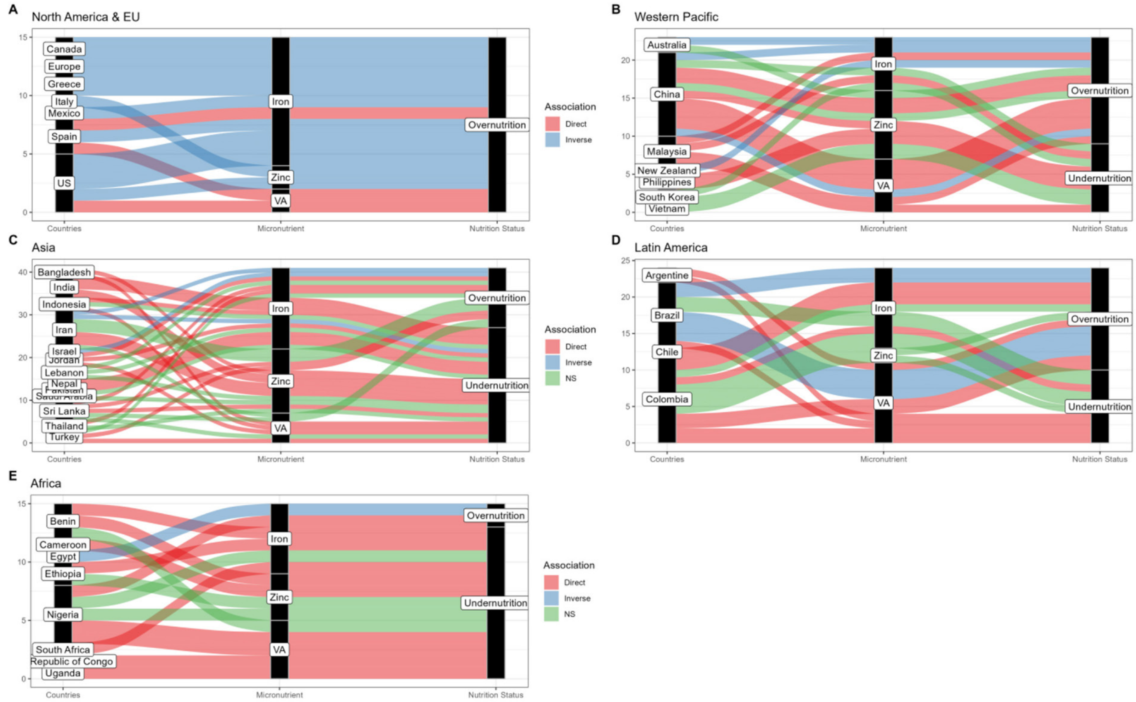

Figure 5 Sankey plots illustrating regional differences in study characteristics and conclusions: (A) North America and Europe, (B) Western Pacific, (C) Asia (excluding Western Pacific), (D) Latin America and (E) Africa. Each line represents a reported association for different micronutrient and nutritional status in different country. The left black column illustrates the countries studies originated from, the middle black column illustrates the relative proportion of studies investigating either iron, zinc or vitamin A (VA) and the right black column illustrates the relative proportion of studies investigating either overnutrition or undernutrition. NS: not significant.

overnutrition had a higher risk (pooled OR (95% CI): 1.51 (1.20 to 1.82)) of ID, with those living with obesity having even higher risk (pooled OR (95% CI): 1.88 (1.33 to 2.43)) compared with those with normal weight. In contrast, zinc and VA deficiencies were most observed in children and young people with undernutrition. While in aggregate, the studies underscore the increased risks for iron, zinc and VA deficiencies with undernutrition in childhood and adolescence, there was more heterogeneity in study conclusions (ie, several studies finding no relationship) for iron and zinc. Such heterogeneity in part relates to the methodological challenges of assessing the status of these micronutrients in humans. Indeed, our results highlight how variable the approaches to measuring and reporting dietary nutrient deficiencies have been, as well as regional data gaps, with important implications for future study design.

Excess adiposity is associated with low-grade inflammation, widely proposed to be the mechanism behind reduced iron status observed in adults living with obesity.[91 92] With the expansion of adipose tissue comes macrophage infiltration and release of inflammatory cytokines such as interleukin-6 (IL-6), which stimulate the synthesis of acute phase proteins such as ferritin and hepcidin, the main regulator of systemic iron homoeostasis.[91] Hepcidin prevents iron absorption from the enterocytes and iron release from splenic macrophages, thereby reducing circulating iron levels overall.[92] In acute infection, this serves to deprive a pathogen of iron,[93] but in the context of chronic disease with prolonged immune activation can lead to anaemia of chronic disease.[94] The results of our meta-analysis, showing a higher risk of ID with overnutrition, particularly in children and young people living with obesity, are consistent with those seen in adults[16] and suggest inflammation-mediated increases in hepcidin as the potential mechanism. This would explain the difference between the observation of ID, but not zinc or VA deficiencies, in children with overweight or obesity. Examining hepcidin and inflammatory markers before and after weight loss intervention would permit testing this association as a causal mechanism. However, as noted in a recent review of studies investigating hepcidin and IL-6 levels in children with obesity,[95] this has only rarely been done. But in two small studies, one 8-month exercise intervention (n=73)[96] and one 6-month weight loss intervention (n=15),[97] decreases in IL-6 and hepcidin were observed in conjunction with weight loss and improvements in iron status, in line with this hypothesis.

Inflammatory status is particularly relevant as ferritin, the primary blood biomarker of iron status used, was consistently found higher in obese groups compared with children with normal weight, with direct linear association reported in multiple studies.[25 46–49 56 66 85 98–105] However, as ferritin is an acute phase reactant, inflammation can obscure ID[106]. Therefore when the WHO reviewed their guidance on the use of ferritin to assess iron status in 2020,[44] they made the strong recommendation that in

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areas of widespread infection or inflammation, serum ferritin should be measured alongside both C-reactive protein (CRP) and α-1 acid glycoprotein (AGP), which reflect different phases of the immune response from acute infection to chronic inflammation. In addition, they recommend that thresholds to define ID in individuals with infection or inflammation should be raised to 30 mg/L for children under 5 and 70 mg/L serum ferritin for all age groups over 5.[44] However, very few studies (n=4 out of 23 studies that used ferritin with or without other biomarkers to define ID) measured and excluded participants with elevated CRP level.[46 104 105 107] Only one study measured AGP[108] and only two studies from Colombia[85] and Brazil[109] used the higher thresholds for ferritin to define ID in the context of inflammation. Interestingly, the WHO serum ferritin concentration thresholds were based on expert opinion,[44] and a recent analysis of serial cross-sectional National Health and Nutrition Examination Survey data concluded thresholds for ferritin for iron-deficient erythropoiesis should be higher, at least for healthy American children and women.[110] Specifically, from regression models of the distributions of Hb and soluble transferrin receptor with serum ferritin in 2569 and 7498 healthy children under 5 and women (15–49 years old), they derived 20 mg/L for children under 5 and 25 mg/L in women as physiologically based serum ferritin thresholds for ID. These data suggest that the global burden of ID in children and young people may well be underestimated.

In contrast to iron, our results show that zinc and VA deficiencies were most observed in undernutrition, with limited evidence for a higher risk for deficiency with overnutrition. While variability in the outcomes measured and statistical approaches between studies precluded meta-analyses, critical review of the data in aggregate suggests an exponential plateau curve relationships between zinc or VA status and bodyweight, with children and young people living with severe undernutrition having the highest risk for these MNDs. Nonetheless, considerable uncertainty in the evidence base remains, particularly for overnutrition. This is not least of all because of efficient homeostatic mechanisms that buffer plasma zinc and VA levels to either dietary deficiency or excess, thereby maintaining plasma concentrations within a narrow range and preventing toxicity in the case of VA.[77 111] Therefore, more moderate deficiencies in overnutrition may be masked. In addition, mechanistically there are complicated interactions between the micronutrients themselves (eg, VA deficiency impairs iron mobilisation and VA supplementation will improve Hb concentrations[111]) and between overnutrition, inflammation and micronutrient metabolism.

Indeed, our comprehensive review highlights the challenges of micronutrient assessment at an individual and population level with important implications for future study design and reporting in the context of the double burden of malnutrition. The most commonly used biomarkers of micronutrient status (plasma/serum ferritin, zinc and retinol levels) are sensitive to a variety of stimuli, including infection and inflammation,[78] and a primary recommendation for future work investigating MNDs in either undernutrition or overnutrition is that CRP and AGP are routinely measured and inflammation accounted for in line with current expert guidelines. While in the case of iron, ferritin increases with inflammation and ID may be underestimated and thresholds for deficiency should be raised[112]; in the cases of zinc and VA, deficiencies may be overestimated as both plasma/serum zinc and retinol are, at least transiently, lowered in acute infection or inflammation.[113 114] Conversely, additional challenges with zinc measurement exist as careful sample collection and handling is critical to prevent haemolysis or contamination from adventitious zinc in the environment,[64] which may mask deficiencies, a potential confounder in the studies that surprisingly did not find zinc deficiency associated with undernutrition. If CRP and AGP are measured, inflammation can be adjusted for by either exclusion, the use of correction factors or linear regression approaches recently proposed by the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia project.[115] Regression approaches have now been systematically developed and used to adjust for ferritin,[116] zinc[114] and VA[113] values on a continuous scale.

In addition, our work highlights that many studies did not apply consensus-based cut-offs for defining either iron, zinc or VA deficiencies but rather compared lower to upper quartiles of plasma/serum biomarkers within their populations, often not specifying the measured ranges of biomarkers within quartiles. Such calculations may overestimate risks of deficiencies in largely replete populations, and their widespread use may explain some of the seeming contradictory conclusions. Lastly, our data highlights regional data gaps and differences in study focus, with most studies from Africa and Asia focused on undernutrition and those from North America and Europe focused entirely on overnutrition. This is concerning as both Africa and Asia experienced dramatic increases in the number of overweight children under 5 between 2000 and 2017 (from 6.6 to 9.7 million children in Africa and from 13.9 to 17.5 million children in Asia).[117] Moreover, the regions of Africa and Asia have the highest double burden of malnutrition with large numbers of stunted and wasted children and the number of stunted children under 5 having increased from 50.6 to 58.7 million children in Africa.[117] These stark data underscore that the investigation of MNDs in relation to the double burden of malnutrition remains critically important for child health. Interestingly, a study published after our literature search assessed the risk of ID (serum ferritin <12 µg/L) in relation to BMI in healthy children (n=2575, aged 12–29 months) living in Canada.[118] A rare example of a study investigating the double burden of malnutrition in a high-income country, it is notable that no association between underweight and ID was found. However, they did find that toddlers with overweight (BAZ>2) had higher risk of ID (OR=2.15 (1.22 to 3.78), p=0.008) in line with the results of our meta-analysis (we note that as they employed convenience sampling, the study did not meet our inclusion criteria).

This is the first study to concurrently, comprehensively review the associations between iron, zinc and VA deficiencies and the double burden of malnutrition in children and young people. In general, undernutrition groups were reported to have lower plasma/serum ferritin, zinc and retinol levels or found to have higher risks for iron, zinc and VA deficiencies. Notwithstanding evidence gaps, we conclude that overnutrition was associated with ID, but not zinc or VA deficiencies. Strengths of this work included our comprehensive search strategy with robust inclusion and exclusion criteria and a priori registration of detailed review protocol in line with PRISMA guidelines[32] and using the Population-Investigation-Comparison-Outcome approach.[119] In addition, this systematic review included populations across the globe (including North American and Europe, Latin American, Western Pacific, Asia and Africa continents), which allowed us to identify regional data gaps and differences in term of their nutritional outcomes or micronutrients of interests and the associations reported. While we excluded studies with small sample size (<100) and those that employed convenience sampling methods to reduce the bias, this review has also highlighted the importance of addressing the challenges and weaknesses in study design, analytical methods and diagnostic criteria for MNDs, to ensure the validity and reliability of data in future study for interpretation. Nonetheless, this work also has some limitations. First, all observational studies are limited by confounding and causality should not be inferred. Second, only four databases (Medline, Scopus, Embase and Cochrane) were searched, and only studies written in English were included, which may have limited the scope. Last but not least, MND status assessment is not trivial in humans, and the underlying studies included in this review were heterogeneous in the populations studied and approaches taken, conferring some limitations in data interpretation.

CONCLUSION

Iron, zinc and VA deficiencies were commonly associated with undernutrition in children and young people. Overnutrition increased the risk of ID, but not zinc or VA deficiencies, with an inverted U-shaped relationship observed between iron status and bodyweight. Heterogeneity between studies was attributable to the diversity of participants, diagnostic criteria and approaches to data analysis. Inflammation status was rarely adequately assessed, and we conclude the burden of ID may well be under-recognised, particularly in children and young people living with overnutrition.

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REFERENCES

1 Bailey RL, West KP Jr, Black RE. The epidemiology of global Micronutrient deficiencies. *Ann Nutr Metab* 2015;66 Suppl 2(suppl 2):22–33.
2 Black RE, Victora CG, Walker SP, *et al*. Maternal and child Undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013;382:427–51.
3 Tam E, Keats EC, Rind F, *et al*. Micronutrient supplementation and Fortification interventions on health and development outcomes among children under-five in Low- and middle-income countries: A systematic review and meta-analysis. *Nutrients* 2020;12:289.
4 da Silva Lopes K, Yamaji N, Rahman MO, *et al*. Nutrition-specific interventions for preventing and controlling anaemia throughout the life cycle: an overview of systematic reviews. *Cochrane Database Syst Rev* 2021;9:CD013092.
5 Stevens GA, Beal T, Mbuya MNN, *et al*. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health* 2022;10:e1590–9.
6 Yue T, Zhang Q, Li G, *et al*. Global burden of nutritional deficiencies among children under 5 years of age from 2010 to 2019. *Nutrients* 2022;14:2685.
7 Camaschella C. Iron deficiency. *Blood* 2019;133:30–9.
8 Gupta S, Brazier AKM, Lowe NM. Zinc deficiency in Low- and middle-income countries: prevalence and approaches for mitigation. *J Hum Nutr Diet* 2020;33:624–43.

9 Belay A, Gashu D, Joy EJM, *et al*. Zinc deficiency is highly prevalent and spatially dependent over short distances in Ethiopia. *Sci Rep* 2021;11:6510.
10 Laillou A, Pham TV, Tran NT, *et al*. Micronutrient deficits are still public health issues among women and young children in Vietnam. *PLoS One* 2012;7:e34906.
11 Sahile Z, Yilma D, Tezera R, *et al*. Prevalence of vitamin A deficiency among preschool children in Ethiopia: A systematic review and meta-analysis. *Biomed Res Int* 2020;2020:8032894.
12 Van Nhien N, Khan NC, Ninh NX, *et al*. Micronutrient deficiencies and anemia among preschool children in rural Vietnam. *Asia Pac J Clin Nutr* 2008;17:48–55.
13 World Health Organization. Malnutrition. 2023. Available: https://www.who.int/health-topics/malnutrition#tab=tab_1 [Accessed 10 Mar 2023].
14 Alderman H, Behrman JR, Glewwe P, *et al*. Child and adolescent health and development. In: Bundy DAP, Silva ND, Horton S, eds. *Evidence of Impact of Interventions on Growth and Development during Early and Middle Childhood*. Washington (DC): The International Bank for Reconstruction and Development / The World Bank©2017, 2017.
15 Astrup A, Bügel S. Overfed but Undernourished: recognizing nutritional inadequacies/deficiencies in patients with overweight or obesity. *Int J Obes (Lond)* 2019;43:219–32.
16 Zhao L, Zhang X, Shen Y, *et al*. Obesity and iron deficiency: a quantitative meta-analysis. *Obes Rev* 2015;16:1081–93.
17 Gu K, Xiang W, Zhang Y, *et al*. The association between serum zinc level and overweight/obesity: a meta-analysis. *Eur J Nutr* 2019;58:2971–82.
18 Saeed A, Dullaart RPF, Schreuder TCMA, *et al*. Disturbed vitamin A metabolism in non-alcoholic fatty liver disease (NAFLD). *Nutrients* 2017;10:29.
19 Lowe NM. The global challenge of hidden hunger: perspectives from the field. *Proc Nutr Soc* 2021;80:283–9.
20 Poti JM, Braga B, Qin B. Ultra-processed food intake and obesity: what really matters for health-processing or nutrient content *Curr Obes Rep* 2017;6:420–31.
21 Moore JB. COVID-19, childhood obesity, and NAFLD: Colliding Pandemics. *The Lancet Gastroenterology & Hepatology* 2022;7:499–501.
22 Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the double burden of malnutrition and the changing nutrition reality. *The Lancet* 2020;395:65–74.
23 Di Cesare M, Sorić M, Bovet P, *et al*. The Epidemiological burden of obesity in childhood: a worldwide epidemic requiring urgent action. *BMC Med* 2019;17.
24 Castillo-Valenzuela O, Duarte L, Arredondo M, *et al*. Childhood obesity and plasma Micronutrient deficit of Chilean children between 4 and 14 years old. *Nutrients* 2023;15:1707.
25 Tan PY, Mohd Johari SN, Teng K-T, *et al*. High prevalence of malnutrition and vitamin A deficiency among schoolchildren of rural areas in Malaysia using a multi-school assessment approach. *Br J Nutr* 2023;129:454–67.
26 Goyena E, Maniego MaL, Ducay AJ, *et al*. Dietary zinc intake and the underlying factors of serum zinc deficiency among preschool children in the Philippines. *Philipp J Sci* 2021;150:799–812.
27 Ssentongo P, Ba DM, Ssentongo AE, *et al*. Association of vitamin A deficiency with early childhood Stunting in Uganda: A population-based cross-sectional study. *PLoS One* 2020;15:e0233615.
28 Cobayashi F, Augusto RA, Lourenço BH, *et al*. Factors associated with Stunting and overweight in Amazonian children: a population-based, cross-sectional study. *Public Health Nutr* 2014;17:551–60.
29 Prentice AM. The triple burden of malnutrition in the era of globalization. *Nestle Nutr Inst Workshop Ser* 2023;97:51–61.
30 Malden S, Gillespie J, Hughes A, *et al*. Obesity in young children and its relationship with diagnosis of asthma, vitamin D deficiency, iron deficiency, specific allergies and flat-Footedness: A systematic review and meta-analysis. *Obes Rev* 2021;22:e13129.
31 Fiamenghi VI, Mello ED de. Vitamin D deficiency in children and adolescents with obesity: a meta-analysis. *Jornal de Pediatria* 2021;97:273–9.
32 Moher D, Liberati A, Tetzlaff J, *et al*. Reprint--preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther* 2009;89:873–80.
33 Sawyer SM, Azzopardi PS, Wickremarathne D, *et al*. The age of adolescence. *Lancet Child Adolesc Health* 2018;2:223–8.
34 Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan—a web and mobile App for systematic reviews. *Syst Rev* 2016;5:210.
35 Academy of Nutrition and Dietetics. *Evidence Analysis Manual: Academy of Nutrition and Dietetics*. 2016.
36 Jackson D, Turner R. Power analysis for random-effects meta-analysis. *Res Synth Methods* 2017;8:290–302.
37 Wickham H. Ggplot2. In: *ggplot2: Elegant Graphics for Data Analysis*. Cham: Springer-Verlag New York, 2016.
38 Brunson JC. Ggalluvial: layered grammar for alluvial plots. *J Open Source Softw* 2020;5:49.
39 South A. Rworldmap: a new R package for mapping global data. *The R Journal* 2011;3:35.
40 R: A language and environment for statistical computing program. Vienna, Austria R Foundation for Statistical Computing; 2023.
41 Park JS, Chang JY, Hong J, *et al*. Nutritional zinc status in Weaning infants: association with iron deficiency, age, and growth profile. *Biol Trace Elem Res* 2012;150:91–102.
42 Lu J, Zhang H, Cao W, *et al*. Study on the zinc nutritional status and risk factors of Chinese 6-18-year-old children. *Nutrients* 2023;15:1685.
43 Kernan KF, Carcillo JA. Hyperferritinemia and inflammation. *Int Immunol* 2017;29:401–9.
44 World Health Organization. *WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations*. Geneva, 2020.
45 Nead KG, Halterman JS, Kaczorowski JM, *et al*. Overweight children and adolescents: a risk group for iron deficiency. *Pediatrics* 2004;114:104–8.
46 Ortíz Pérez M, Vázquez López MA, Ibáñez Alcalde M, *et al*. Relationship between obesity and iron deficiency in healthy adolescents. *Child Obes* 2020;16:440–7.
47 Pompano LM, Correa-Burrows P, Burrows R, *et al*. Adjusting Ferritin concentrations for Nonclinical inflammation in adolescents with overweight or obesity. *J Pediatr* 2022;244:125–32.
48 Suteerojntrakool O, Khongcharoensombat T, Chomtho S, *et al*. Anthropometric markers and iron status of 6-12-year-old Thai children: associations and predictors. *J Nutr Metab* 2021;2021:9629718.
49 Ferrari M, Cuenca-García M, Valtueña J, *et al*. Inflammation profile in overweight/obese adolescents in Europe: an analysis in relation to iron status. *Eur J Clin Nutr* 2015;69:247–55.
50 Kurniawan YAI, Muslimatun S, Achadi EL, *et al*. Anaemia and iron deficiency anaemia among young adolescent girls from the peri urban Coastal area of Indonesia. *Asia Pac J Clin Nutr* 2006;15:350–6.
51 Sethy PGS, Bulliyya G, Rautray TR, *et al*. Nutritional status of preschool children in association with some trace elements in rural gram Panchayatas of Bhubaneswar, Odisha, India. *Adv Sci Lett* 2014;20:868–73.
52 Ghosh A, Chowdhury SD, Ghosh T. Undernutrition in Nepalese children: a biochemical and haematological study. *Acta Paediatr* 2012;101:671–6.
53 Brotanek JM, Gosz J, Weitzman M, *et al*. Iron deficiency in early childhood in the United States: risk factors and racial/ethnic disparities. *Pediatrics* 2007;120:568–75.
54 Tussing-Humphreys LM, Liang H, Nemeth E, *et al*. Excess Adiposity, inflammation, and iron-deficiency in female adolescents. *J Am Diet Assoc* 2009;109:297–302.
55 Cepeda-Lopez AC, Osendarp SJ, Melse-Boonstra A, *et al*. Sharply higher rates of iron deficiency in obese Mexican women and children are predicted by obesity-related inflammation rather than by differences in dietary iron intake. *Am J Clin Nutr* 2011;93:975–83.
56 Cabañas Pujadas G, Ortiz-Marrón H, Ortiz-Pinto MA, *et al*. Changes in obesity and iron deficiency between 4 and 9 years of age. longitudinal study of childhood obesity (ELOIN). *Int J Obes (Lond)* 2022;46:1992–9.
57 Manios Y, Moschonis G, Chrousos GP, *et al*. The double burden of obesity and iron deficiency on children and adolescents in Greece: the healthy growth study. *J Hum Nutr Diet* 2013;26:470–8.
58 Moschonis G, Chrousos GP, Lionis C, *et al*. Association of total body and visceral fat mass with iron deficiency in Preadolescents: the healthy growth study. *Br J Nutr* 2012;108:710–9.
59 Higgins JT, Chandler J, Cumpston M, *et al*. Cochrane Handbook for systematic reviews of interventions version 6.4. *Cochrane* 2023.
60 Eftekhari M, Mozaffari-Khosravi H, Shidfar F. The relationship between BMI and iron status in iron-deficient adolescent Iranian girls. *Public Health Nutr* 2009;12:2377–81.
61 Yalçın SS, Fırat MÇ, Tosun E, *et al*. A possible Etiological factor in obesity: element status in blood and tooth of overweight versus normal-weight children. *Int J Environ Health Res* 2018;2018:1–13.
62 Freake HC, Sankavaram K. Zinc: physiology, dietary sources, and requirements. In: Caballero B, ed. *Encyclopedia of Human Nutrition*. Fourth Edition. Oxford: Academic Press, 2013: 584–92.

63 Naupal-Forcadilla RT, Barba CV, Talavera MTM, *et al*. Determinants of zinc status of 2-3-year-old children in Laguna, Philippines. *Malays J Nutr* 2017;23.
64 International Zinc Nutrition Consultative Group. Assessing population zinc status with serum zinc concentration. 2012. Available: https://static1.squarespace.com/static/56424f6ce4b0552eb7fdc4e8/t/5774378f414fb5410541b748/1467234199261/IZiNCG_TechBrief2_2012-3.pdf
65 Lowe NM, Fekete K, Decsi T. Methods of assessment of zinc status in humans: a systematic review. *Am J Clin Nutr* 2009;89:2040S–2051S.
66 Thillan K, Lanerolle P, Thoradeniya T, *et al*. Micronutrient status and associated factors of Adiposity in primary school children with normal and high body fat in Colombo municipal area, Sri Lanka. *BMC Pediatr* 2021;21:14.
67 Zhu Q, Dai Y, Zhang J, *et al*. Association between serum zinc concentrations and metabolic risk factors among Chinese children and adolescents. *Br J Nutr* 2021;126:1529–36.
68 Fan Y, Zhang C, Bu J. Relationship between selected serum metallic elements and obesity in children and adolescent in the U.S. *Nutrients* 2017;9:104.
69 Perrone L, Gialanella G, Moro R, *et al*. Zinc, copper, and iron in obese children and adolescents. *Nutrition Research* 1998;18:183–9.
70 Dehghani SM, Katibeh P, Haghighat M, *et al*. Prevalence of zinc deficiency in 3-18 years old children in Shiraz-Iran. *Iran Red Crescent Med J* 2011;13:4–8.
71 Habib A, Molayemat M, Habib A, *et al*. Vitamin D and zinc are interlinked but affected by different growth factors in Iranian children and adolescents: vitamin D and zinc in Iranian children and adolescents. *Iran J Pediatr* 2022;32.
72 Sharif Y, Sadeghi O, Dorosty A, *et al*. Serum levels of vitamin D, Retinol and zinc in relation to overweight among toddlers: findings from a national study in Iran. *Arch Iran Med* 2019;22:174–81.
73 Li W, Herrán OF, Villamor E. Trends in iron, zinc, and vitamin A status biomarkers among Colombian children: results from 2 nationally representative surveys. *Food Nutr Bull* 2017;38:146–57.
74 Ho M, Baur LA, Cowell CT, *et al*. Zinc status, dietary zinc intake and metabolic risk in Australian children and adolescents; Nepean longitudinal study. *Eur J Nutr* 2017;56:2407–14.
75 Zou Y, Zhang R, Huang L, *et al*. Serum levels of vitamin D, Retinol, zinc, and CRP in relation to obesity among children and adolescents. *Eur J Med Res* 2022;27:51.
76 Lin C-N, Wilson A, Church BB, *et al*. Pediatric reference intervals for serum copper and zinc. *Clin Chim Acta* 2012;413:612–5.
77 EFSA Panel on Dietetic Products, Nutrition and Allergies. Scientific opinion on dietary reference values for zinc. *EFSA Journal* 2014;12:10.
78 Centers for Disease Control and Prevention, World Health Organization, Nutrition International, *et al*. *Micronutrient survey manual*. Geneva: World Health Organization, 2020.
79 Gunanti IR, Marks GC, Al-Mamun A, *et al*. Low serum concentrations of carotenoids and vitamin E are associated with high Adiposity in Mexican-American children. *J Nutr* 2014;144:489–95.
80 Hu W, Tong S, Oldenburg B, *et al*. Serum vitamin A concentrations and growth in children and adolescents in Gansu province, China. *Asia Pac J Clin Nutr* 2001;10:63–6.
81 Ortega-Senovilla H, de Oya M, Garcés C. Relationship of NEFA concentrations to Rbp4 and to Rbp4/Retinol in Prepubertal children with and without obesity. *J Clin Lipidol* 2019;13:301–7.
82 Tian T, Wang Y, Xie W, *et al*. Associations between serum vitamin A and metabolic risk factors among Eastern Chinese children and adolescents. *Nutrients* 2022;14:610.
83 Yang C, Chen J, Liu Z, *et al*. Association of vitamin A status with Overnutrition in children and adolescents. *Int J Environ Res Public Health* 2015;12:15531–9.
84 Disalvo L, Varea A, Matamoros N. Vitamin A deficiency and associated factors in Preschoolers from the outskirts of La Plata, Buenos Aires. *Arch Argent Pediat* 2019;117:19–25.
85 Maslova E, Mora-Plazas M, Forero Y, *et al*. Are vitamin A and iron deficiencies re-emerging in urban Latin America? A survey of schoolchildren in Bogota, Colombia. *Food Nutr Bull* 2009;30:103–11.
86 Abd-El Wahed MA, Mohamed MH, Ibrahim SS, *et al*. Iron profile and dietary pattern of primary school obese Egyptian children. *J Egypt Public Health Assoc* 2014;89:53–9.
87 de Souza Valente da Silva L, Valeria da Veiga G, Ramalho RA. Association of serum concentrations of Retinol and carotenoids with overweight in children and adolescents. *Nutrition* 2007;23:392–7.
88 Paes-Silva RP, Gadelha PCFP, Lemos M da CC de, *et al*. Adiposity, inflammation and fat-soluble vitamins in adolescents. *Jornal de Pediatria* 2019;95:575–83.
89 Dallazen C, Tietzmann DC, da Silva SA, *et al*. Vitamin A deficiency and associated risk factors in children aged 12-59 months living in poorest municipalities in the South region of Brazil. *Public Health Nutr* 2023;26:132–42.
90 Wei X, Peng R, Cao J, *et al*. Serum vitamin A status is associated with obesity and the metabolic syndrome among school-age children in Chongqing, China. *Asia Pac J Clin Nutr* 2016;25:563–70.
91 Hutchinson C. A review of iron studies in overweight and obese children and adolescents: a double burden in the young *Eur J Nutr* 2016;55:2179–97.
92 González-Domínguez Á, Visiedo-García FM, Domínguez-Riscart J, *et al*. Iron metabolism in obesity and metabolic syndrome. *Int J Mol Sci* 2020;21:15.
93 Haschka D, Hoffmann A, Weiss G. Iron in immune cell function and host defense. *Semin Cell Dev Biol* 2021;115:27–36.
94 Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. *Blood* 2019;133:40–50.
95 Berton PF, Gambero A. Hepcidin and inflammation associated with iron deficiency in childhood obesity - A systematic review. *J Pediatr (Rio J)* 2024;100:124–31.
96 Coimbra S, Catarino C, Nascimento H, *et al*. Physical exercise intervention at school improved Hepcidin, inflammation, and iron metabolism in overweight and obese children and adolescents. *Pediatr Res* 2017;82:781–8.
97 Amato A, Santoro N, Calabrò P, *et al*. Effect of body mass index reduction on serum Hepcidin levels and iron status in obese children. *Int J Obes (Lond)* 2010;34:1772–4.
98 Zimmermann MB, Zeder C, Muthayya S, *et al*. Adiposity in women and children from transition countries predicts decreased iron absorption, iron deficiency and a reduced response to iron Fortification. *Int J Obes (Lond)* 2008;32:1098–104.
99 Perng W, Mora-Plazas M, Marin C, *et al*. Iron status and linear growth: a prospective study in school-age children. *Eur J Clin Nutr* 2013;67:646–51.
100 Zhu Y, He B, Xiao Y, *et al*. Iron metabolism and its association with Dyslipidemia risk in children and adolescents: a cross-sectional study. *Lipids Health Dis* 2019;18:50.
101 Cheng HL, Bryant CE, Rooney KB, *et al*. Iron, Hepcidin and inflammatory status of young healthy overweight and obese women in Australia. *PLoS One* 2013;8:e68675.
102 Onabanjo OO, Balogun OL. Anthropometric and iron status of adolescents from selected secondary schools in Ogun state. *ICAN: Infant, Child, & Adolescent Nutrition* 2014;6:109–18.
103 Kassem E, Na'amnih W, Shapira M, *et al*. Comparison between school-age children with and without obesity in nutritional and inflammation biomarkers. *J Clin Med* 2022;11:23.
104 Shattnawi KK, Alomari MA, Al-Sheyab N, *et al*. The relationship between plasma Ferritin levels and body mass index among adolescents. *Sci Rep* 2018;8:15307.
105 Sypes EE, Parkin PC, Birken CS, *et al*. Higher body mass index is associated with iron deficiency in children 1 to 3 years of age. *J Pediatr* 2019;207:198–204.
106 Pasricha S-R, Tye-Din J, Muckenthaler MU, *et al*. Iron deficiency. *The Lancet* 2021;397:233–48.
107 El Khoury R, Sleilaty G, Gannagé-Yared M-H. Prevalence of iron deficiency in Lebanese schoolchildren. *Eur J Clin Nutr* 2020;74:1157–63.
108 Tessema M, De Groote H, D. Brouwer I, *et al*. Soil zinc is associated with serum zinc but not with linear growth of children in Ethiopia. *Nutrients* 2019;11:221.
109 Araújo LKAR de, Faria JCP, Sarni ROS. Iron deficiency anemia in infants in Sousa (PB), Brazil: an association with nutritional status. *Rev Assoc Med Bras* 2022;68:1698–704.
110 Mei Z, Addo OY, Jefferds ME, *et al*. Physiologically based serum Ferritin thresholds for iron deficiency in children and non-pregnant women: a US national health and nutrition examination surveys (NHANES) serial cross-sectional study. *The Lancet Haematology* 2021;8:e572–82.
111 EFSA Panel on Dietetic Products, Nutrition and Allergies. Scientific opinion on dietary reference values for vitamin A. *EFSA Journal* 2015;13:4028.
112 Thurnham DI, McCabe LD, Haldar S, *et al*. Adjusting plasma Ferritin concentrations to remove the effects of Subclinical inflammation in the assessment of iron deficiency: a meta-analysis. *Am J Clin Nutr* 2010;92:546–55.
113 Larson LM, Guo J, Williams AM, *et al*. Approaches to assess vitamin A status in settings of inflammation: biomarkers reflecting

inflammation and nutritional determinants of anemia (BRINDA) project. *Nutrients* 2018;10:1100.
114 McDonald CM, Suchdev PS, Krebs NF, *et al*. Adjusting plasma or serum zinc concentrations for inflammation: biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. *Am J Clin Nutr* 2020;111:927–37.
115 Namaste SM, Aaron GJ, Varadhan R, *et al*. Methodologic approach for the biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. *Am J Clin Nutr* 2017;106:Suppl.
116 Namaste SM, Rohner F, Huang J, *et al*. Adjusting Ferritin concentrations for inflammation: biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. *Am J Clin Nutr* 2017;106(Suppl 1):359S–371S.
117 UNICEF, WHO. *World Bank Group Joint Child Malnutrition Estimates. Levels and Trends in Child Malnutrition*. 2018.
118 Borkhoff SA, Parkin PC, Birken CS, *et al*. Examining the double burden of Underweight, overweight/obesity and iron deficiency among young children in a Canadian primary care setting. *Nutrients* 2023;15:3635.
119 Aslam S, Emmanuel P. Formulating a researchable question: A critical step for facilitating good clinical research. *Indian J Sex Transm Dis AIDS* 2010;31:47–50.

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SUPPLEMENTARY MATERIAL

Overnutrition is a risk factor for iron, but not zinc or vitamin A deficiency in children and young people: a systematic review and meta-analysis

Authors

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1 **Table S1 Search strategy for Medline.**

# ▲	Searches	Results
1	Anaemia, Iron-Deficiency/bl, di, ep, et, me [Blood, Diagnosis, Epidemiology, Etiology, Metabolism]	7101
2	Iron/bl, df [Blood, Deficiency]	17580
3	((iron or ferritin or hemoglobin) and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	16221
4	1 or 2 or 3	33690
5	Zinc/bl, df [Blood, Deficiency]	11105
6	(zinc and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	4505
7	5 or 6	13387
8	Vitamin A Deficiency/bl, di, ep, et, pc [Blood, Diagnosis, Epidemiology, Etiology, Prevention & Control]	2240
9	Vitamin A/bl [Blood]	5182
10	((retinol or "vitamin A") and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	2923
11	8 or 9 or 10	8055
12	4 or 7 or 11	51425
13	Obesity/bl, di, ep, et, me, pc [Blood, Diagnosis, Epidemiology, Etiology, Metabolism, Prevention & Control]	98565
14	Obesity, Abdominal/bl, di, ep, me, pc [Blood, Diagnosis, Epidemiology, Metabolism, Prevention & Control]	2530
15	Pediatric Obesity/bl, di, ep, et, me, pc [Blood, Diagnosis, Epidemiology, Etiology, Metabolism, Prevention & Control]	6908
16	Overweight/bl, di, ep, et, me, pc [Blood, Diagnosis, Epidemiology, Etiology, Metabolism, Prevention & Control]	13827
17	Malnutrition/bl, di, ep, et, me, pc [Blood, Diagnosis, Epidemiology, Etiology, Metabolism, Prevention & Control]	9368
18	Protein-Energy Malnutrition/bl, di, ep, et, me, pc [Blood, Diagnosis, Epidemiology, Etiology, Metabolism, Prevention & Control]	4276
19	Thinness/bl, di, ep, et, pc [Blood, Diagnosis, Epidemiology, Etiology, Prevention & Control]	2585
20	Body Mass Index/	130582
21	Anthropometry/	39336
22	(malnutrition or malnourish* or overnutrition or undernutrition or obese or obesity or overweight or adiposity or stunting or stunted or underweight or (wasting adj2 disease) or wasted or "body mass index" or BMI or anthropometr*).ti,ab,kw.	586872
23	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	644487
24	12 and 23	4893
25	limit 24 to english	4565
26	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or	5094920

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	paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.	
27	25 and 26	2549
28	limit 27 to (address or case reports or comment or editorial or letter or meta analysis or news or "review" or "systematic review")	302
29	27 not 28	2247

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4 **Table S2 Search strategy for Embase.**

# ▲	Searches	Results
1	iron/ec [Endogenous Compound]	20090
2	iron deficiency/co, di, dm, ep, et, pc [Complication, Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	2292
3	iron deficiency anaemia/co, di, dm, ep, et, pc [Complication, Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	6259
4	((iron or ferritin or hemoglobin) and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	24033
5	or/1-4	46391
6	zinc/ec [Endogenous Compound]	8578
7	zinc deficiency/co, di, ep, et, pc [Complication, Diagnosis, Epidemiology, Etiology, Prevention]	825
8	(zinc and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	5061
9	or/6-8	12886
10	retinol/ec [Endogenous Compound]	4437
11	retinol deficiency/co, di, ep, et, pc [Complication, Diagnosis, Epidemiology, Etiology, Prevention]	1424
12	((retinol or "vitamin A") and (serum or blood or plasma) and (inadequa* or insufficien* or deficien*)).ti,ab,kw.	2905
13	or/10-12	7461
14	5 or 9 or 13	60740
15	overnutrition/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	234
16	obesity/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	47924
17	abdominal obesity/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	1226
18	childhood obesity/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	3482
19	malnutrition/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	7850
20	protein calorie malnutrition/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	1032
21	underweight/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	789
22	stunting/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	355
23	chronic wasting disease/di, dm, ep, et, pc [Diagnosis, Disease Management, Epidemiology, Etiology, Prevention]	234
24	body mass index/	404144
25	anthropometry/	47377
26	(malnutrition or malnourish* or overnutrition or undernutrition or obese or obesity or overweight or adiposity or stunting or stunted or underweight or (wasting adj2 disease) or wasted or "body mass index" or BMI or anthropometr*).ti,ab,kw.	859208
27	or/15-26	961836
28	14 and 27	7182
29	limit 28 to english	6810

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30	exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neo-nat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in. or (teen* or toddler? or underage? or under-age? or youth*).ti,ab,kw.	4255302
31	29 and 30	2812
32	limit 31 to conference abstracts	541
33	limit 31 to (book or book series)	10
34	limit 31 to (books or chapter or conference abstract or letter or note or "review" or short survey)	774
35	limit 31 to (meta analysis or "systematic review")	38
36	32 or 33 or 34 or 35	794
37	31 not 36	2018

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7 **Table S3 Search strategy for Scopus.**

#	Searching words	Results
#1	TITLE-ABS-KEY ((iron OR ferritin OR hemoglobin OR zinc OR "vitamin A" OR retinol) AND (serum OR blood OR plasma) AND (inadequa* OR insufficien* OR deficien*))	60369
#2	TITLE-ABS-KEY (malnutrition OR malnourish* OR overnutrition OR undernutrition OR obese OR obesity OR overweight OR adiposity OR stunting OR stunted OR underweight OR (wasting W/2 disease) OR wasted OR "body mass index" OR bmi OR anthropometr*)	887265
#3	(TITLE-ABS-KEY ((iron OR ferritin OR hemoglobin OR zinc OR "vitamin W/0 A" OR retinol) AND (serum OR blood OR plasma) AND (inadequa* OR insufficien* OR deficien*))) AND (TITLE-ABS (malnutrition OR malnourish* OR overnutrition OR undernutrition OR obese OR obesity OR overweight OR adiposity OR stunting OR stunted OR underweight OR (wasting W/2 disease) OR wasted OR "body mass index" OR bmi OR anthropometr*))	7,726
#4	(TITLE-ABS-KEY ((iron OR ferritin OR hemoglobin OR zinc OR "vitamin W/0 A" OR retinol) AND (serum OR blood OR plasma) AND (inadequa* OR insufficien* OR deficien*))) AND (TITLE-ABS-KEY (malnutrition OR malnourish* OR overnutrition OR undernutrition OR obese OR obesity OR overweight OR adiposity OR stunting OR stunted OR underweight OR (wasting W/2 disease) OR wasted OR "body mass index" OR bmi OR anthropometr*)) AND (LIMIT-TO (LANGUAGE , "English"))	7,173
#5	(TITLE-ABS-KEY ((iron OR ferritin OR hemoglobin OR zinc OR "vitamin W/0 A" OR retinol) AND (serum OR blood OR plasma) AND (inadequa* OR insufficien* OR deficien*))) AND (TITLE-ABS-KEY (malnutrition OR malnourish* OR overnutrition OR undernutrition OR obese OR obesity OR overweight OR adiposity OR stunting OR stunted OR underweight OR (wasting W/2 disease) OR wasted OR "body mass index" OR bmi OR anthropometr*)) AND ((TITLE-ABS-KEY (adolescen* OR babies OR baby OR boy? OR boyfriend OR boyhood OR girlfriend OR girlhood OR child* OR girl? OR infan* OR juvenil* OR kid? OR minors OR minors* OR neonat* OR neo-nat* OR newborn* OR new-born* OR paediatric* OR peadiatric* OR pediatric* OR perinat* OR preschool* OR puber* OR pubescen* OR school* OR teen* OR toddler? OR underage? OR under-age? OR youth*))) AND (LIMIT-TO (LANGUAGE , "English"))	3,036
#6	(TITLE-ABS-KEY ((iron OR ferritin OR hemoglobin OR zinc OR "vitamin W/0 A" OR retinol) AND (serum OR blood OR plasma) AND (inadequa* OR insufficien* OR deficien*))) AND (TIT	2,683

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	LE-ABS-KEY (malnutrition OR malnourish* OR overnutrition OR undernutrition OR obese OR obesity OR overweight OR adiposity OR stunting OR stunted OR underweight OR (wasting W/2 disease) OR wasted OR "body mass index" OR bmi OR anthropometr*)) AND ((TITLE-ABS-KEY (adolescen* OR babies OR baby OR boy? OR boyfriend OR boyhood OR girlfriend OR girlhood OR child* OR girl? OR infan* OR juvenil* OR kid? OR minors OR minors* OR neonat* OR neo-nat* OR newborn* OR new-born* OR paediatric* OR peadiatric* OR pediatric* OR perinat* OR preschool* OR puber* OR pubescen* OR school* OR teen* OR toddler? OR underage? OR under-age? OR youth*))) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (DOCTYPE , "ar"))	

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Table S4 Search strategy for Cochrane.

#1	MeSH descriptor: [Iron, Dietary] explode all trees and with qualifier(s): [blood - BL]	54
#2	MeSH descriptor: [Iron] explode all trees and with qualifier(s): [blood - BL, deficiency - DF]	933
#3	(((iron or ferritin or hemoglobin) and (serum or blood or plasma)) and (inadequa* or insufficien* or deficien*)):ti,ab,kw	5477
#4	MeSH descriptor: [Anaemia, Iron-Deficiency] explode all trees	1330
#5	#1 or #2 or #3 or #4	6310
#6	MeSH descriptor: [Zinc] explode all trees and with qualifier(s): [blood - BL, deficiency - DF]	648
#7	(((zinc) and (serum or blood or plasma)) and (inadequa* or insufficien* or deficien*)):ti,ab,kw	870
#8	#6 or #7	1243
#9	MeSH descriptor: [Vitamin A] tree(s) exploded and with qualifier(s): [blood - BL]	497
#10	(((retinol or "vitamin A") and (serum or blood or plasma)) and (inadequa* or insufficien* or deficien*)):ti,ab,kw	706
#11	#9 or #10	977
#12	#5 or #8 or #11	7724
#13	MeSH descriptor: [Obesity] explode all trees	14007
#14	MeSH descriptor: [Thinness] explode all trees and with qualifier(s): [blood - BL, diagnosis - DI, etiology - ET, metabolism - ME, epidemiology - EP, prevention & control - PC]	111
#15	MeSH descriptor: [Malnutrition] explode all trees and with qualifier(s): [blood - BL, diagnosis - DI, etiology - ET, metabolism - ME, epidemiology - EP, prevention & control - PC]	1969
#16	MeSH descriptor: [Overweight] explode all trees and with qualifier(s): [blood - BL, diagnosis - DI, etiology - ET, metabolism - ME, epidemiology - EP, prevention & control - PC]	6395
#17	MeSH descriptor: [Protein-Energy Malnutrition] explode all trees	250
#18	MeSH descriptor: [Body Mass Index] explode all trees	10188
#19	MeSH descriptor: [Anthropometry] explode all trees	23419
#20	(malnutrition or malnourish* or overnutrition or undernutrition or obese or obesity or overweight or adiposity or stunting or stunted or underweight or (wasting NEAR/2 disease) or wasted or "body mass index" or BMI or anthropometr*):ti,ab,kw	99958
#21	#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20	109600
#22	#12 and #21	1831
#23	MeSH descriptor: [Adolescent] explode all trees	104274
#24	MeSH descriptor: [Child] explode all trees	56347
#25	MeSH descriptor: [Infant] explode all trees	32245
#26	(infant disease* or childhood disease*):ti,ab,kw or (adolescen* or babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born*	308863

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	or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*):ti,ab,kw	
#27	#23 or #24 or #25 or #26	308863
#28	#22 and #27 in trials	882

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Table S5 Characteristics of studies (n=46) assessing the association between iron and under- and overnutrition.

First Author, Year, Country	Study Design, Participant (n), Age	Malnutrition and Biochemical Indicators[1]	Findings[2]	Association	Quality Rating
Both (n=10)					
Cobayashi, 2013, Brazil[1]	Cross-sectional, 1139, 0-10 y	OW: BAZ>1; stunting ID: SF<12µg/L (<5 y), <15µg/L (≥5 y), or sTfR>8.3mg/L	**Overnutrition**: BAZ↑ ID↑ OW/ID: PR= 1.64 (1.07, 2.53) for <5 y **Undernutrition:** NS	Inverse NS	Positive
El Khoury, 2020, Lebanon[2]	Cross-sectional, 903, 8-18 y	BMI category ID: SF<15ng/mL; CRP>10mg/L excluded	**Both over- and undernutrition:** NS	NS	Neutral
Eftekhari, 2009, Iran[3]	Cross-sectional, 431, 13-20 y	BMI category ID: SF<12µg/L, TS<16%	**Both over- and undernutrition:** BMI↑ SF↓ β= -0.21 for girls with ID	Inverse	Neutral
Li, 2017, Colombia[4]	Cross-sectional, 14559, 1-17 y	HAZ, BAZ PF	**Both over- and undernutrition:** NS	NS	Positive
Maslova, 2009, Colombia[5]	Cross-sectional, 2811, 5-12 y	BAZ ID: PF<15 or 30µg/L if CRP>10mg/L	**Both over- and undernutrition:** PF↓ BAZ↓ ID/BAZ: β= -0.22 (-0.42, -0.03)	Direct	Positive
Onabanjo, 2014, Nigeria[6]	Cross-sectional, 127, 10-19 y	Underweight: BAZ<5^{th} centile OW, OB: BAZ>85^{th} & 95^{th} centiles SF	**Overnutrition**: BMI↑ SF↑ OW, OB: r= 0.505, 0.556 (male); OW, OB: r= 0.782, 0.838 (female) **Undernutrition**: NS	Direct NS	Neutral

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Perng, 2013, Colombia[7]	Cohort study, 2714, 5-12y	BAZ, HAZ PF	**Overnutrition:** BAZ↑ PF↑ **Undernutrition:** NS	Direct NS	Positive
Tan, 2023, Malaysia[8]	Cross-sectional, 776, 7-11y	BAZ, WAZ, HAZ, stunting ID: SF<15µg/L; Anaemia: Hb<115g/L; IDA: ID + Anaemia	**Overnutrition**: BAZ↑ SF↑; WAZ↑ SF↑ **Undernutrition:** SF↓ HAZ↓ ID/stunting COR= 2.4 (1.6, 3.7) SF, Hb↓ HAZ↓ IDA/stunting AOR= 2.3 (1.2, 4.3)	Direct	Positive
Zhu, 2019, China[9]	Cross-sectional, 1866, 7-18 y	BMI category (Working Group on Obesity in China) SF, SI ID: SI<45µg/dL	**Overnutrition**: BMI↑ Prevalence of ID ↑ SI↓ BMI↑ SF↑ **Undernutrition:** NS	Inverse NS	Neutral
Zimmermann, 2008, Morocco, India[10]	Cross-sectional, 1688, 9.3±2.5y	BAZ SF, TfR BIS (SF/TfR)	**Both over- and undernutrition:** BAZ↑ BIS↓ y= -0.6256x+3.194; β= -0.658 (-0.466, -0.850) BAZ↑ SF↑ β= 1.873 (1.587, 2.519) BAZ↑ sTfR↑ β= 1.873 (1.587, 2.159)	Inverse	Neutral
Overnutrition (n=21)					
Abd-El-Wahed, 2014, Egypt[11]	Case-control, 120 (60+60), 6-12 y	NW, OB: BMI<85th & >95th centiles ID: ≥2 abnormal parameters: MCV<76fL, TS<15%, SF<10µg/mL	BMI↑ ID↑ ID/OB: COR= 7.09 (3.16, 15.92)	Inverse	Neutral
Brotanek, 2007, US[12]	Cross-sectional, 1641, 1-3 y	OW, OB: WHZ>85th & 95th centiles ID: ≥2 abnormal parameters: TS<10%, SF<10µg/L, red blood cells EP>1.42µmol/L (1-2 y); <12%, 10µmol/L, and>1.24µmol/L (3y)	WHZ↑ ID↑ ID/OW: AOR= 3.34 (1.10, 10.12)	Inverse	Positive
Cabañas Pujadas, 2022, Spain[13]	Cohort study, 1347, 9 y	OB: BAZ>2 SF, Serum transferrin, CRP ID: TS<16%	BAZ↑ TS↓ β= −2.4 (−4.6, −0.1) BAZ↑ SF↑ β= 13.9 (7.2, 20.5) BAZ↑ serum transferrin↑ β= 12.0 (3.9, 20.1)	Inverse	Positive

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Cepeda-Lopez, 2011, Mexico[14]	Cross-sectional, 1174, 5-12 y	OB, OW: BMIz>1 & 2 SD TIBC, CRP ID: low SI or TIBC >36 μg/L; TS<20%.	BMIz↑ ID↑ ID/OB: AOR= 3.96 (1.34, 11.67) BMIz↑ TIBC↑ r= 0.04	Inverse	Positive
Cheng, 2013, Australia[15]	Cross-sectional, 114, 18-25 y	BMI≥27.5 SI, TS, SF	**in OW/OB women** BMI↑ SI↓ β= -0.379 (0.139) BMI↑ TS↓ β= -0.588 (0.222) BMI↑ SF↑	Inverse	Positive
de Araújo, 2022, Brazil[16]	Cross-sectional, 104, 7-9 m	WHZ ID: Hb>11g/dL, ferritin<12μg/L if CRP≤5mg/L, or 30μg/L if CRP>5mg/L	WHZ↑ ID↑ WHZ/ID: AOR= 2.86 (1.38, 5.6); BAZ, WHZ, WAZ↑, ferritin↓	Inverse	Neutral
Ferrari, 2015, Europe[317]	Cross-sectional, 876, 13.9-16 y	Thinness: BMI<18; OW, OB: BMI>25 & 30 SF, sTfR, CRP	BMI↑ SF↑ male: β= 0.055 (0.029, 0.082) BMI↑ sTfR↑ female: β= 0.017 (0.001, 0.033) BMI↑ CRP↑	Inverse	Positive
Grant, 2007, New Zealand[18]	Cross-sectional, 416, 6-23 m	BMI>16.5 & 18.5 ID: NHANES standard: ≥2 abnormal parameters: SF, TS and EP.	BMI↑ ID↑ BMI>18.5/ID: RR= 4.34 (1.08, 10.67) relative to BMI<16.5	Inverse	Positive
Higgins, 2020, Canada[19]	Cross-sectional, 1332, 5.1-<19.0 y	NW, OW, OB: BMI>3rd, 85th & 97th centiles SI, serum transferrin	BMIz↑ serum transferrin↑ β:BMIz/transferrin: 0.061 (0.037, 0.085) BMIz↑ SI↓ BMIz/iron: β= -0.768 (-1.31, -0.229) (male), -0.870 (-1.41- -0.329) (female)	Inverse	Positive
Kassem, 2022, Israel[20]	Cross-sectional, 146, 10-12 y	OW, OB: WHO standard SF, TS ID: SF<15μg/dL	BAZ↑ prevalence of ID↑ BAZ↑ TS↓, SF↑	Inverse	Positive
Manios, 2013, Greece[21]	Cross-sectional, 2492, 9-13 y	OW, OB (International Obesity Task Force) ID:TS<16% IDA: ID + Hb<120g/L	BMI↑ ID, IDA↑ OB/ID: AOR= 2.46 (1.52, 3.96) (male), AOR= 2.05 (1.19, 3.51) (female) OB/IDA: AOR= 3.13 (1.01, 7.91) (male), AOR= 3.28 (1.15, 9.33) (female)	Inverse	Positive

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Moschonis, 2012, Greece[22]	Cross-sectional, 1493, 9-13 y	OW, OB (International Obesity Task Force) ID:TS<16% IDA: ID + Hb<120g/L	BMI↑ ID↑ OW/ID: AOR= 2.13 (1.27, 3.60) (male) OB/ID: AOR= 2.25 (1.14, 4.46) (female)	Inverse	Neutral
Nead, 2004, US[23]	Cross-sectional, 9698, 2-16 y	OW, OB: BMI>85th & 95th centiles ID: ≥ 2 abnormal parameters: TS, EP and SF	BMI↑ ID ↑ ID/OW: AOR= 2.0 (1.2, 3.5) ID/OB: AOR= 2.3 (1.4, 3.9)	Inverse	Positive
Ortiz Perez, 2020, Spain[24]	Cross-sectional, 405, 12-16 y	OW, OB (International Obesity Task Force) SF, CRP, sTfR, SI elevated CRP were excluded.	BAZ↑ SF, CRP, sTfR↑ r= 0.14, r= 0.43, r= 0.17, respectively	Direct	Neutral
Pompano, 2022, Chile[25]	Cross-sectional, 518, 16-17 y	OW, OB: WHO standard SF	BAZ↑ SF↑ r= 0.12	Direct	Positive
Shattnawi, 2018, Jordan[26]	Cross-sectional, 873, 14.6±1.0 y	OW: BMIz: CDC standard PF, elevated CRP were excluded.	BMI↑ PF↑	Direct	Positive
Suteerojntrakool, 2021, Thailand[27]	Cross-sectional, 336, 6-12 y	OW, OB: WHO standard ID: ≥2 abnormal parameters: TS<16%, SF<15μg/mL, and sTfR>5mg/L IDA: ID + anaemia	BAZ↑ SF↑ r= 0.214; BAZ↑ sTfR↑ r= 0.207; BAZ↑ TS↓ r= -0.132; BAZ↑ TIBC↑ r= 0.209	Direct	Neutral
Sypes, 2018, Canada[28]	Cross-sectional, 1607 children, 1-3 y	BMIz ID: SF<12μg/L CRP>10mg/L was excluded	BMI↑ ID, SF↑ BMIz/ID: AOR= 1.28 (1.10, 1.50) BMIz/median SF: β= -0.062 (-0.093, -0.031)	Inverse	Positive
Thillan, 2021, Sri Lanka[29]	Case-control, 324, 8-9 y	OW, OB: WHO standard SF	BMI↑ SF↑ in boys	Direct	Positive

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Tussing-Humphreys, 2009, US[30]	Cross-sectional, 210, 12-17 y	Heavier weight: BMI≥85th centile ID: ≥2 abnormal parameters: MCV<82fL for 12-14y and<85fL for 15-17y, free EP >70μg/dL and TS<16%.	BMI↑ ID↑ BMI>85th/ID: AOR= 2.32 (1.14, 4.71) BMI↑ log SI↓ β= -0.004	Inverse	Positive
Yalcin, 2019, Turkey[31]	Case-control, 120, 6-10 y	OW, OB: BAZ>1 & 2 SD Whole blood iron	NS	NS	Positive
Undernutrition (n=15)					
Alaofe, 2017, Benin[32]	Cross-sectional, 647, 6-59 m	Stunting Anaemia: WHO standard ID: SF adjusted by medical status at birth IDA: anaemia + ID	HAZ↑ ID, IDA↑ Stunting/ID: AOR= 2.17 (1.17, 4.02) Stunting/IDA: AOR= 2.16 (1.05, 4.46)	Direct	Positive
Al-Hussaini, 2022, Saudi Arabia[33]	Case-control, 7931, 6-16 y	Thinness (wasting): BAZ<-2 SD SI, SF	NS	NS	Neutral
Andre, 2017, Brazil[34]	Cross-sectional, 457, 4-7 y	HAZ SF	NS	NS	Positive
Chitekwe, 2022, Nepal[35]	Cross-sectional, 1709, 6-59 m	Stunting ID: SF<12.0ug/L or StfR>8.3mg/L	HAZ↓ ID↑ Stunting/ID (Ferritin): AOR= 1.61 (1.18, 2.18); Stunting/ID (StfR): AOR= 1.69 (1.20, 2.38)	Direct	Positive
Ernawati, 2021, Indonesia[36]	Cross-sectional, 1008, 11-16 y	Stunting, severe stunting SF	NS	NS	Positive
Ghosh, 2012, Nepal[37]	Cross-sectional, 192, 6-10 y	Stunting: HAZ<-1 SD SF	HAZ↑ SF↑ β= 0.217	Direct	Negative

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Habib, 2016, Pakistan[38]	Cross-sectional, 7138, 6-59 m	Stunting, Underweight: WAZ<-2 SD IDA: Hb<110g/L, SF<12μg/L Hb adjusted for altitudes	HAZ↓ IDA↑ stunting/IDA: AOR= 1.42 (1.23, 1.63) WAZ↓ IDA↑ underweight/IDA COR= 1.28 (1.15, 1.43)	Direct	Positive
Indriastuti Kurniawan, 2006, Indonesia[39]	Cross-sectional, 133, 10-12 y	Thinness: BAZ<-2 SD Anaemia: Hb<120g/L IDA: Anaemia + SF<12μg/L, sTfR>8.5mg/L, ZnPP>40μmol/mol heme.	**Comparing with female patients with anaemia:** BAZ↓ IDA↑ thinness/IDA: AOR= 5.1 (1.34, 19.00)	Direct	Negative
Khatib, 2009, Jordan[40]	Cross-sectional, 560, 5.5-10 y	Stunting SF	HAZ↓ SF↓	Direct	Neutral
Kumari, 2022, India[41]	Case-control, 202, 1-5 y	WHZ, BAZ SI	WHZ↑ SI↑ BMI↑ SI↑ r= 0.301	Direct	Neutral
Matsungo, 2017, South Africa[42]	Cross-sectional, 750, 0-6 m	Stunting: LAZ<-2 SD Anaemia: Hb<110g/L ID: sTfR>8·3mg/L; IDA: ID + anaemia	LAZ↓ ID↑, IDA↑	Direct	Positive
Orsango, 2021, Ethiopia[43]	Cross-sectional, 331, 2-5 y	HAZ, WHZ IDA: Hb <110g/L, adjusted SF<12μg/L	HAZ ↑ IDA↓ HAZ/IDA: AOR= 0.74 (0.56, 0.98)	Direct	Positive
Park, 2012, South Korea[44]	Cross-sectional, 101, 11.1±2.0 m	HAZ, WAZ, WHZ ID: SF<12ng/mL and/or TS<15%	NS	NS	Positive
Sethy, 2014, India[45]	Cross-sectional, 144, 2-5 y	Underweight: WAZ<-2SD Stunting SI	WHZ↓ SI↓ (mean level, but r= -0.175) HAZ↓ SI↓	Direct	Negative

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Shukla, 2023, India[46]	Case-control, 442, 6-60 m	SAM: MUAC<11.5cm SF	MUAC↓ SF↓	Direct	Neutral

[1]Stunting refers to HAZ<-2 SD unless noted

[2]OR shown as OR (95%CI) unless noted; β coefficient shown as β (95%CI) unless noted

Abbreviations:

AOR: adjusted odds ratio; BAZ: BMI-age z score; BIS: body iron store; BMI: body mass index; COR: crude odds ratio; CRP: C-reaction protein; HAZ: height-for-age z score; Hb: haemoglobin; fL: femtoliter; ID: iron deficiency; IDA: iron deficiency anaemia; EP: erythrocyte protoporphyrin, NW: normal weight; NS: not significant; MCV: mean corpuscular volume; OB: obese; OR: odds ratio; OW: overweight; PF: plasma ferritin; PR: prevalence ratio; SF: serum ferritin; SI: serum iron; sTfR: serum transferrin receptor; TfR: transferrin receptor; TS: transferrin saturation; WAZ: weight-for-age z score; WHO: World Health Organization; WHZ: weight-for-height z score; SAM: severe acute malnutrition; ZnPP: zinc protoporphyrin.

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Table S6 Characteristics of the studies (n=28) assessing the association between zinc and weight status.

First Author, Year, Country	**Study Design, Participant (n), age**	**Malnutrition and Biochemical Indicators[1]**	**Significant findings[2]**	**Association**	**Quality Rating**
Both (n=4)					
Dehghani, 2011, Iran[47]	Cross-sectional, 902, 3-18 y	Wasting, stunting, BMI percentiles Serum Zn	**Overnutrition**: NS **Undernutrition**: Serum Zn↓ prevalence of mild wasting, stunting ↑	NS Direct	Neutral
Habib, 2022, Iran[48]	Cross-sectional, 454, 2-18 y	BMI percentiles, HAZ Serum Zn	**Overnutrition**: NS **Undernutrition**: HAZ ↓Serum Zn↓	NS Direct	Positive
Li, 2017, Colombia[4]	Cross-sectional, 4279, 1-17 y	HAZ, BAZ Serum Zn	**Both over- and undernutrition:** NS	NS	Positive
Lu, 2023, China[49]	Cross-sectional, 64850, 6-18 y	Stunting: WS/T 456-2014 OW, OB: WS/T 586-2018 Serum Zn	**Overnutrition:** BMI↑ ZD↓ ZD/OW: AOR= 0.881 (0.808, 0.960); ZD/OB: AOR= 0.776 (0.702, 0.857) **Undernutrition:** HAZ↓ ZD↑ AOR= 1.443 (1.19, 1.75)	Direct	Positive
Overnutrition (n=8)					
Fan, 2017, US[50]	Cross-sectional, 5404, 6-19 y	OW, OB: BMI percentiles Serum Zn (vs Q1)	Serum Zn↑ BMI↓ Serum Zn Q4/OW: AOR= 0.65 (0.47, 0.89) Serum Zn Q3/OB: AOR= 0.62 (0.41, 0.92) (Serum Zn-BMI) male: β= -0.161 (-0.315, -0.007), female: β= -0.184 (-0.343, -0.025)	Inverse	Positive
Ho, 2017, Australia[51]	Cross-sectional, 726, 8 y (n=436), 15 y (n=290)	OW, OB (BMI z scores) Plasma Zn	NS	NS	Neutral
Perrone, 1998, Italy[52]	Case-control, 207 (143+164), 4-16 y	OB: BMI>95^{th} centile Serum Zn	BMI↑ Serum Zn↓	Inverse	Neutral

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Sharif, 2019, Iran[53]	Cross-sectional, 4261, 15-23 m	OW: BAZ≥1 SD Quartiles of Zn levels (vs Q1);	NS	NS	Positive
Thillan, 2021, Sri Lanka[29]	Case-control, 324, 8-9 y	OW, OB: WHO standard Serum Zn	BMI↑ Serum Zn↑ (male)	Direct	Positive
Yalcin, 2019, Turkey[31]	Case-control, 120 (40+80), 6-10 y	OW, OB: BAZ>1 & 2 SD Whole blood Zn	BMI↑ Whole blood Zn↑	Direct	Neutral
Zhu, 2021, China[54]	Cross-sectional, 3241, 6-17 y	OW, OB: BMI (WS/T 586—2018) Quartiles of Zn levels (vs Q1);	Serum Zn ↑ BMI ↑	Direct	Positive
Zou, 2022, China[55]	Cross-sectional, 2818, 6-17 y	OW, OB: BMI (WS/T 586—2018) Serum Zn	NS	NS	Positive
Undernutrition (n=16)					
Al-Hussaini, 2022, Saudi Arabia[33]	Case-control, 7931, 6-16 y	Thinness(wasting): BAZ<-2SD Serum Zn	NS	NS	Neutral
Engle-Stone, 2014, Cameroon[56]	Cross-sectional, 817, 12-59 m	HAZ, WHZ Plasma Zn	HAZ, WHZ↓ Plasma Zn↓	Direct	Positive
Galetti, 2016, Benin[57]	Cross-sectional, 598, 1-10 y	HAZ Plasma Zn	Plasma Zn↑ HAZ↑ HAZ/Plasma Zn: β= 0.15 (SE= 0.06)	Direct	Positive
Gibson, 2007, Thailand[58]	Case-control, 230 (58+172), 6-13 y	Stunting Serum Zn	NS	NS	Positive
Goyena, 2021, Philippine[59]	Cross-sectional, 2892, 6-71 m	Stunting ZD: IZiNCG standard	HAZ↓ ZD↑ ZD/stunting: AOR= 1.36 (1.06, 1.76)	Direct	Positive
Kongsbak, 2006, Bangladesh[60]	Cross-sectional, 579, 3-7 y	Stunting Serum Zn	HAZ↓ Serum Zn↓ stunting was associated with 0.2μmol/L lower Serum Zn.	Direct	Positive
Kumari, 2022,	Case-control, 202,	WHZ, BAZ Serum Zn	BMI↑ Serum Zn↑ r= 0.201 WHZ↑ Serum Zn↑	Direct	Neutral

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India[41]	1-5 y				
Marashinghe, 2015, Sri Lanka[61]	Cross-sectional, 340, 2-5 y	Underweight: WAZ<-2 SD, stunting, wasting/thinness: WHZ<-2 SD Serum Zn	HAZ↑ Serum Zn↑ severe stunting vs. normal WAZ↑ Serum Zn↑ severe underweight vs. normal	Direct	Neutral
Nasiri-Babadi, 2021, Iran[62]	Cross-sectional, 425, 5-7 y	Wasting (BAZ<-1) Serum Zn, tertiles of Zn levels (vs T1)	Serum Zn↑ weight, BAZ↑ Wasting/Zn T3: AOR= 0.53 (0.31, 0.91)	Direct	Positive
Naupal-Forcadilla, 2017, Philippines[63]	Cross-sectional, 149, 2-3 y	HAZ ZD: IZiNCG standard	HAZ↑ ZD↓ HAZ/ZD: AOR= 0.86 (0.78, 0.96) ZD was less likely to occur among children with normal HAZ	Direct	Positive
Okafor, 2021, Nigria[64]	Cross-sectional, 380, 6-12 y	Stunting Serum Zn ZD: serum Zn<80µg/dL	NS	NS	Positive
Park, 2012, South Korea[44]	Cross-sectional, 101, 6-24 m	HAZ, WAZ, WHZ: <-1 SD Hypozincaemia: serum Zn<70µg/dL	NS	NS	Positive
Sethy, 2014, India[45]	Cross-sectional, 144, 2-5 y	Stunting, wasting: WHZ<-2 SD Serum Zn	HAZ↓ Serum Zn↓ (mean level, but r= -0.193); WHZ↓ Serum Zn↓ (mean level, but r= -0.278)	Direct	Negative
Tessema, 2019, Ethiopia[65]	Cross-sectional, 1776, 6-59 m	HAZ, WAZ Serum Zn, adjusted by CRP, AGP	NS	NS	Neutral
Van Nhien, 2009, Vietnam[66]	Cross-sectional, 245, 11-17 y	BMI<17 Serum Zn	NS	NS	Neutral
Yazbeck, 2016, Lebanon[67]	Case-control, 161(78+83), 1-10 y	FTT: WAZ<5th centile; Short stature: HAZ<-2 SD or <2.5th centile ZD: Plasma Zn<65µg/dL	NS	NS	Neutral

[1]Stunting refers to HAZ<-2 SD, severe stunting refers to HAZ<-3SD unless specific noted.
[2]OR were shown as OR (95%CI) unless specific noted; β coefficient were shown as β (95%CI) unless specific noted. NS: not significant.
AGP: α-acid glycoprotein; AOR: adjusted odds ratio; AOR: adjusted odds ratio; BAZ: BMI-age z score; BMI: body mass index; CRP: C-reaction protein; FTT: Failure to thrive; HAZ: height-for-age z score; IZiNCG: International Zinc Nutrition Consultative Group; MUAC: mid-upper arm circumference; OB: obese; OR: odds ratio; OW: overweight; SE: standard error; WAZ: weight-for-age z score; WHZ: weight-for-height z score; Zn: zinc; zinc deficiency: ZD.

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25 **Table S7 Characteristics of the studies (n=27) assessing the association between vitamin A and weight status.**

First Author, Year, Country	Study Design, Participant (n), age	Malnutrition and Biochemical Indicators[1]	Significant findings[2]	Association	Quality Rating
Both (n=5)					
Dallazen, 2023, Brazil[68]	Cross-sectional, 1503, 12-59 m	HAZ, BAZ VAD: plasma retinol<0.7μmol/L	**Overnutrition**: BAZ↑ plasma retinol↓ **Undernutrition**: HAZ↓ VAD↑ APR= 4.75 (2.10, 10.73) plasma retinol↓	Inverse Direct	Positive
Disalvo, 2019, Argentina[69]	Cross-sectional, 624, 1-6 y	WAZ, BMIz Serum retinol	**Overnutrition**: BMIz↑ Serum VA↑ **Undernutrition**: WAZ↓ Serum retinol↓	Direct	Neutral
Li, 2017, Colombia[4]	Cross-sectional, 3844, 1-17 y	HAZ, BAZ Serum VA	**Both under- and overnutrition**: BAZ↑ Serum VA↑	Direct	Positive
Maslova, 2009, Colombia[5]	Cross-sectional, 2811, 5-12 y	BAZ Plasma retinol	**Both under- and overnutrition**: Plasma retinol↑ BAZ↑	Direct	Positive
Tan, 2023, Malaysia[8]	Cross-sectional, 776, 7-11 y	BAZ, HAZ, WAZ VAD: Both plasma retinol and RBP<0.7μmol/L	**Overnutrition**: BAZ↑ retinol, RBP↑; WAZ↑ retinol, RBP↑ **Undernutrition**: Serum VA↓ HAZ↓ VAD/stunting: COR= 2.9 (1.8, 4.7)	Direct	Positive
Overnutrition (n=12)					
Cobayashi, 2013, Brazil[1]	Cross-sectional, 582, 0-10 y	OW: BAZ>1 VAD: plasma VA<20μg/dL	OW↑ VAD↑ PR= 1.97 (1.13, 3.41) for ≥5y	Inverse	Positive
de Souza Valente da Silva,	Cross-sectional, 471, 7-17 y	OW, OB: BMI>85th & 95th centiles Low serum carotenoids:<40 μg/dL	BMI↑ serum carotenoids↓ r= -0.192 BMI/low serum carotenoids: β= 0.92, AOR= 2.51 (1.43, 4.39)	Inverse	Positive

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2007, Brazil[70]					
Gunanti, 2014, US[71]	Cross-sectional, 1154, 8-15 y	OW, OB: BMI>85th & 95th centiles Serum retinol and quartiles	BMI↑ serum retinol↑ β= 5.56 (3.36, 7.75) OW/retinol quartile: AOR= 2.01(1.26, 3.22) OB/retinol quartile: AOR= 2.90(1.65, 5.09)	Direct	Positive
Hu, 2001, China[72]	Cross-sectional, 793, 0-19 y	BMI Serum VA	BMI↑ VA↑ r= 0.26, β= 4.32±0.93 Weight↑ VA↑ r= 0.37, β= 10.39±1.85	Direct	Positive
Ortega-Senovilla, 2019, Spain[73]	Case-control, 141 (70+71), 6-8 y	OB (Cole et al, 2000) Plasma all-trans-retinol	BMI↑ plasma retinol↑	Direct	Neutral
Paes-Silva, 2018, Brazil[74]	Cross-sectional, 411, 12-19 y	OW: BAZ>1; Low β-carotene: Serum β-carotene <0.9μmol/L	BAZ↑ β-carotene↓ Low β-carotene/OW, PR= 1.46 (1.2, 1.8) (male) Low β-carotene/NW, PR= 1.19 (1.0, 1.4) (female)	Inverse	Neutral
Sharif, 2019, Iran[53]	Cross-sectional, 4261, 15-23 m	OW: BAZ>1 Quartiles of retinol levels (vs Q1)	NS	NS	Positive
Thillan, 2021, Sri Lanka[29]	Case-control, 324, 8-9 y	OW; OB: WHO standard Serum VA	NS	NS	Positive
Tian, 2022, China[75]	Cross-sectional, 3025, 7-17 y	General OB: WS/T 586-2018 Central OB: WC≥90th centile Quartiles of Serum VA levels (vs Q1)	serum VA↑ general OB↑ Q4/general OB: AOR= 4.10 (2.88, 5.85) serum VA↑ central OB↑ Q4/central OB: AOR= 4.14 (3.07, 5.56)	Direct	Positive
Wei, 2016, China[76]	Cross-sectional, 1928, 7-11 y	OB: BMI>95th centile VAD: Serum VA <20μg/dL	BMI↑ VAD/OB: AOR= 2.37 (1.59, 3.55) BMI↑ Serum VA↓	Inverse	Positive
Yang, 2015, China[77]	Cross-sectional, 3457, 7-17 y	OW, OB: BMI>85th & 95th centiles VAD: serum retinol<30μg/dL	BMI↑ serum retinol↑ VAD/NW: AOR= 1.34 (1.10, 1.63), β= 0.29	Direct	Positive
Zou, 2022,	Cross-sectional, 2818	OW; OB: WS/T 586-2018 VAI: Serum VA 20-30μg/dL;	serum VA↑ BMI↑ sufficient VA/OW: AOR= 1.55 (1.19, 2.02)	Direct	Positive

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China[55]	6-17 y	VAD: Serum VA<20μg/dL			
Undernutrition (n=10)					
Adamu, 2016, Nigeria[78]	Case-control, 550 (275+275), 6 m-5 y	WHZ Serum retinol	WHZ↓ Serum VA↓	Direct	Neutral
Ahmed, 2006, Bangladesh[79]	Cross-sectional, 381, 11-16 y	BMI Serum VA	BMI↓ Serum VA↓ r= 0.33, β= 0.26	Direct	Positive
Alaofe, 2017, Benin[32]	Cross-sectional, 647 children, 6-59 m	Stunting VAD: serum retinol<20μg/dL, corrected by infection	NS	NS	Positive
Ernawati, 2021, Indonesia[36]	Cross-sectional, 1008, 11-16 y	Stunting; severe stunting Serum retinol	HAZ↓ serum retinol↓	Direct	Positive
Khatib, 2009, Jordan[40]	Cross-sectional, 560, 5.5-10 y	BMI; stunting Serum VA	BMI↓ serum VA↓ r= 0.114	Direct	Neutral
Kurugol, 2000, Turkey[80]	Cross-sectional, 160, 6-59 m	Stunting Serum retinol	HAZ↓ Serum retinol↓	Direct	Neutral
Marashinghe, 2015, Sri Lanka[61]	Cross-sectional, 340, 2-5 y	Underweight: WAZ<-2; stunting; wasting/thinness: WHZ<-2 Serum VA	NS	NS	Neutral
Oso, 2003, Nigeria[81]	Cross-sectional, 213, 6 m-6 y	Stunting Serum retinol	HAZ↓ serum retinol↓	Direct	Negative
Samba, 2006, Congo[82]	Cross-sectional, 5722, 0-71 m	WHZ <-2 SD Serum retinol	WHZ↓ Serum retinol↓	Direct	Neutral

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Ssentongo, 2020, Uganda[83]	Cross-sectional, 4765, 6–59 m	Stunting; severe stunting VAD: RBP<0.83μmol/L, adjusted by CRP	RBP↓ HAZ↓ VAD/stunting: AOR= 1.43 (1.08, 1.89) VAD/severe stunting: AOR= 1.64 (1.14, 2.35)	Direct	Positive

[1]Stunting refers to HAZ<-2 SD, severe stunting refers to HAZ<-3SD unless specific noted.
[2]OR were shown as OR (95%CI) unless specific noted; β coefficient were shown as β (95%CI) unless specific noted.

AOR: adjusted odds ratio; BAZ: BMI-age z score; BMI: body mass index; CRP: C-reaction protein; HAZ: height-for-age z score; NS: not significant; NW: normal weight; OB: obese; OR: odds ratio; OW: overweight; RBP: retinol binding protein; VAD: vitamin A deficiency; WAZ: weight-for-age z score; WHZ: weight-for-height z score.

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Table S8 Risk of bias assessment for included studies.

First Author, Year	Micronutrient	Nutrition	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall Rating
Abd-El-Wahed, 2014	Iron	Overnutrition	YES	YES	NO	NO	YES	YES	YES	NO	YES	NO	NEUTRAL
Adamu, 2016	VA	Undernutrition	YES	YES	NO	NO	YES	YES	YES	NO	NO	YES	NEUTRAL
Ahmed, 2006	VA	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	POSITIVE
Alaofe, 2017	Iron, VA	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Al-Hussaini, 2022	Iron, zinc	Undernutrition	YES	YES	YES	NO	YES	YES	NO	NO	YES	YES	NEUTRAL
Andre, 2017	Iron	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	NO	NO	POSITIVE
Brotanek, 2007	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Cabanas Pujadas, 2022	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Cepeda-Lopez, 2011	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Cheng, 2013	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Chitekwe, 2022	Iron	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Cobayashi, 2013	Iron, VA	Both	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Dallazen, 2023	VA	Both	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
de Araujo, 2022	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES	NEUTRAL
de Souza Valente da Silva, 2007	VA	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	NO	NO	POSITIVE
Dehghani, 2011	Zinc	Both	YES	YES	NO	NO	YES	YES	YES	NO	NO	YES	NEUTRAL
Disalvo, 2019	VA	Both	YES	YES	YES	NO	YES	NO	YES	YES	YES	YES	NEUTRAL
Eftekhari, 2009	Iron	Both	YES	YES	NO	NO	YES	YES	YES	YES	NO	YES	NEUTRAL
El Khoury, 2020	Iron	Overnutrition	YES	YES	NO	NO	YES	YES	NO	NO	YES	NO	NEUTRAL
Engle-Stone, 2014	Zinc	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	POSITIVE
Ernawati, 2021	Iron, VA	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Fan, 2017	Zinc	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Ferrari, 2015	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Galetti, 2016	Zinc	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	NO	YES	POSITIVE
Ghosh, 2012	Iron	Undernutrition	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	NEGATIVE
Gibson, 2007	Zinc	Undernutrition	YES	YES	YES	YES	YES	YES	YES	NO	NO	YES	POSITIVE

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Goyena, 2021	Zinc	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Grant, 2007	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	POSITIVE
Gunanti, 2014	VA	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Habib, 2016	Iron	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Habib, 2022	Zinc	Both	YES	YES	YES	NO	YES	YES	YES	NO	YES	YES	POSITIVE
Higgins, 2020	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Ho, 2017	Zinc	Overnutrition	YES	Unclear	NO	NO	YES	YES	YES	NO	YES	YES	NEUTRAL
Hu, 2001	VA	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	NO	POSITIVE
Indriastuti Kurniawan, 2006	Iron	Undernutrition	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	NEGATIVE
Kassem, 2022	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	POSITIVE
Khatib, 2009	Iron, VA	Undernutrition	YES	YES	NO	YES	YES	YES	YES	NO	YES	YES	NEUTRAL
Kongsbak, 2006	Zinc	Undernutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Kumari, 2022	Iron, zinc	Undernutrition	YES	NO	YES	NO	YES	YES	YES	NO	YES	YES	NEUTRAL
Kurugol, 2000	VA	Undernutrition	YES	YES	NO	NO	YES	YES	YES	NO	NO	YES	NEUTRAL
Li, 2017	Iron, zinc, VA	Both	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Lu, 2023	Zinc	Both	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Manios,2013	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Marashinghe, 2015	Zinc, VA	Undernutrition	YES	YES	YES	NO	YES	NO	YES	NO	YES	YES	NEUTRAL
Maslova, 2009	Iron, VA	Both	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Matsungo, 2017	Iron	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Moschonis, 2012	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	NO	YES	YES	YES	NEUTRAL
Nasiri-babadi, 2021	Zinc	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Naupal-Forcadilla, 2017	Zinc	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	NO	YES	POSITIVE
Nead, 2004	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	NO	POSITIVE
Okafor, 2021	Zinc	Undernutrition	YES	YES	YES	NO	YES	YES	YES	NO	YES	YES	POSITIVE
Onabanjo, 2014	Iron	Both	YES	NO	NO	YES	YES	YES	NO	NO	YES	YES	NEUTRAL
Orsango, 2021	Iron	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Ortega-Senovilla, 2019	VA	Overnutrition	YES	YES	YES	NO	YES	YES	NO	NO	YES	YES	NEUTRAL
Ortiz Perez, 2020	Iron	Overnutrition	YES	YES	NO	YES	YES	YES	YES	NO	YES	YES	NEUTRAL

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Oso, 2003	VA	Undernutrition	YES	YES	NO	YES	YES	YES	YES	NO	NO	NO	NEUTRAL
Paes-Silva, 2018	VA	Overnutrition	YES	YES	NO	NO	YES	YES	YES	YES	YES	YES	NEUTRAL
Park, 2012	Iron, zinc	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Perng, 2013	Iron	Both	YES	YES	YES	NO	YES	YES	YES	NO	YES	YES	POSITIVE
Perrone, 1998	Zinc	Overnutrition	YES	NO	NO	NO	YES	YES	YES	NO	YES	NO	NEUTRAL
Pompano, 2022	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	POSITIVE
Samba, 2006	VA	Undernutrition	YES	YES	NO	NO	YES	YES	YES	NO	NO	YES	NEUTRAL
Sethy, 2014	Iron, zinc	Undernutrition	YES	NO	NO	NO	YES	YES	YES	NO	NO	NO	NEGATIVE
Sharif, 2019	zinc, VA	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Shattnawi, 2018	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Shukla, 2023	Iron	Undernutrition	YES	NO	YES	NO	YES	YES	NO	NO	NO	YES	NEUTRAL
Ssentongo, 2020	VA	Undernutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Suteerojntrakoo, 2021	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	NO	YES	YES	YES	NEUTRAL
Sypes, 2018	Iron	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Tan, 2023	Iron	Both	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Tessema, 2019	Zinc	Undernutrition	YES	YES	NO	YES	YES	NO	YES	YES	YES	YES	NEUTRAL
Thillan, 2021	Iron, zinc, VA	Overnutrition	YES	YES	YES	NO	YES	YES	YES	NO	YES	YES	POSITIVE
Tian, 2022	VA	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Tussing-Humphreys, 2009	Iron	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE
Van Nhien, 2009	Zinc	Undernutrition	YES	YES	NO	YES	YES	YES	YES	NO	YES	YES	NEUTRAL
Wei, 2016	VA	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Yalcin, 2019	Iron, zinc	Overnutrition	YES	YES	YES	NO	YES	YES	NO	NO	YES	YES	NEUTRAL
Yang, 2015	VA	Overnutrition	YES	YES	YES	NO	YES	YES	YES	NO	YES	YES	POSITIVE
Yazbeck, 2016	Zinc	Undernutrition	YES	YES	NO	NO	YES	YES	YES	NO	YES	YES	NEUTRAL
Zhu, 2019	Iron	Both	YES	YES	YES	NO	YES	YES	NO	YES	YES	UES	NEUTRAL
Zhu, 2021	Zinc	Overnutrition	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	POSITIVE
Zimmermann, 2008	Iron	Both	YES	Unclear	YES	NO	YES	YES	YES	YES	YES	YES	NEUTRAL
Zou, 2022	Zinc, VA	Overnutrition	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	POSITIVE

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Figure S1 Subgroup analysis of associations between iron deficiency and overnutrition stratified by gender. The vertical line represents no effect (OR=1.00) and the dashed line the overall effect (OR=1.51).

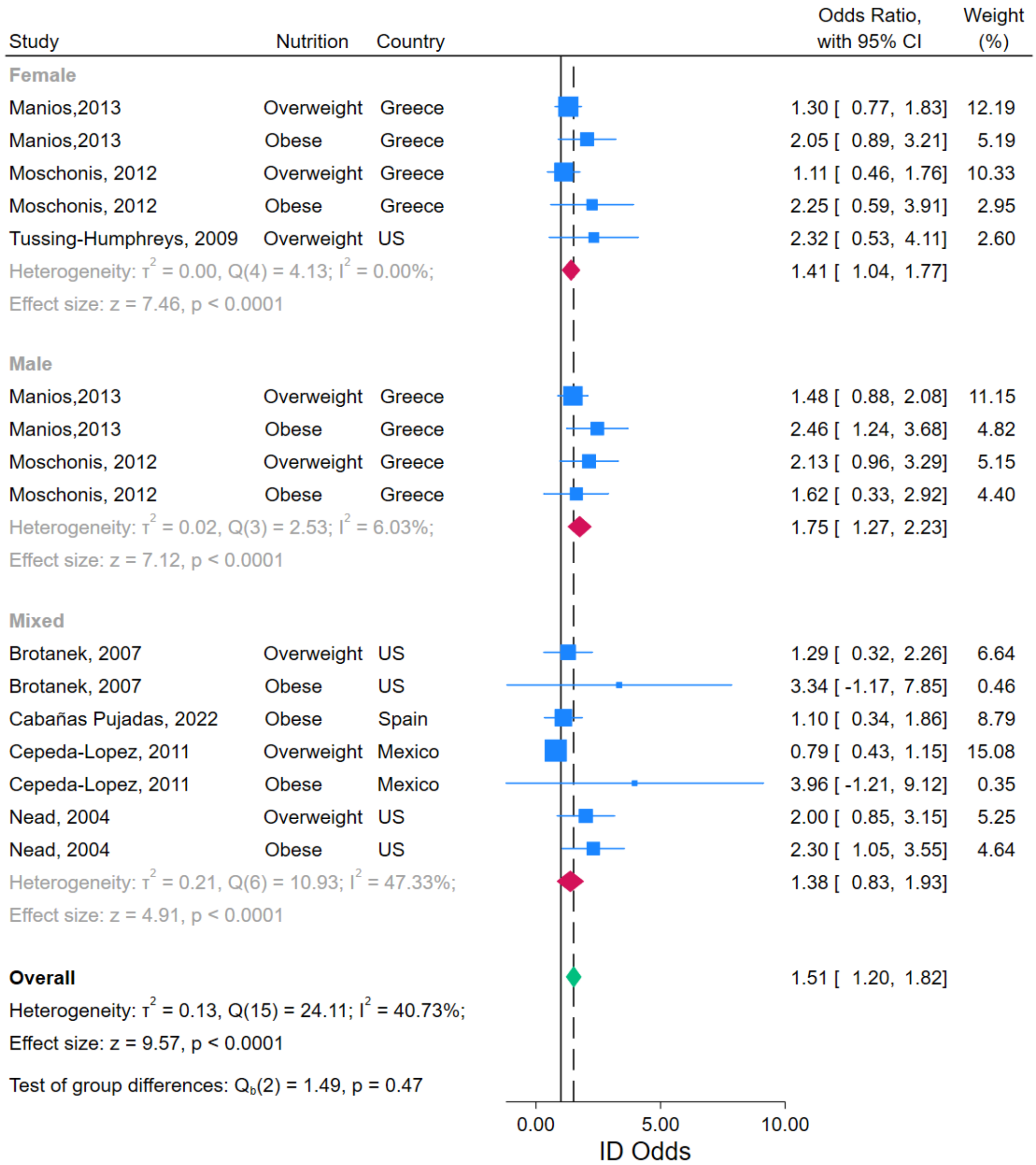

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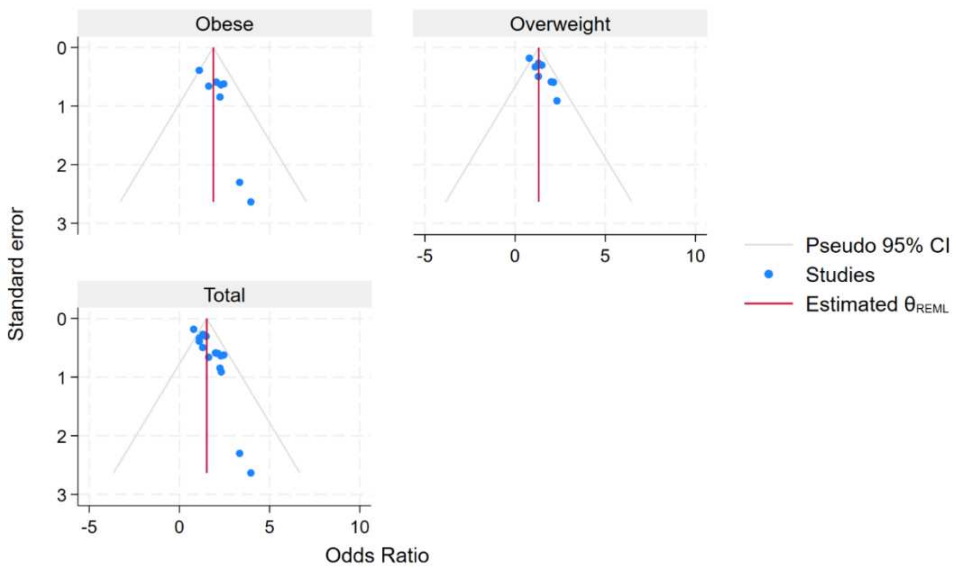
Figure S2 Funnel plots for nutrition status and gender. **A.** nutrition status and **B.** gender. The red line represents the odds ratio for each group.

A.



B.

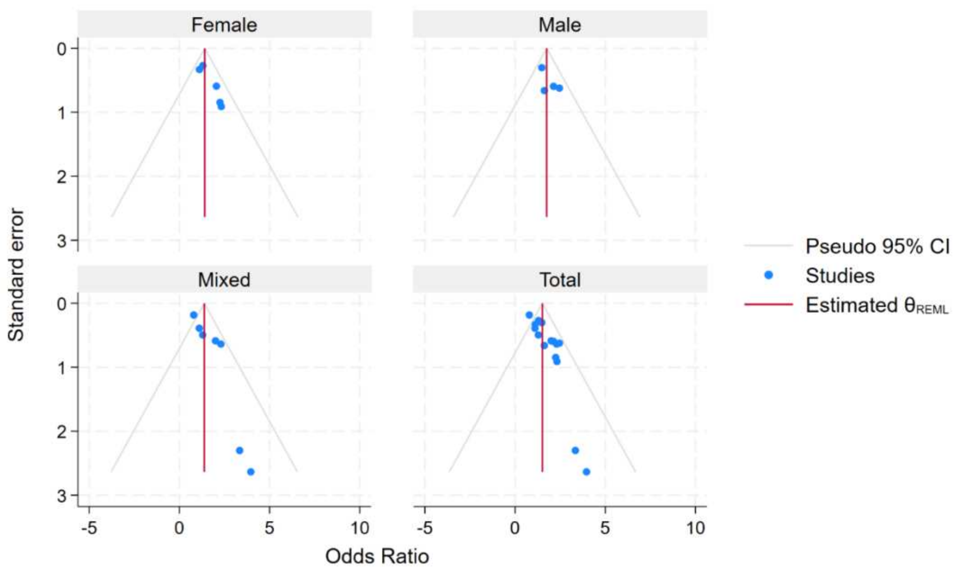


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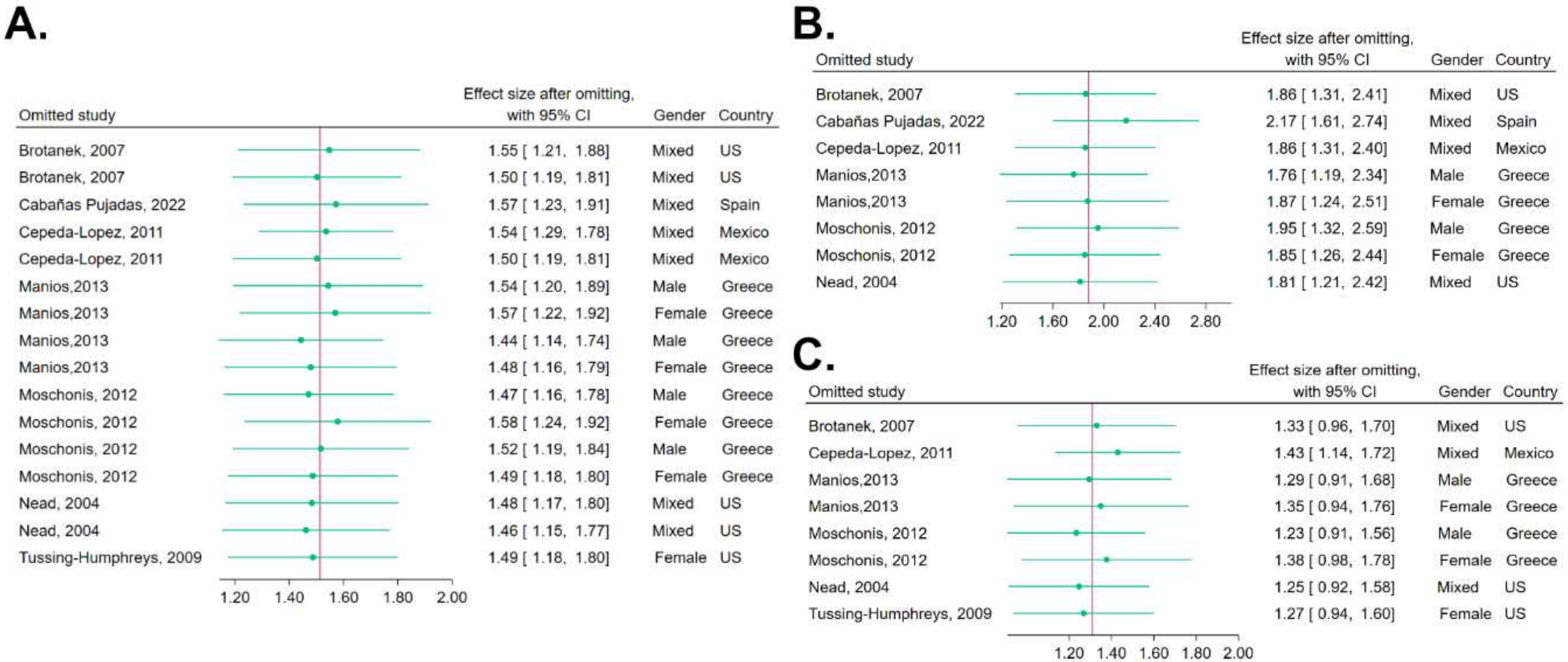
Figure S3 Leave-one-out sensitivity test for overall and subgroup effect sizes. The red line represents the effect size before omitting any study. **A.** Overall, **B.** obese, **C.** overweight.



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References

1. Cobayashi F, Augusto RA, Lourenco BH, et al. Factors associated with stunting and overweight in Amazonian children: a population-based, cross-sectional study. *Public Health Nutr* 2014;17(3):551-60. doi: 10.1017/S1368980013000190
2. El Khoury R, Sleilaty G, Gannage-Yared MH. Prevalence of Iron deficiency in Lebanese schoolchildren. *Eur J Clin Nutr* 2020;74(8):1157-63. doi: 10.1038/s41430-020-0590-y
3. Eftekhari M, Mozaffari-Khosravi H, Shidfar F. The relationship between BMI and iron status in iron-deficient adolescent Iranian girls. *Public Health Nutr* 2009;12(12):2377-81. doi: 10.1017/S1368980009005187
4. Li W, Herran OF, Villamor E. Trends in Iron, Zinc, and Vitamin A Status Biomarkers Among Colombian Children: Results From 2 Nationally Representative Surveys. *Food Nutr Bull* 2017;38(2):146-57. doi: 10.1177/0379572117700976
5. Maslova E, Mora-Plazas M, Forero Y, et al. Are Vitamin A and Iron Deficiencies Re-Emerging in Urban Latin America? A Survey of Schoolchildren in Bogota, Colombia. *Food Nutr Bull* 2009;30(2):103-11. doi: 10.1177/156482650903000201
6. Onabanjo OO, Balogun OL. Anthropometric and Iron Status of Adolescents From Selected Secondary Schools in Ogun State, Nigeria. *ICAN: Infant, Child, & Adolescent Nutrition* 2014;6(2):109-18. doi: 10.1177/1941406414520703
7. Perng W, Mora-Plazas M, Marin C, Villamor E. Iron status and linear growth: a prospective study in school-age children. *Eur J Clin Nutr* 2013;67(6):646-51. doi: 10.1038/ejcn.2013.56
8. Tan PY, Mohd Johari SN, Teng KT, et al. High prevalence of malnutrition and vitamin A deficiency among schoolchildren of rural areas in Malaysia using a multi-school assessment approach. *Br J Nutr* 2023;129(3):454-67. doi: 10.1017/S0007114522001398
9. Zhu Y, He B, Xiao Y, Chen Y. Iron metabolism and its association with dyslipidemia risk in children and adolescents: a cross-sectional study. *Lipids Health Dis* 2019;18(1):50. doi: 10.1186/s12944-019-0985-8
10. Zimmermann MB, Zeder C, Muthayya S, et al. Adiposity in women and children from transition countries predicts decreased iron absorption, iron deficiency and a reduced response to iron fortification. *Int J Obes (Lond)* 2008;32(7):1098-104. doi: 10.1038/ijo.2008.43
11. Abd-El Wahed MA, Mohamed MH, Ibrahim SS, El-Naggar WA. Iron profile and dietary pattern of primary school obese Egyptian children. *J Egypt Public Health Assoc* 2014;89(2):53-9. doi: 10.1097/01.EPX.0000451827.84315.5c
12. Brotanek JM, Gosz J, Weitzman M, Flores G. Iron deficiency in early childhood in the United States: risk factors and racial/ethnic disparities. *Pediatrics* 2007;120(3):568-75. doi: 10.1542/peds.2007-0572
13. Cabañas Pujadas G, Ortiz-Marrón H, Ortiz-Pinto MA, et al. Changes in obesity and iron deficiency between 4 and 9 years of age. Longitudinal study of childhood obesity (ELOIN). *Int J Obes (Lond)* 2022;46(11):1992-99. doi: 10.1038/s41366-022-01196-y
14. Cepeda-Lopez AC, Osendarp SJ, Melse-Boonstra A, et al. Sharply higher rates of iron deficiency in obese Mexican women and children are predicted by obesity-related inflammation rather than by differences in dietary iron intake. *Am J Clin Nutr* 2011;93(5):975-83. doi: 10.3945/ajcn.110.005439
15. Cheng HL, Bryant CE, Rooney KB, et al. Iron, hepcidin and inflammatory status of young healthy overweight and obese women in Australia. *PLoS One* 2013;8(7):e68675. doi: 10.1371/journal.pone.0068675
16. de Araújo LKAR, Faria JCP, Sarni ROS. Iron deficiency anemia in infants in Sousa (PB), Brazil: an association with nutritional status. *Revista da Associacao Medica Brasileira* 2022;68(12):1698-704. doi: 10.1590/1806-9282.20220761
17. Ferrari M, Cuenca-Garcia M, Valtuena J, et al. Inflammation profile in overweight/obese adolescents in Europe: an analysis in relation to iron status. *Eur J Clin Nutr* 2015;69(2):247-55. doi: 10.1038/ejcn.2014.154

Tan *et al.* Supplementary Material

18. Grant CC, Wall CR, Brunt D, et al. Population prevalence and risk factors for iron deficiency in Auckland, New Zealand. *J Paediatr Child Health* 2007;43(7-8):532-8. doi: 10.1111/j.1440-1754.2007.01129.x
19. Higgins V, Omidi A, Tahmasebi H, et al. Marked Influence of Adiposity on Laboratory Biomarkers in a Healthy Cohort of Children and Adolescents. *J Clin Endocrinol Metab* 2020;105(4) doi: 10.1210/clinem/dgz161
20. Kassem E, Na'amnih W, Shapira M, et al. Comparison between School-Age Children with and without Obesity in Nutritional and Inflammation Biomarkers. *J Clin Med* 2022;11(23):6973. doi: 10.3390/jcm11236973
21. Manios Y, Moschonis G, Chrousos GP, et al. The double burden of obesity and iron deficiency on children and adolescents in Greece: the Healthy Growth Study. *J Hum Nutr Diet* 2013;26(5):470-8. doi: 10.1111/jhn.12025
22. Moschonis G, Chrousos GP, Lionis C, et al. Association of total body and visceral fat mass with iron deficiency in preadolescents: the Healthy Growth Study. *Br J Nutr* 2012;108(4):710-9. doi: 10.1017/S0007114511005952
23. Nead KG, Halterman JS, Kaczorowski JM, et al. Overweight children and adolescents: a risk group for iron deficiency. *Pediatrics* 2004;114(1):104-8. doi: 10.1542/peds.114.1.104
24. Ortiz Perez M, Vazquez Lopez MA, Ibanez Alcalde M, et al. Relationship between Obesity and Iron Deficiency in Healthy Adolescents. *Child Obes* 2020;16(6):440-47. doi: 10.1089/chi.2019.0276
25. Pompano LM, Correa-Burrows P, Burrows R, et al. Adjusting Ferritin Concentrations for Nonclinical Inflammation in Adolescents with Overweight or Obesity. *J Pediatr* 2022;244:125-32.e1. doi: 10.1016/j.jpeds.2022.01.012
26. Shattnawi KK, Alomari MA, Al-Sheyab N, Bani Salameh A. The relationship between plasma ferritin levels and body mass index among adolescents. *Sci Rep* 2018;8(1):15307. doi: 10.1038/s41598-018-33534-4
27. Suteerojntrakool O, Khongcharoensombat T, Chomtho S, et al. Anthropometric Markers and Iron Status of 6-12-Year-Old Thai Children: Associations and Predictors. *J Nutr Metab* 2021;2021 doi: 10.1155/2021/9629718
28. Sypes EE, Parkin PC, Birken CS, et al. Higher Body Mass Index Is Associated with Iron Deficiency in Children 1 to 3 Years of Age. *J Pediatr* 2019;207:198-204 e1. doi: 10.1016/j.jpeds.2018.11.035
29. Thillan K, Lanerolle P, Thoradeniya T, et al. Micronutrient status and associated factors of adiposity in primary school children with normal and high body fat in Colombo municipal area, Sri Lanka. *BMC Pediatrics* 2021;21(1):14. doi: 10.1186/s12887-020-02473-3
30. Tussing-Humphreys LM, Liang H, Nemeth E, et al. Excess adiposity, inflammation, and iron-deficiency in female adolescents. *J Am Diet Assoc* 2009;109(2):297-302. doi: 10.1016/j.jada.2008.10.044
31. Yalcin SS, Firat MC, Tosun E, Yalcin S. A possible etiological factor in obesity: element status in blood and tooth of overweight versus normal-weight children. *Int J Environ Health Res* 2018:1-13. doi: 10.1080/09603123.2018.1531115
32. Alaofe H, Burney J, Naylor R, Taren D. Prevalence of anaemia, deficiencies of iron and vitamin A and their determinants in rural women and young children: a cross-sectional study in Kalale district of northern Benin. *Public Health Nutr* 2017;20(7):1203-13. doi: 10.1017/S1368980016003608
33. Al-Hussaini AA, Alshehry Z, AlDehaimi A, Bashir MS. Vitamin D and iron deficiencies among Saudi children and adolescents: A persistent problem in the 21st century. *Saudi Journal of Gastroenterology* 2022;28(2):157-64. doi: 10.4103/sjg.sjg_298_21
34. AndrÉ HP, Vieira SA, Franceschini SdCC, et al. Factors associated with the iron nutritional status of Brazilian children aged 4 to 7 years. *Revista de Nutrição* 2017;30(3):345-55. doi: 10.1590/1678-98652017000300007

Tan *et al.* Supplementary Material

35. Chitekwe S, Parajuli KR, Paudyal N, et al. Individual, household and national factors associated with iron, vitamin A and zinc deficiencies among children aged 6–59 months in Nepal. *Matern Child Nutr* 2022;18(S1) doi: 10.1111/mcn.13305
36. Ernawati F, Syauqy A, Arifin AY, et al. Micronutrient deficiencies and stunting were associated with socioeconomic status in indonesian children aged 6–59 months. *Nutrients* 2021;13(6) doi: 10.3390/nu13061802
37. Ghosh A, Chowdhury SD, Ghosh T. Undernutrition in Nepalese children: a biochemical and haematological study. *Acta Paediatr* 2012;101(6):671-6. doi: 10.1111/j.1651-2227.2012.02613.x
38. Habib MA, Black K, Soofi SB, et al. Prevalence and Predictors of Iron Deficiency Anemia in Children under Five Years of Age in Pakistan, A Secondary Analysis of National Nutrition Survey Data 2011-2012. *PLoS One* 2016;11(5):e0155051. doi: 10.1371/journal.pone.0155051
39. Kurniawan YA, Muslimatun S, Achadi EL, Sastroamidjojo S. Anaemia and iron deficiency anaemia among young adolescent girls from the peri urban coastal area of Indonesia. *Asia Pac J Clin Nutr* 2006;15(3):350-6.
40. Khatib IM, Elmadfa I. High prevalence rates of anemia, vitamin A deficiency and stunting imperil the health status of Bedouin schoolchildren in North Badia, Jordan. *Ann Nutr Metab* 2009;55(4):358-67. doi: 10.1159/000258632
41. Kumari N, Goyal M, Tiwari RK. Correlation of Serum Biochemical Parameters and Oxidative Stress in Malnourished Children: A Case-control Study. *Journal of Clinical and Diagnostic Research* 2022;16(10):BC01-BC05. doi: 10.7860/JCDR/2022/58226.16890
42. Matsungo TM, Kruger HS, Faber M, et al. The prevalence and factors associated with stunting among infants aged 6 months in a peri-urban South African community. *Public Health Nutr* 2017;20(17):3209-18. doi: 10.1017/S1368980017002087
43. Orsango AZ, Habtu W, Lejisa T, et al. Iron deficiency anemia among children aged 2–5 years in southern Ethiopia: a community-based cross-sectional study. *PeerJ* 2021 doi: 10.7717/peerj.11649
44. Park JS, Chang JY, Hong J, et al. Nutritional zinc status in weaning infants: association with iron deficiency, age, and growth profile. *Biol Trace Elem Res* 2012;150(1-3):91-102. doi: 10.1007/s12011-012-9509-3
45. Sethy PGS, Bulliyya G, Rautray TR, et al. Nutritional Status of Preschool Children in Association with Some Trace Elements in Rural Gram Panchayatas of Bhubaneswar, Odisha, India. *Adv Sci Lett* 2014;20(3):868-73. doi: 10.1166/asl.2014.5414
46. Shukla P, Pandey SK, Singh J, et al. Clinico-Etiopathogenesis of Vitamin B12, Folic Acid and Iron Deficiency in Severe Acute Malnutrition Children: A Tertiary Care Hospital Experience from Central India. *Indian J Clin Biochem* 2023 doi: 10.1007/s12291-022-01100-5
47. Dehghani SM, Katibeh P, Haghighat M, et al. Prevalence of zinc deficiency in 3-18 years old children in shiraz-iran. *Iran Red Crescent Med J* 2011;13(1):4-8.
48. Habib A, Molayemat M, Habib A, et al. Vitamin D and Zinc are Interlinked But Affected by Different Growth Factors in Iranian Children and Adolescents: Vitamin D and Zinc in Iranian Children and Adolescents. *Iran J Pediatr* 2022;32(6) doi: 10.5812/ijp-127158
49. Lu J, Zhang H, Cao W, et al. Study on the Zinc Nutritional Status and Risk Factors of Chinese 6-18-Year-Old Children. *Nutrients* 2023;15(7) doi: 10.3390/nu15071685
50. Fan Y, Zhang C, Bu J. Relationship between Selected Serum Metallic Elements and Obesity in Children and Adolescent in the U.S. *Nutrients* 2017;9(2) doi: 10.3390/nu9020104
51. Ho M, Baur LA, Cowell CT, et al. Zinc status, dietary zinc intake and metabolic risk in Australian children and adolescents; Nepean Longitudinal Study. *Eur J Nutr* 2017;56(7):2407-14. doi: 10.1007/s00394-016-1280-3
52. Perrone L, Gialanella G, Moro R, et al. Zinc, copper, and iron in obese children and adolescents. *Nutr Res* 1998;18(2):183-89.

Tan *et al.* Supplementary Material

53. Sharif Y, Sadeghi O, Dorosty A, et al. Serum Levels of Vitamin D, Retinol and Zinc in Relation to overweight among Toddlers: Findings from a National Study in Iran. *Arch Iran Med* 2019;22(4):174-81.
54. Zhu Q, Dai Y, Zhang J, et al. Association between serum zinc concentrations and metabolic risk factors among Chinese children and adolescents. *Br J Nutr* 2021;126(10):1529-36. doi: 10.1017/S0007114521000258
55. Zou Y, Zhang R, Huang L, et al. Serum levels of vitamin D, retinol, zinc, and CRP in relation to obesity among children and adolescents. *Eur J Med Res* 2022;27(1):51. doi: 10.1186/s40001-022-00670-7
56. Engle-Stone R, Ndjebayi AO, Nankap M, et al. Stunting prevalence, plasma zinc concentrations, and dietary zinc intakes in a nationally representative sample suggest a high risk of zinc deficiency among women and young children in Cameroon. *J Nutr* 2014;144(3):382-91. doi: 10.3945/jn.113.188383
57. Galetti V, Mitchikpè CE, Kujinga P, et al. Rural Beninese Children Are at Risk of Zinc Deficiency According to Stunting Prevalence and Plasma Zinc Concentration but Not Dietary Zinc Intakes. *J Nutr* 2016;146(1):114-23. doi: 10.3945/jn.115.216606
58. Gibson RS, Manger MS, Krittaphol W, et al. Does zinc deficiency play a role in stunting among primary school children in NE Thailand? *Br J Nutr* 2007;97(1):167-75. doi: 10.1017/S0007114507250445
59. Goyena EA, Maniego MLV, Ducay AJD, et al. Dietary zinc intake and the underlying factors of serum zinc deficiency among preschool children in the Philippines. *Philipp J Sci* 2021;150(3):799-812.
60. Kongsbak K, Wahed MA, Friis H, Thilsted SH. Acute Phase Protein Levels, T. trichiura, and Maternal Education Are Predictors of Serum Zinc in a Cross-Sectional Study in Bangladeshi Children. *J Nutr* 2006;136(8):2262-68. doi: 10.1093/jn/136.8.2262
61. Marasinghe E, Chackrewarthy S, Abeysena C, Rajindrajith S. Micronutrient status and its relationship with nutritional status in preschool children in urban Sri Lanka. *Asia Pac J Clin Nutr* 2015;24(1):144-51. doi: 10.6133/apjcn.2015.24.1.17
62. Nasiri-babadi P, Sadeghian M, Sadeghi O, et al. The association of serum levels of zinc and vitamin D with wasting among Iranian pre-school children. *Eat Weight Disord* 2021;26(1):211-18. doi: 10.1007/s40519-019-00834-1
63. Naupal-Forcadilla RT, Barba CV, Talavera MTM, Dy MR. Determinants of Zinc Status of 2-3-Year-Old Children in Laguna, Philippines. *Malays J Nutr* 2017;23(1)
64. Okafor AMA, Ikwumere CM, Egumgbe UD, et al. Prevalence and determining factors of stunting among school-aged children in a rural nigerian community: A cross-sectional study. *Curr Res Nutr Food Sci* 2021;9(2):409-22. doi: 10.12944/CRNFSJ.9.2.05
65. Tessema M, De Groote H, I DB, et al. Soil Zinc Is Associated with Serum Zinc But Not with Linear Growth of Children in Ethiopia. *Nutrients* 2019;11(2) doi: 10.3390/nu11020221
66. Van Nhien N, Yabutani T, Khan NC, et al. Association of low serum selenium with anemia among adolescent girls living in rural Vietnam. *Nutrition* 2009;25(1):6-10. doi: 10.1016/j.nut.2008.06.032
67. Yazbeck N, Hanna-Wakim R, El Rafei R, et al. Dietary Zinc Intake and Plasma Zinc Concentrations in Children with Short Stature and Failure to Thrive. *Ann Nutr Metab* 2016;69(1):9-14. doi: 10.1159/000447648
68. Dallazen C, Tietzmann DC, Da Silva SA, et al. Vitamin A deficiency and associated risk factors in children aged 12-59 months living in poorest municipalities in the South Region of Brazil. *Public Health Nutr* 2023;26(1):132-42. doi: 10.1017/S1368980022000325
69. Disalvo L, Varea A, Matamoros N, et al. Vitamin A deficiency and associated factors in preschoolers from the outskirts of La Plata, Buenos Aires. *Arch Argent Pediatr* 2019;117(1):19-25. doi: 10.5546/aap.2019.eng.19
70. de Souza Valente da Silva L, Valeria da Veiga G, Ramalho RA. Association of serum concentrations of retinol and carotenoids with overweight in children and adolescents. *Nutrition* 2007;23(5):392-7. doi: 10.1016/j.nut.2007.02.009

Tan *et al.* Supplementary Material

71. Gunanti IR, Marks GC, Al-Mamun A, Long KZ. Low serum concentrations of carotenoids and vitamin E are associated with high adiposity in Mexican-American children. *J Nutr* 2014;144(4):489-95. doi: 10.3945/jn.113.183137
72. Hu W, Tong S, Oldenburg B, Feng X. Serum vitamin A concentrations and growth in children and adolescents in Gansu Province, China. *Asia Pac J Clin Nutr* 2001;10(1):63-6. doi: 10.1046/j.1440-6047.2001.00208.x
73. Ortega-Senovilla H, de Oya M, Garces C. Relationship of NEFA concentrations to RBP4 and to RBP4/retinol in prepubertal children with and without obesity. *J Clin Lipidol* 2019;13(2):301-07. doi: 10.1016/j.jacl.2019.01.006
74. Paes-Silva RP, Gadelha P, Lemos M, et al. Adiposity, inflammation and fat-soluble vitamins in adolescents. *J Pediatr* 2019;95(5):575-83. doi: 10.1016/j.jped.2018.05.008
75. Tian T, Wang Y, Xie W, et al. Associations between Serum Vitamin A and Metabolic Risk Factors among Eastern Chinese Children and Adolescents. *Nutrients* 2022;14(3):610. doi: 10.3390/nu14030610
76. Wei X, Peng R, Cao J, et al. Serum vitamin A status is associated with obesity and the metabolic syndrome among school-age children in Chongqing, China. *Asia Pac J Clin Nutr* 2016;25(3):563-70. doi: 10.6133/apjcn.092015.03
77. Yang C, Chen J, Liu Z, et al. Association of Vitamin A Status with Overnutrition in Children and Adolescents. *Int J Environ Res Public Health* 2015;12(12):15531-9. doi: 10.3390/ijerph121214998
78. Adamu A, Jiya NM, Ahmed H, et al. Prevalence of Vitamin A Deficiency among Malnourished Children in Usmanu Danfodiyo University Teaching Hospital, Sokoto, Northwestern Nigeria. *Pak J Nutr* 2016;15(9):821-28. doi: 10.3923/pjn.2016.821.828
79. Ahmed F, Rahman A, Noor AN, et al. Anaemia and vitamin A status among adolescent schoolboys in Dhaka City, Bangladesh. *Public Health Nutr* 2006;9(3):345-50. doi: 10.1079/PHN2005858
80. Kurugol Z, Egemen A, Keskinoglu P, et al. Vitamin A deficiency in healthy children aged 6-59 months in Izmir Province of Turkey. *Paediatr Perinat Epidemiol* 2000;14:64-9. doi: 10.1046/j.1365-3016.2000.00229.x
81. Oso OO, Abiodun PO, Omotade OO, Oyewole D. Vitamin A status and nutritional intake of carotenoids of preschool children in Ijaye Orile community in Nigeria. *J Trop Pediatr* 2003;49(1):42-7. doi: 10.1093/tropej/49.1.42
82. Samba C, Tchibindat F, Houze P, et al. Prevalence of infant Vitamin A deficiency and undernutrition in the Republic of Congo. *Acta Trop* 2006;97(3):270-83. doi: 10.1016/j.actatropica.2005.11.008
83. Ssentongo P, Ba DM, Ssentongo AE, et al. Association of vitamin A deficiency with early childhood stunting in Uganda: A population-based cross-sectional study. *PLoS One* 2020;15(5):e0233615. doi: 10.1371/journal.pone.0233615